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Experimental evidence: current insights and future directions

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Aims

- Overview of experimental evidence from acute and short duration trials – focus on metabolic health
- Does the experimental evidence support modification by physical activity or fitness?
- Mechanisms
- Blood pressure and vascular function
- Future directions

Breaking Up Prolonged Sitting With Standing or Walking Attenuates the Postprandial Metabolic Response in Postmenopausal Women: A Randomized Acute Study

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OBJECTIVE

To determine whether breaking up prolonged sitting with short bouts of standing or walking improves postprandial markers of cardiometabolic health in women at high risk of type 2 diabetes.

RESEARCH DESIGN AND METHODS

Twenty-two overweight/obese, dysglycemic, postmenopausal women (mean ± SD age 66.6 ± 4.7 years) each participated in two of the following treatments: prolonged, unbroken sitting (7.5 h) or prolonged sitting broken up with either standing or walking at a self-perceived light intensity (for 5 min every 30 min). Both allocation and treatment order were randomized. The incremental area under the curves (iAUCs) for glucose, insulin, nonesterified fatty acids (NEFA), and triglycerides were calculated for each treatment condition (mean ± SEM). The following day, all participants underwent the 7.5-h sitting protocol.

RESULTS

Compared with a prolonged bout of sitting (iAUC 5.3 ± 0.8 mmol/L · h), both standing (3.5 ± 0.8 mmol/L · h) and walking (3.8 ± 0.7 mmol/L · h) significantly reduced the glucose iAUC (both $P < 0.05$). When compared with prolonged sitting (548.2 ± 71.8 mU/L · h), insulin was also reduced for both activity conditions (standing, 437.2 ± 73.5 mU/L · h; walking, 347.9 ± 78.7 mU/L · h; both $P < 0.05$). Both standing (−1.0 ± 0.2 mmol/L · h) and walking (−0.8 ± 0.2 mmol/L · h) attenuated the suppression of NEFA compared with prolonged sitting (−1.5 ± 0.2 mmol/L · h) (both $P < 0.05$). There was no significant effect on triglyceride iAUC. The effects on glucose (standing and walking) and insulin (walking only) persisted into the following day.

CONCLUSIONS

Breaking up prolonged sitting with 5-min bouts of standing or walking at a self-perceived light intensity reduced postprandial glucose, insulin, and NEFA responses in women at high risk of type 2 diabetes. This simple, behavioral approach could inform future public health interventions aimed at improving the metabolic profile of postmenopausal, dysglycemic women.

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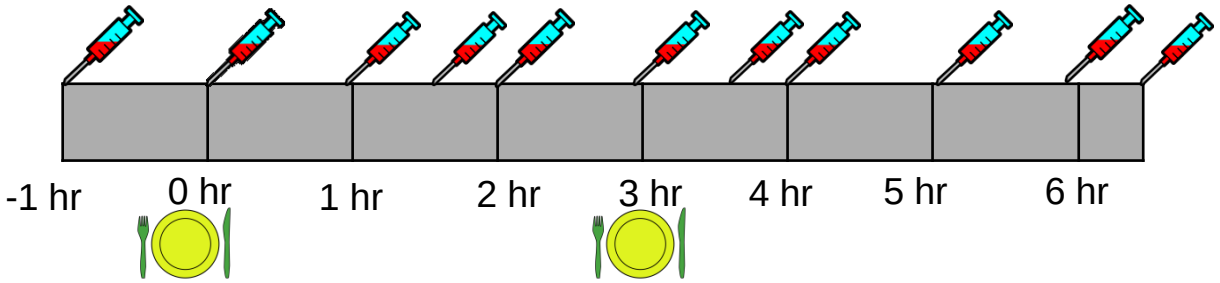
Leicester protocols

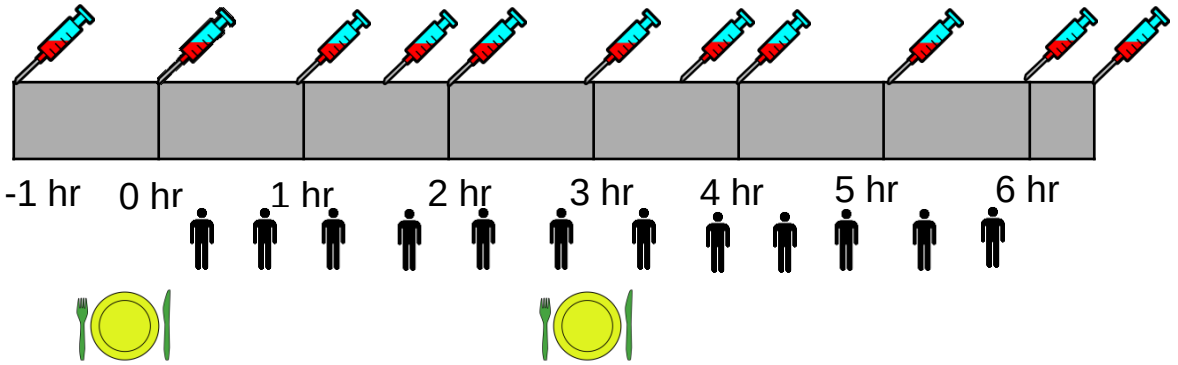
(Henson et al. 2016 Diabetes Care)

Sitting Control



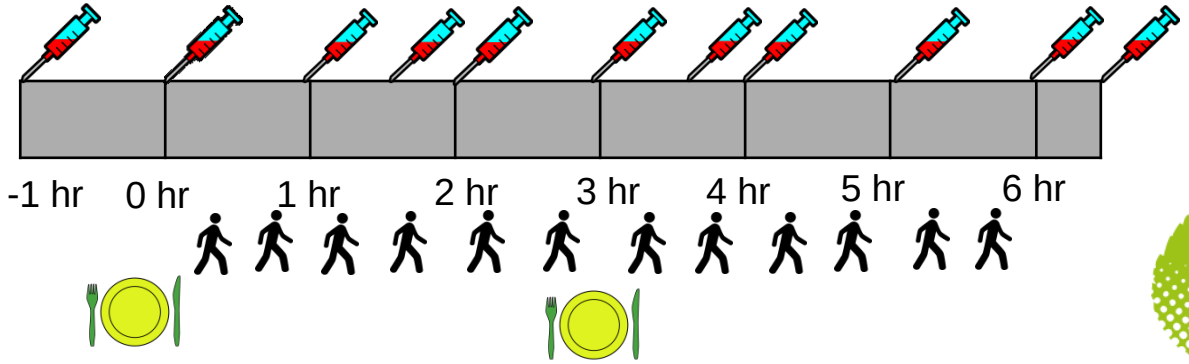
Standing Condition

5 min standing breaks, 2 per hour

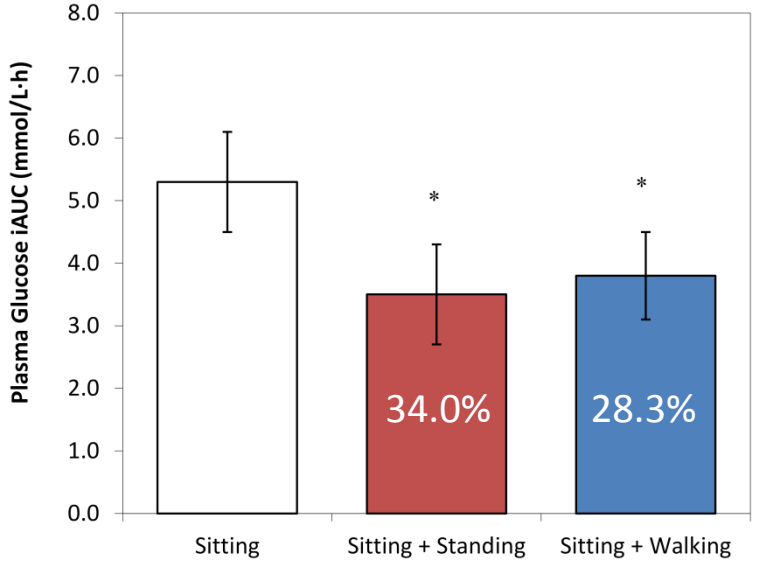


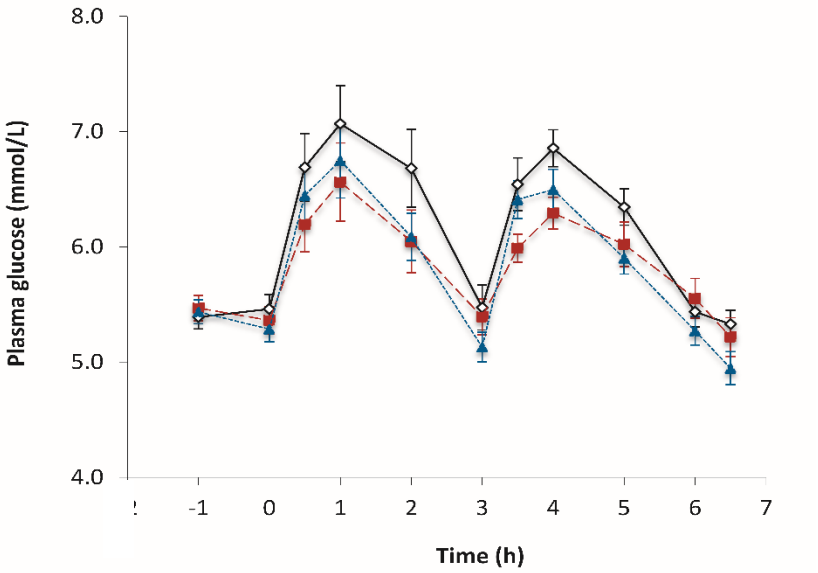
Walking

5 min walking breaks, 2 per hour



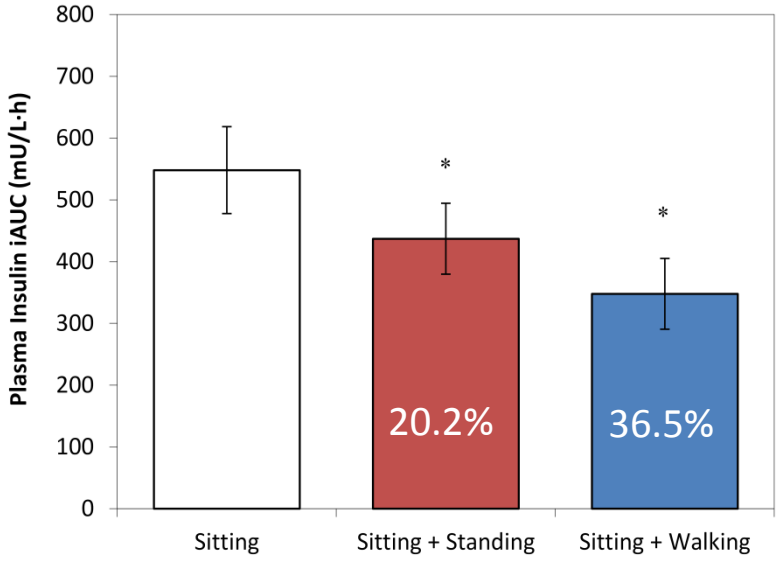
Glucose – Day 1

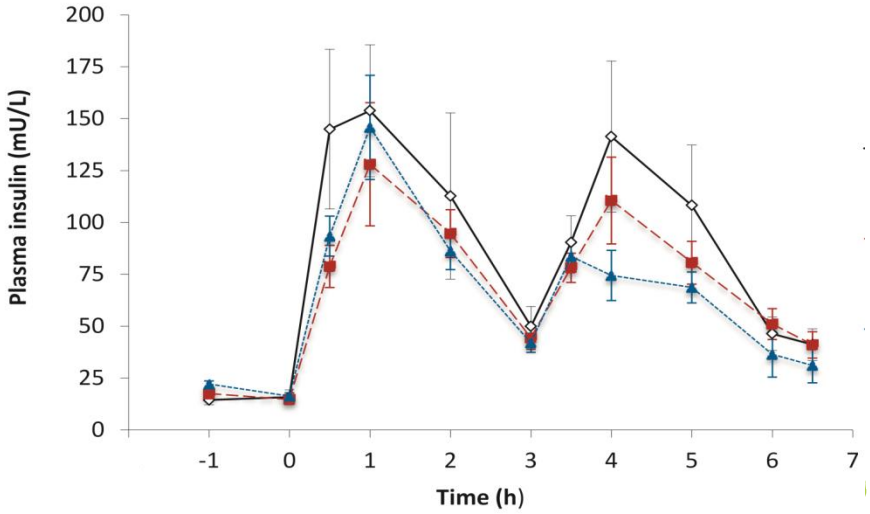




iAUC: Standing vs. sitting p=0.022; Walking vs. sitting p=0.009

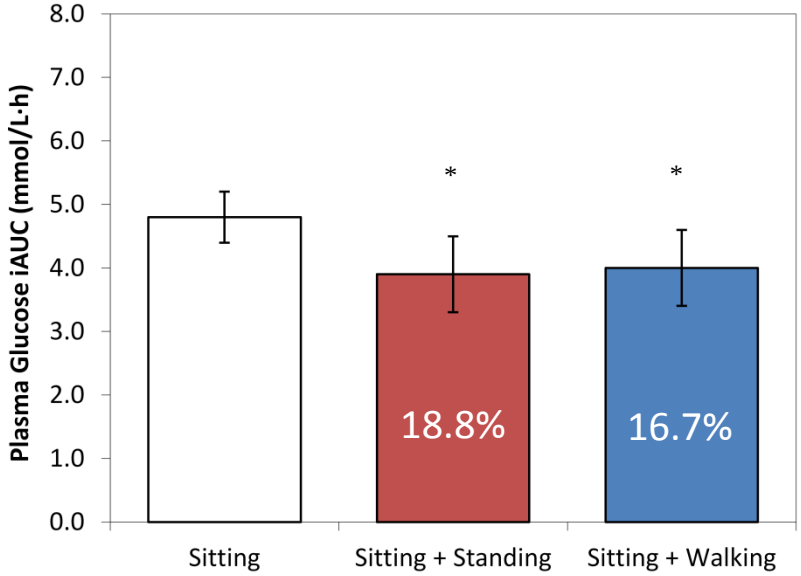
Insulin – Day 1



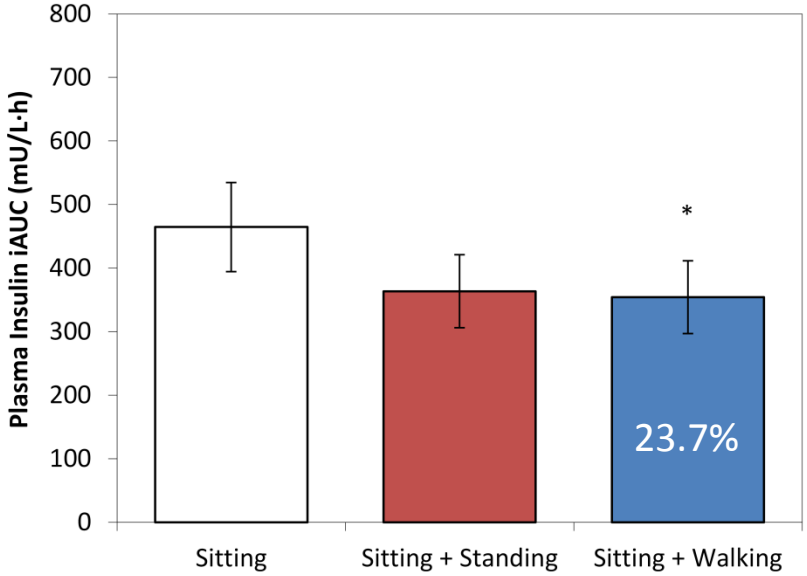


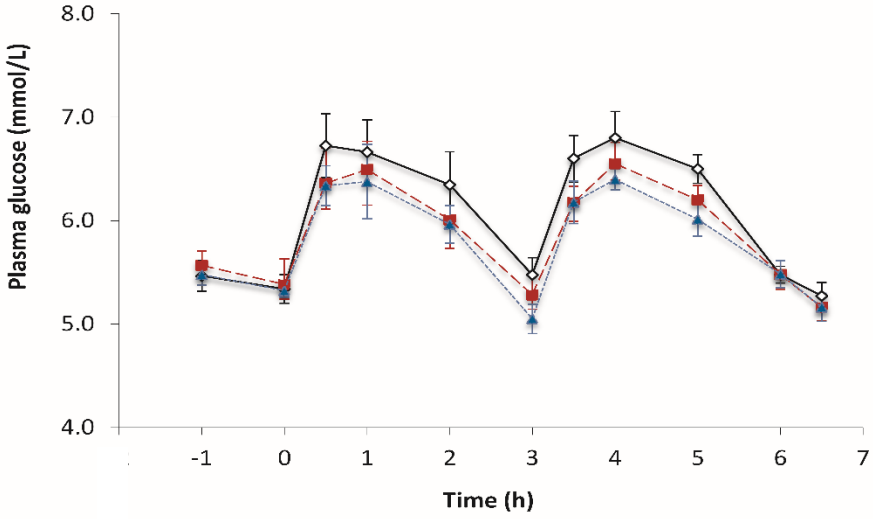
iAUC: Standing vs. sitting p=0.045; Walking vs. sitting p=0.008

Glucose – Day 2

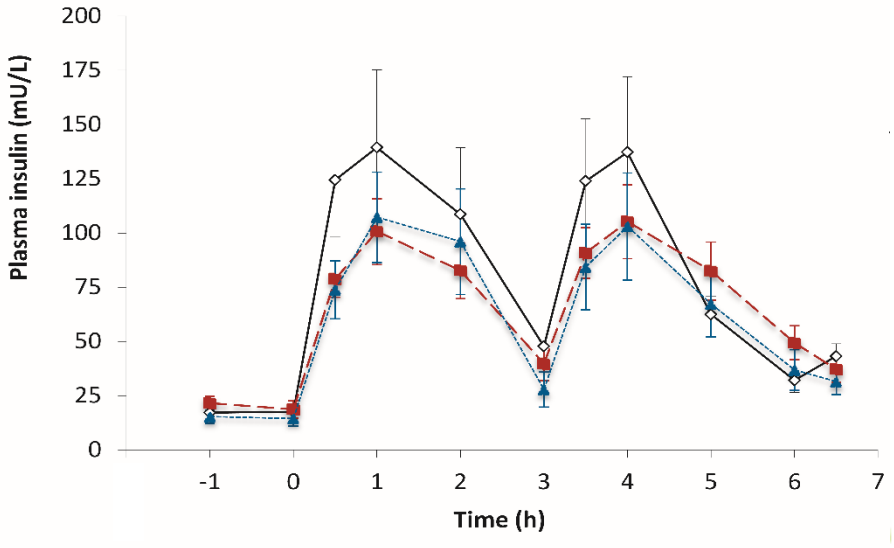


Insulin – Day 2





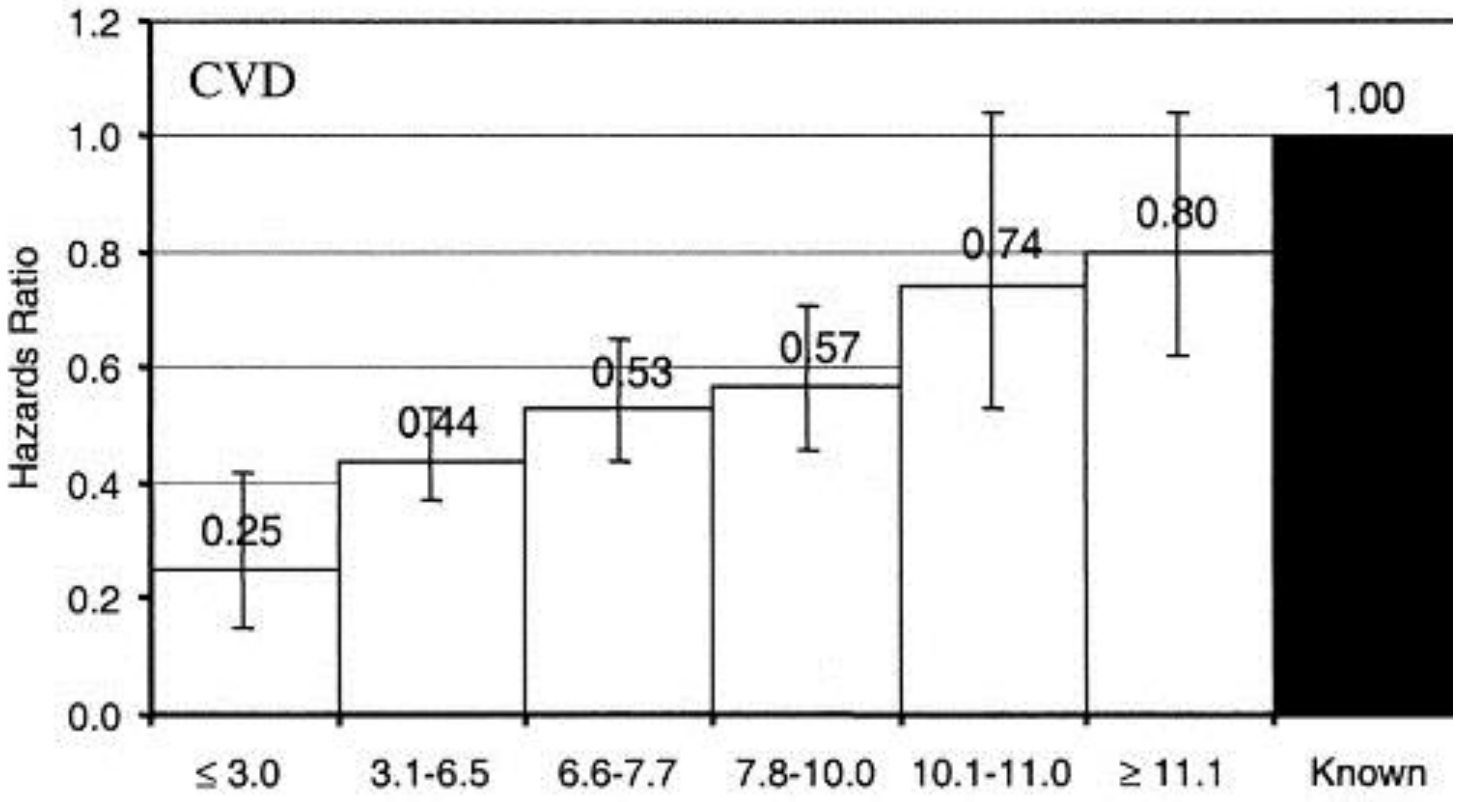
iAUC: Standing vs. sitting p=0.039; Walking vs. sitting p=0.027



iAUC: Standing vs. sitting p=0.325; Walking vs. sitting p=0.038

Postprandial dysmetabolism

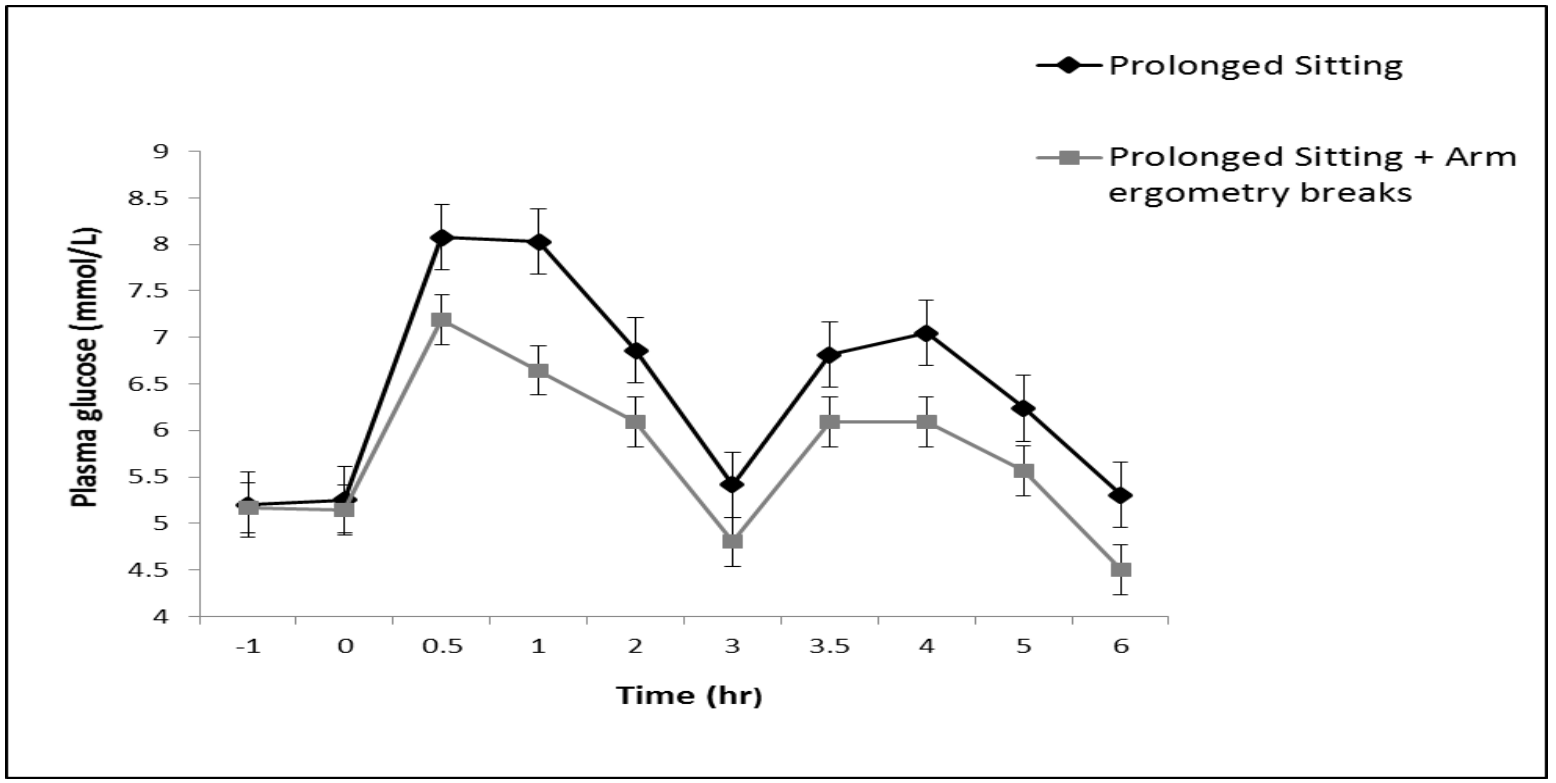
DECODE Study Group 2003, Diabetes Care



Breaking up sedentary behavior with seated upper body activity

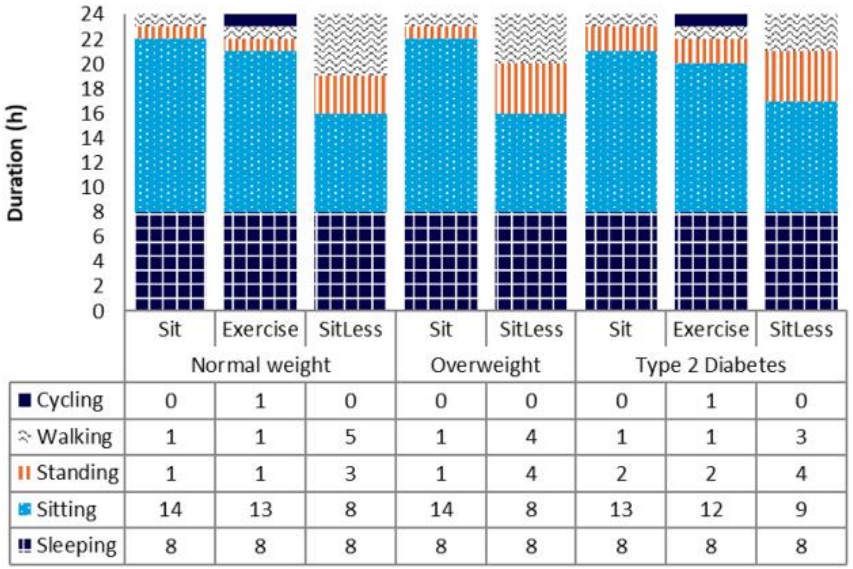
McCarthy et al. 2017 Diabetes, Obesity and Metabolism

ARMING your HEALTH

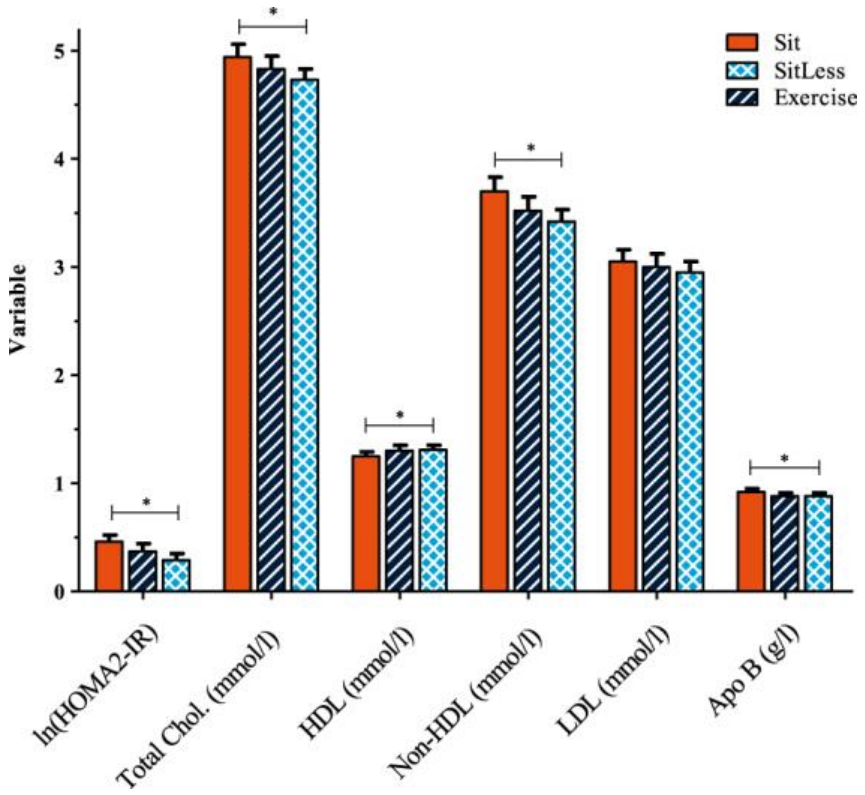


Exercise vs reduced sitting

Duvivier et al. 2018 Scientific Reports

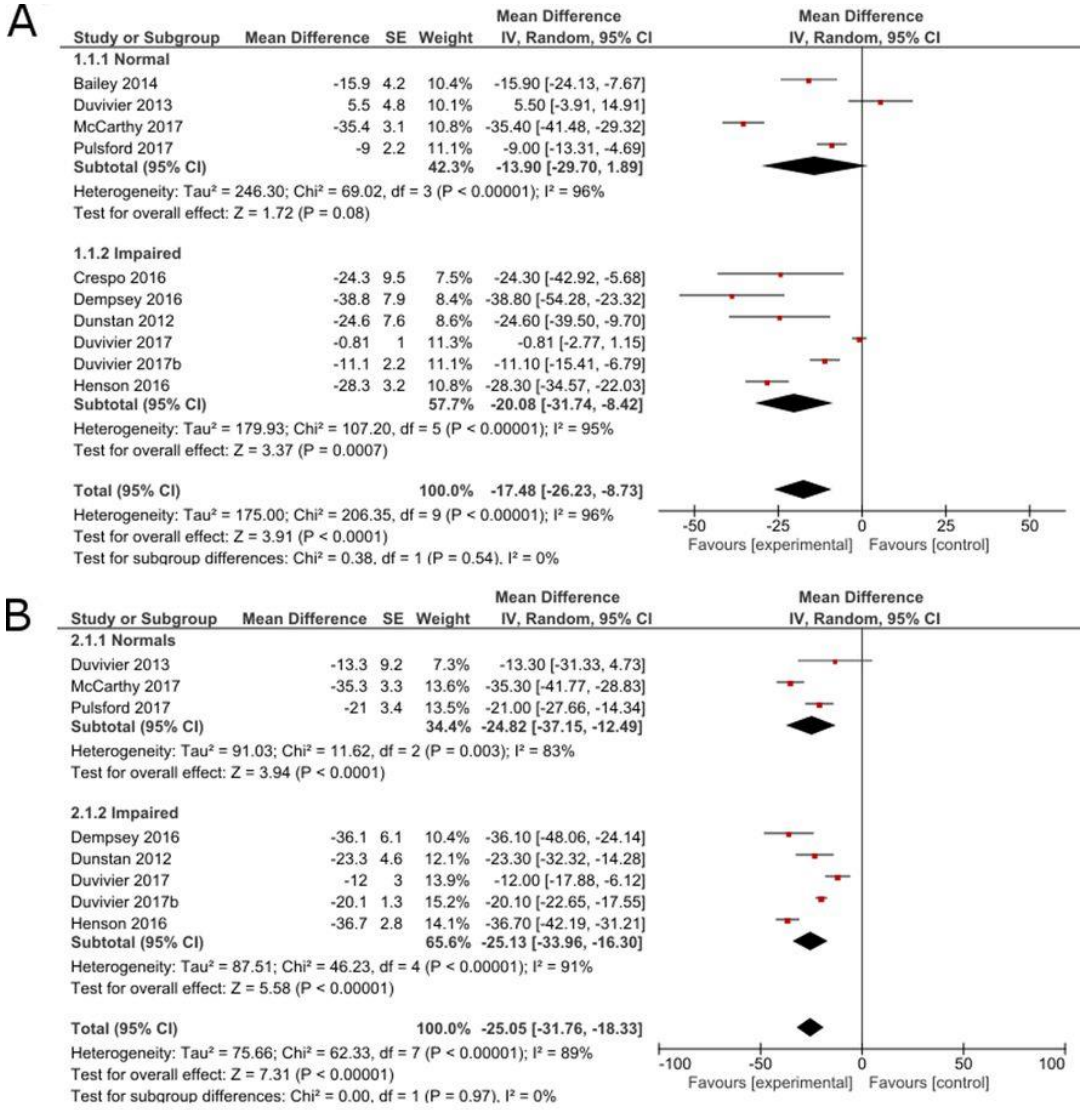


	Sit	Exercise	SitLess	Sit	SitLess	Sit	Exercise	SitLess
	Normal weight			Overweight		Type 2 Diabetes		
Cycling	0	1	0	0	0	0	1	0
Walking	1	1	5	1	4	1	1	3
Standing	1	1	3	1	4	2	2	4
Sitting	14	13	8	14	8	13	12	9
Sleeping	8	8	8	8	8	8	8	8



Meta-analysis

(Chastin et al. BJSM 2018)

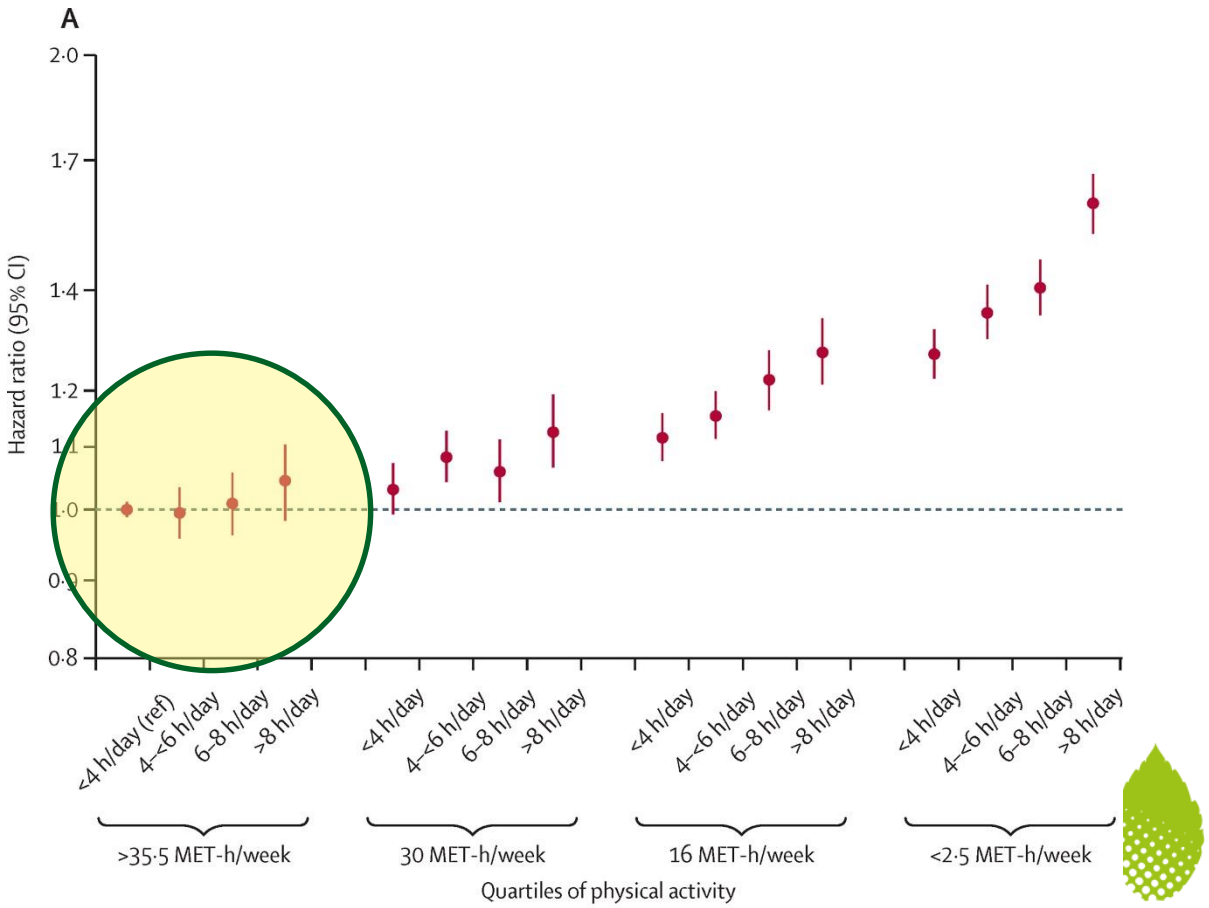


Glucose

Insulin

Physical activity as a modifier

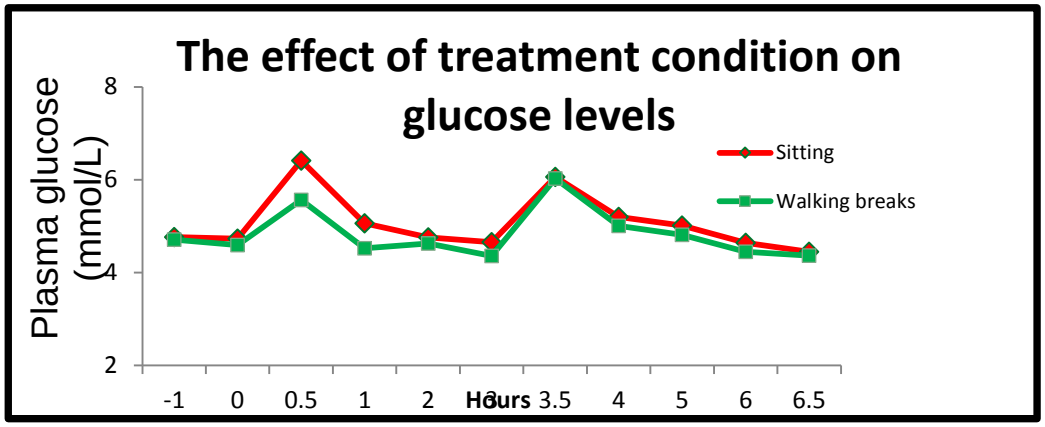
Ekelund et al. 2016 Lancet

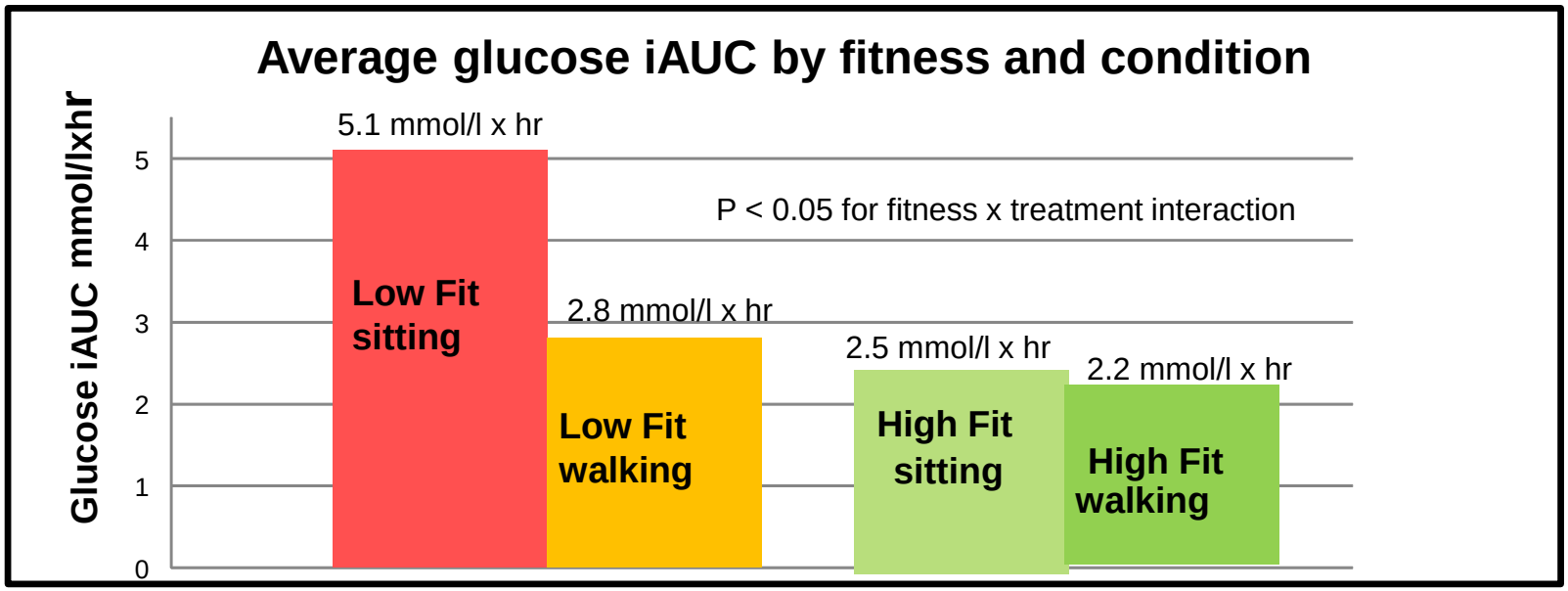


Impact of fitness level on glucose control

McCarthy et al. 2017 MSSE

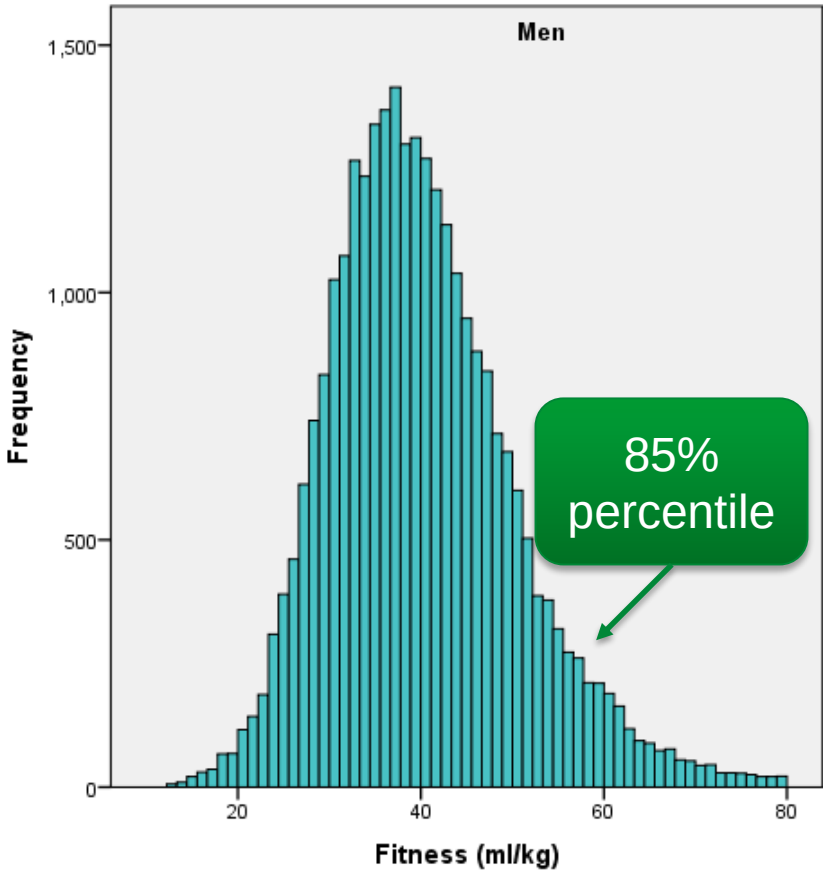
FIT 2 SIT



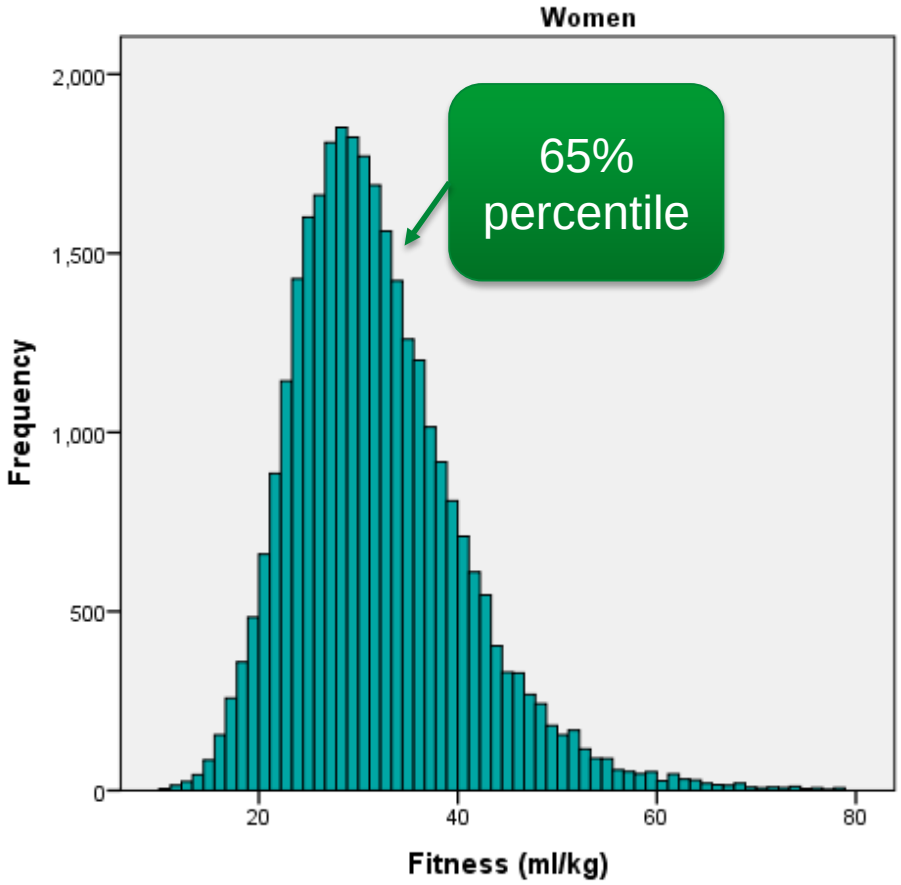


Fitness values compared to UK Biobank

Men = 50 ml/kg

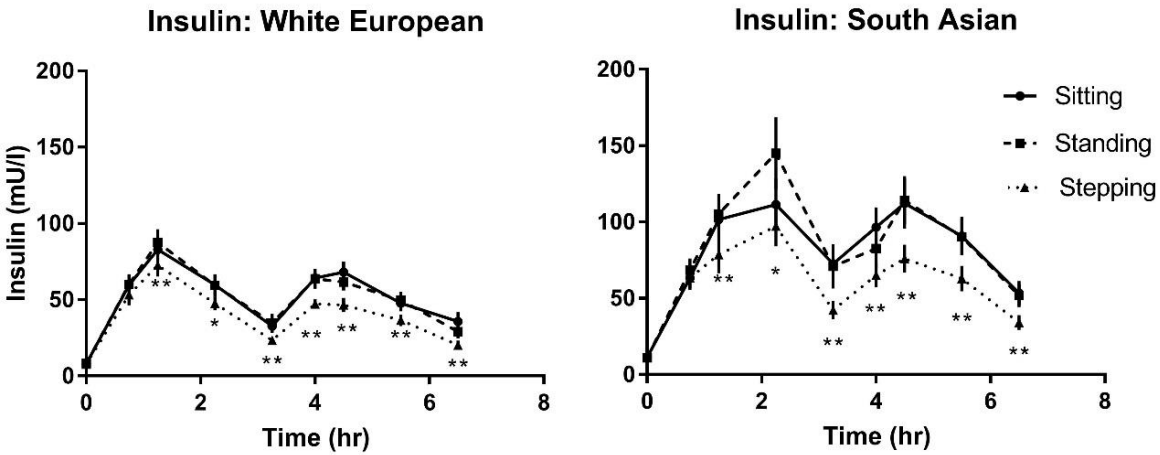


Women = 34 ml/kg

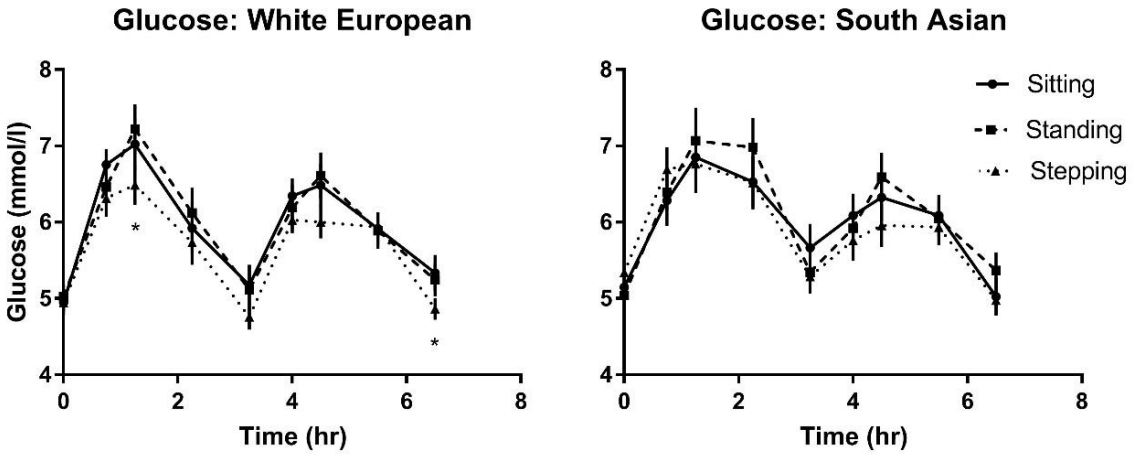


Ethnicity also a modifier

Yates et al J Gerontol A-Biol in press



Insulin: treatment x ethnicity p = 0.029



Glucose: treatment x ethnicity p = 0.772

Pooled Leicester Cohorts

N=130	
Age	63.6±13.6
Sex (female)	73 (56%)
BMI	27.8±4.9
Ethnicity (WE)	85 (65%)
Fasting insulin	10.1±8.4
Fasting glucose	5.0±0.7
HOMA-IR	2.4±2.0
Normoglycaemia	95 (73%)
Non-diabetic hyperglycaemia	35 (27%)
Data presented as mean ± SD or number (column percentage)	

Pooled results from Leicester cohorts

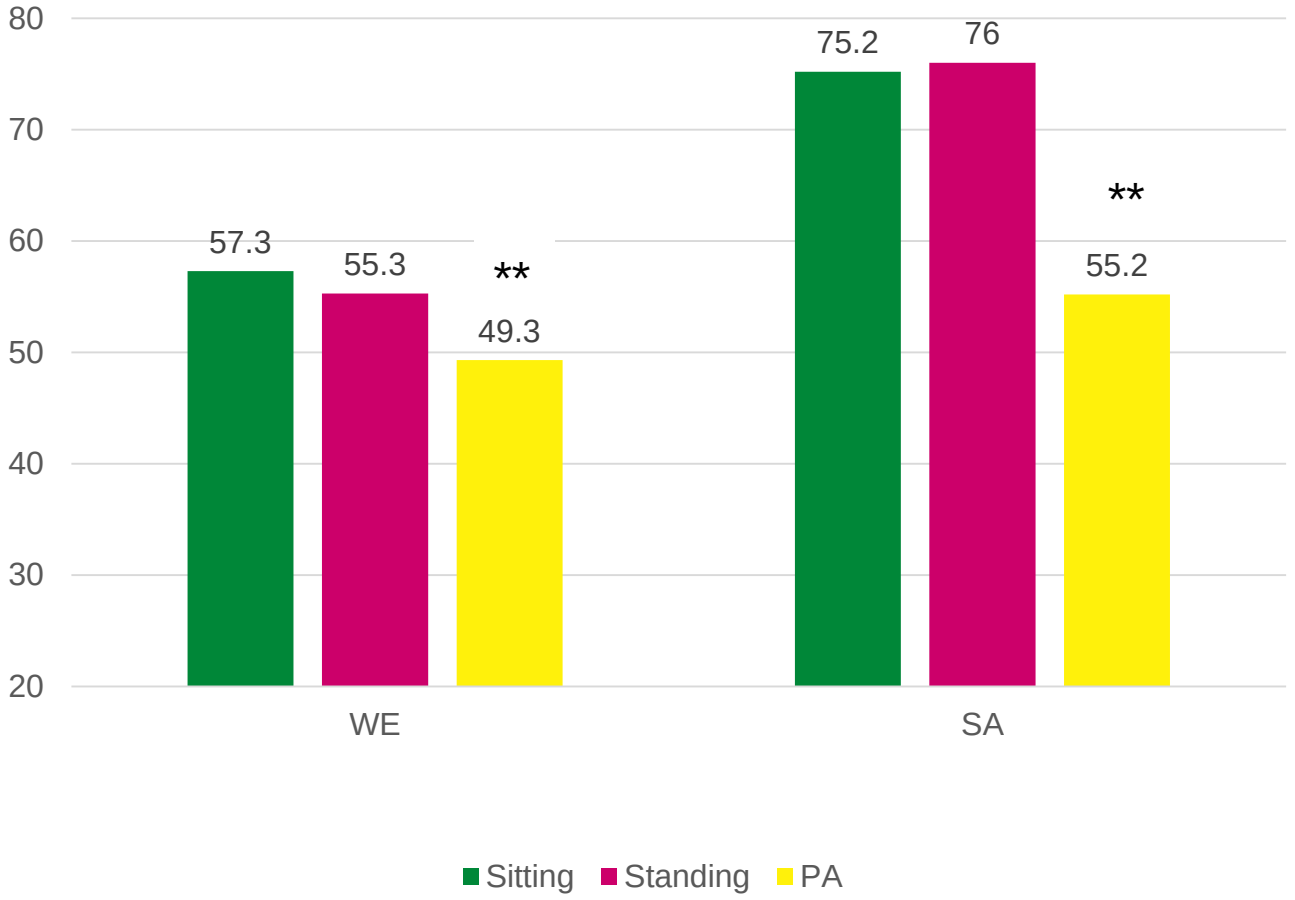
Variable	Sitting	Standing	Light physical activity
Insulin	64.5 (58.2, 70.9)	65.8 (59.1, 72.6)	54.7 (49.6, 59.9)**
Glucose	6.0 (5.8, 6.2)	6.0 (5.8, 6.2)	5.7 (5.6, 5.8)**
Adjusted for fasting values, age, sex and ethnicity			

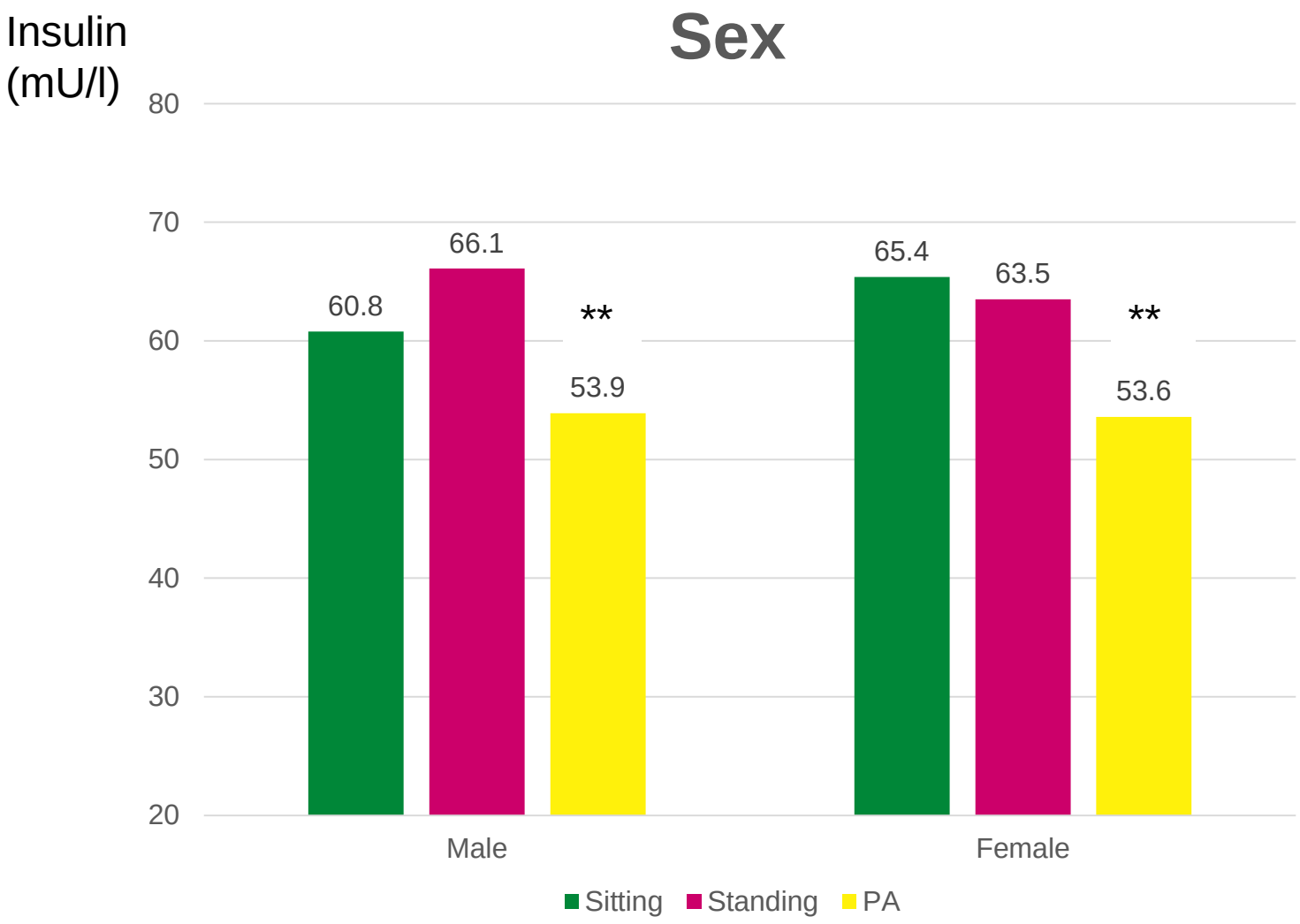
Modifiers in Leicester cohorts

	Insulin	Glucose
Ethnicity	**<0.001**	0.697
Sex	**0.001**	0.333
Age	**0.022**	0.459
BMI	**0.002**	**0.006**
HOMA-IR	0.610	0.935

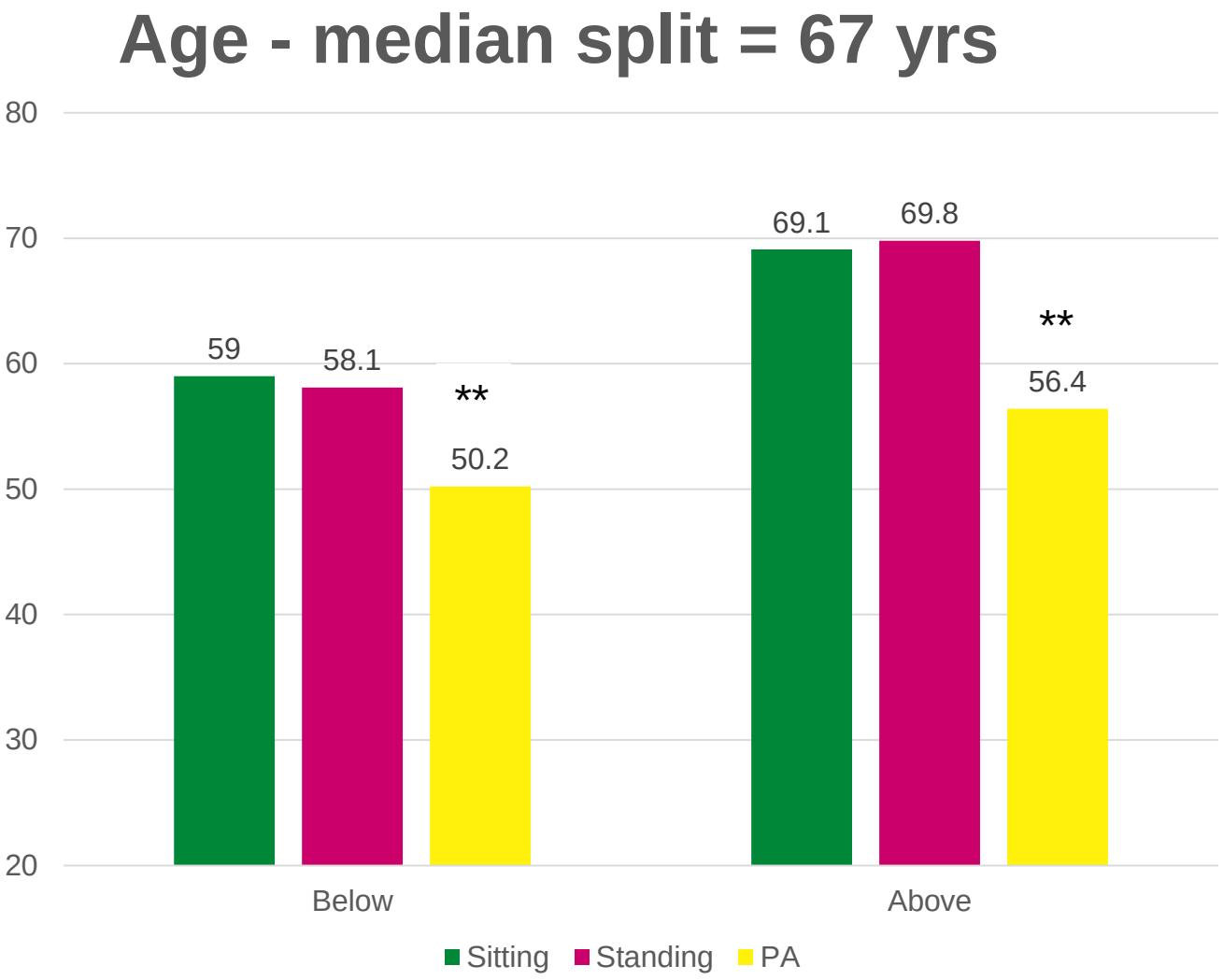
Ethnicity

Insulin (mU/l)

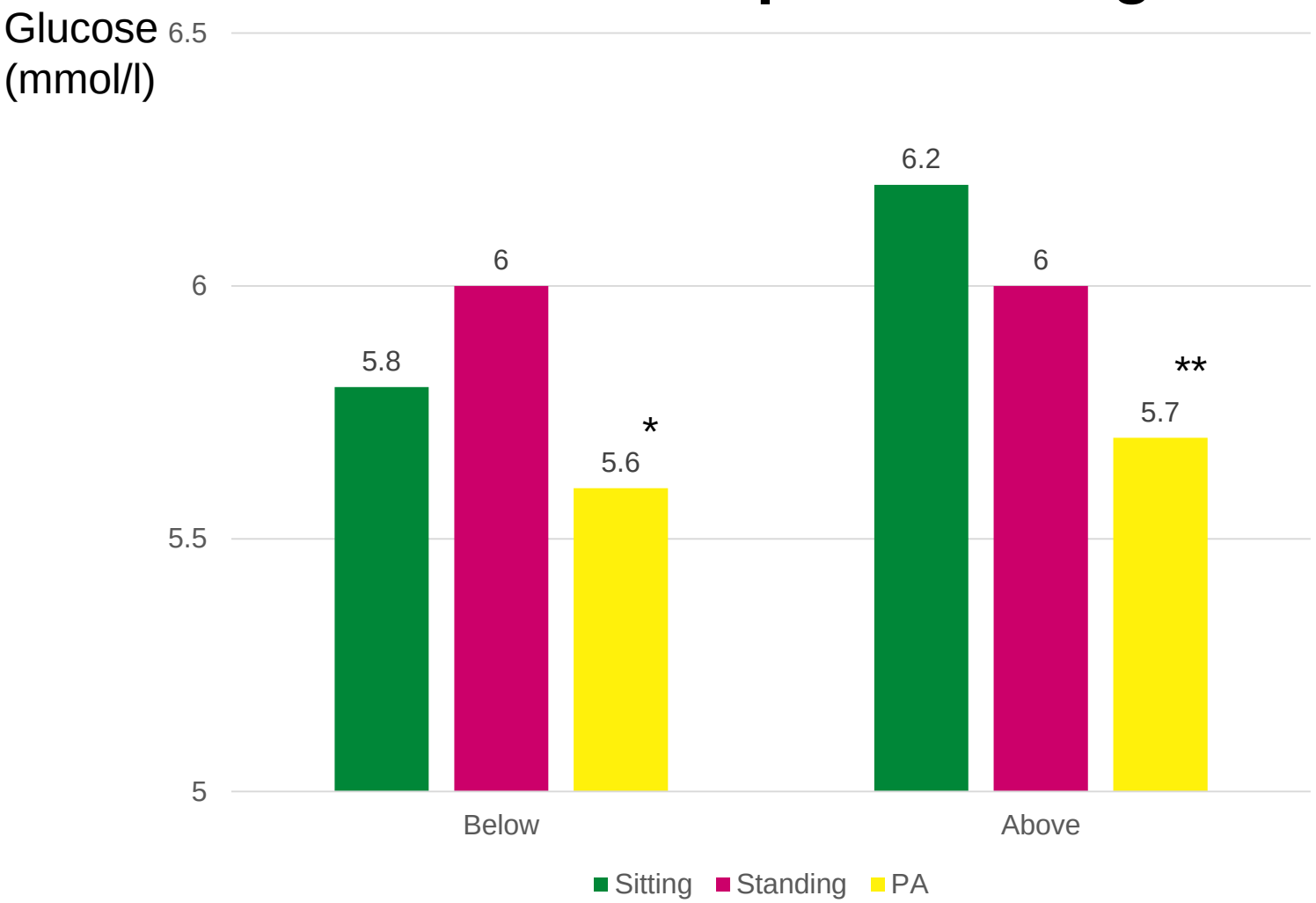



Insulin (mU/l)
Sex
80
70
60
50
40
30
20
60.8
66.1
53.9
**
65.4
63.5
53.6
**
Male
Female
Sitting
Standing
PA

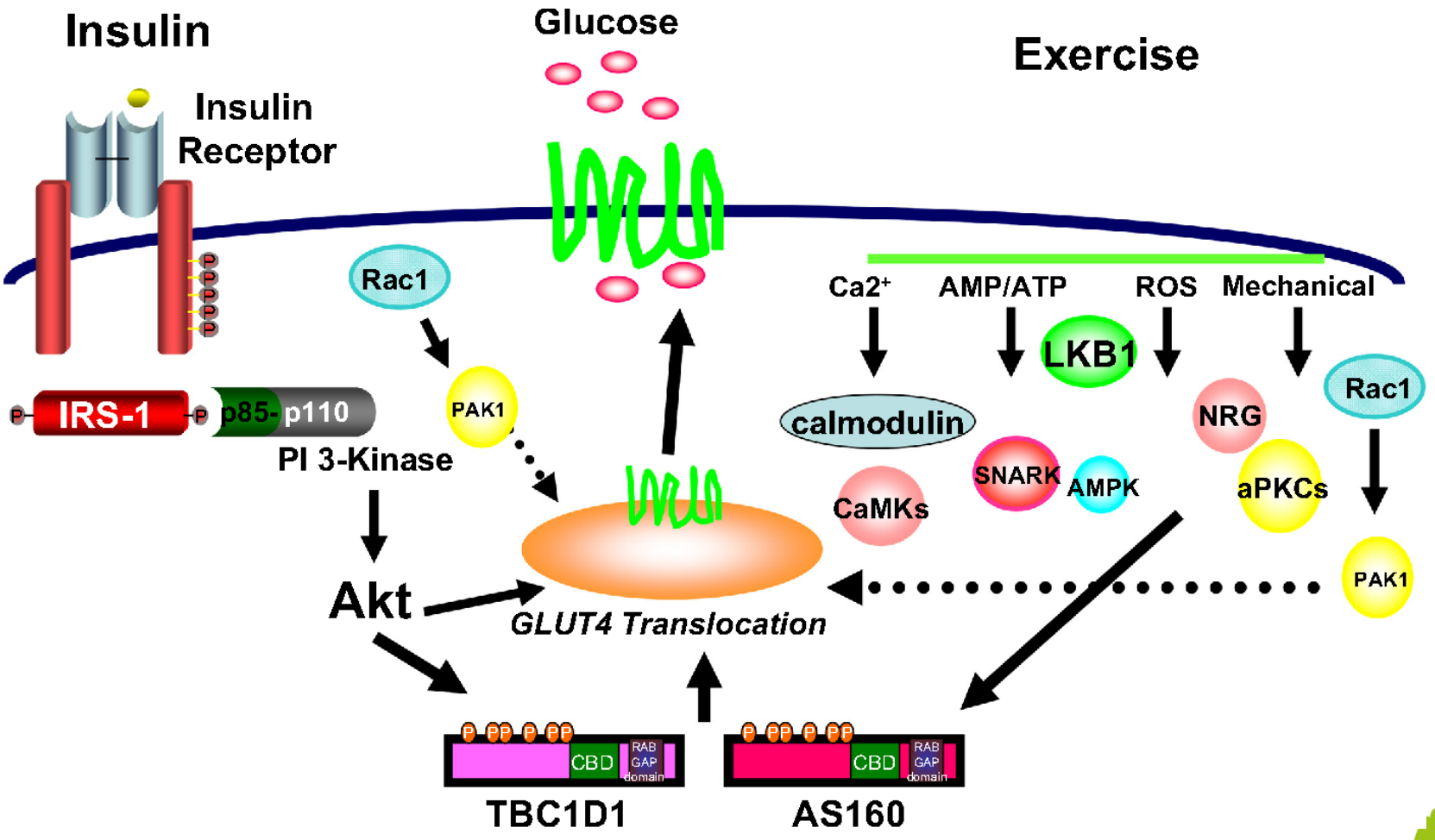
Insulin (mU/l)


Age - median split = 67 yrs
80
70
60
50
40
30
20
59
58.1
**
50.2
69.1
69.8
**
56.4
Below
Above
Sitting
Standing
PA

BMI - median split = 27.2 kg/m2



Mechanisms

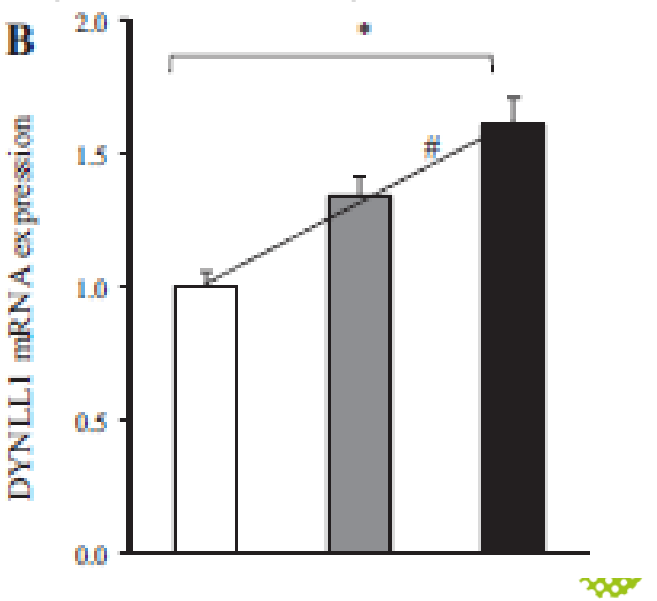


Stanford & Goodyear, 2014. Advances in physiology education

Mechanisms

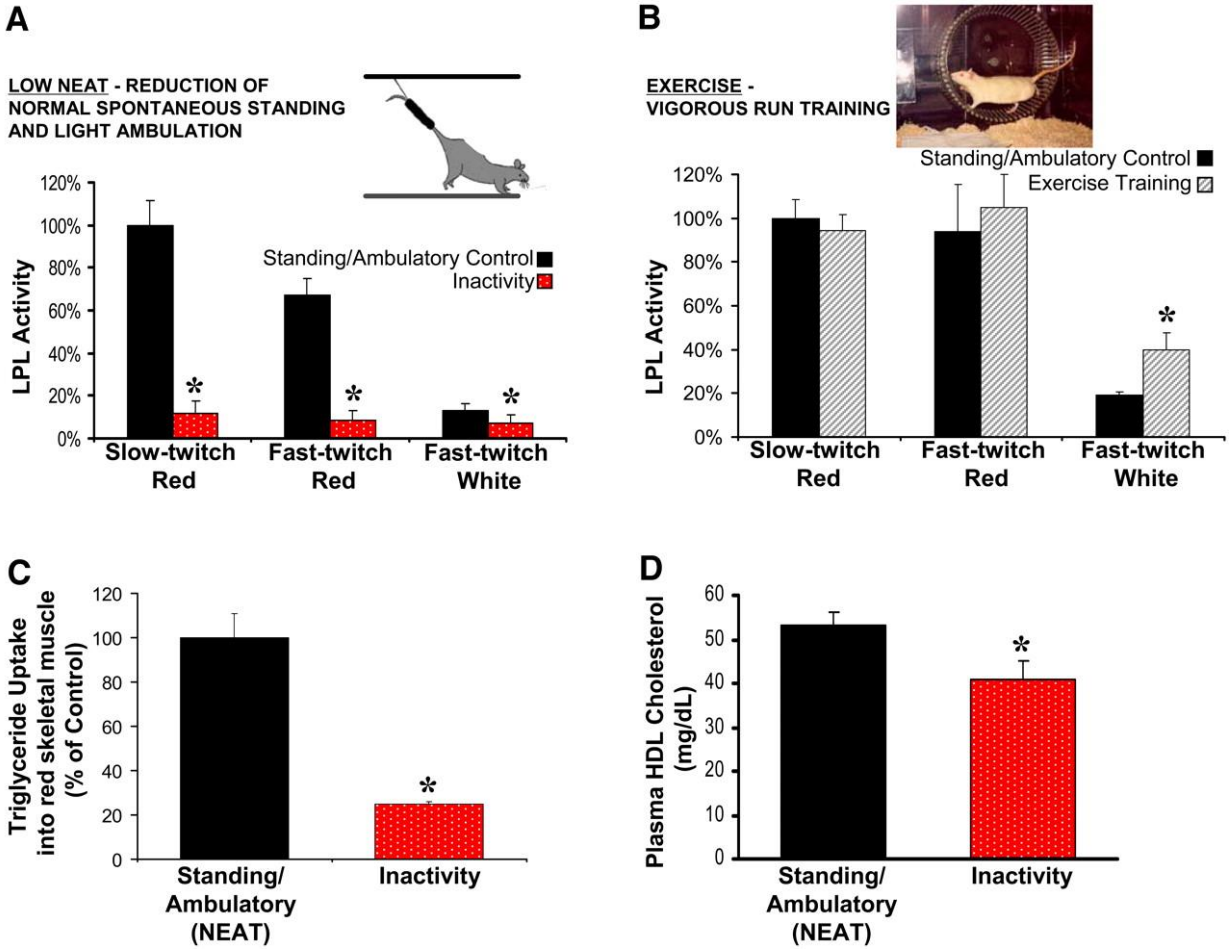
Bergouignan et al., 2016 Scientific Reports & Latouche et al., 2013J Appl Physiol

Pathways	Key proteins	5 hr light- intensity interruptions	5 hr moderate-intensity interruptions	3d light- intensity interruptions
Contraction-mediated glucose uptake	pACC	↑	↑	↑ p = 0.08
	tACC	=	=	↑ p = 0.14
Insulin-mediated glucose uptake	pAKT	=	=	↑ p = 0.14
	tAKT	=	=	↑
GLUT4 Translocation	pTBC1D4	=	=	
	tTBC1D4	=	↑	
Glycogen synthesis	pGSK3β	=	=	
	tGSK3β	=	↑	
Oxidative phosphorylation	ATPase	=	↑	



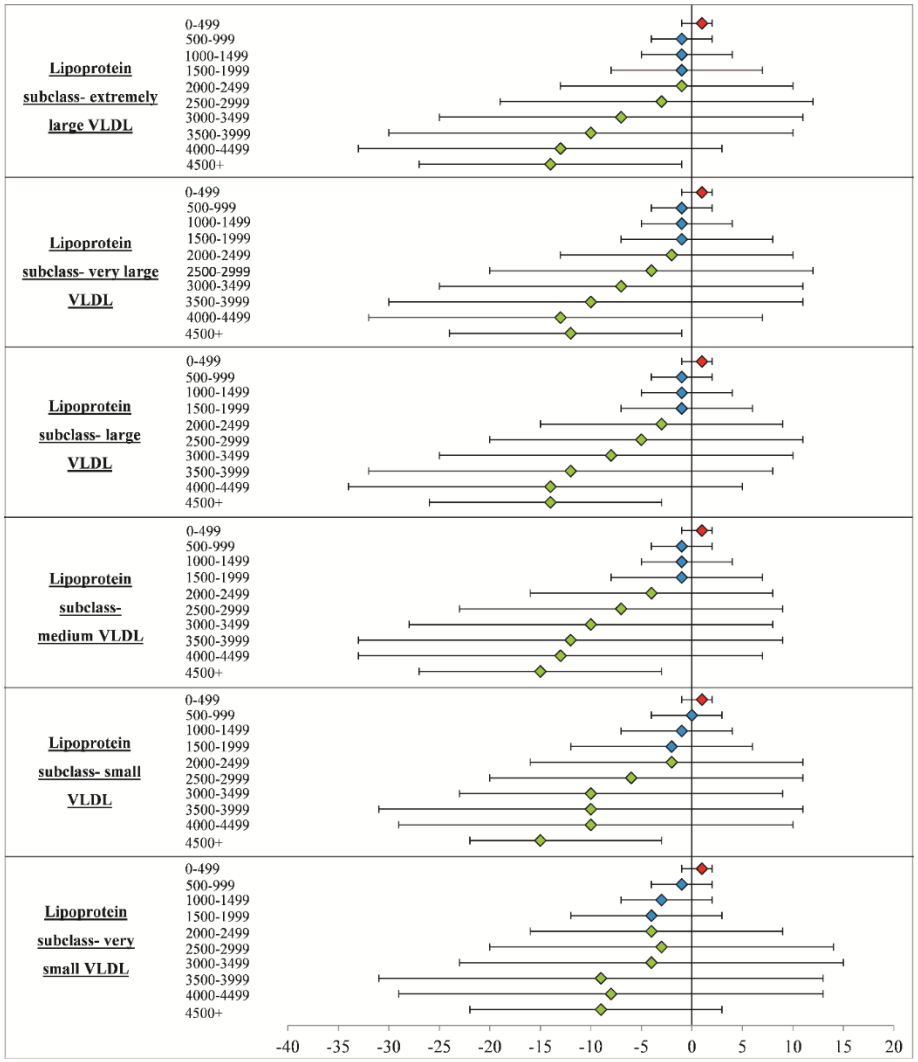
Lipid metabolism

Hamilton et al. 2007 Diabetes Care

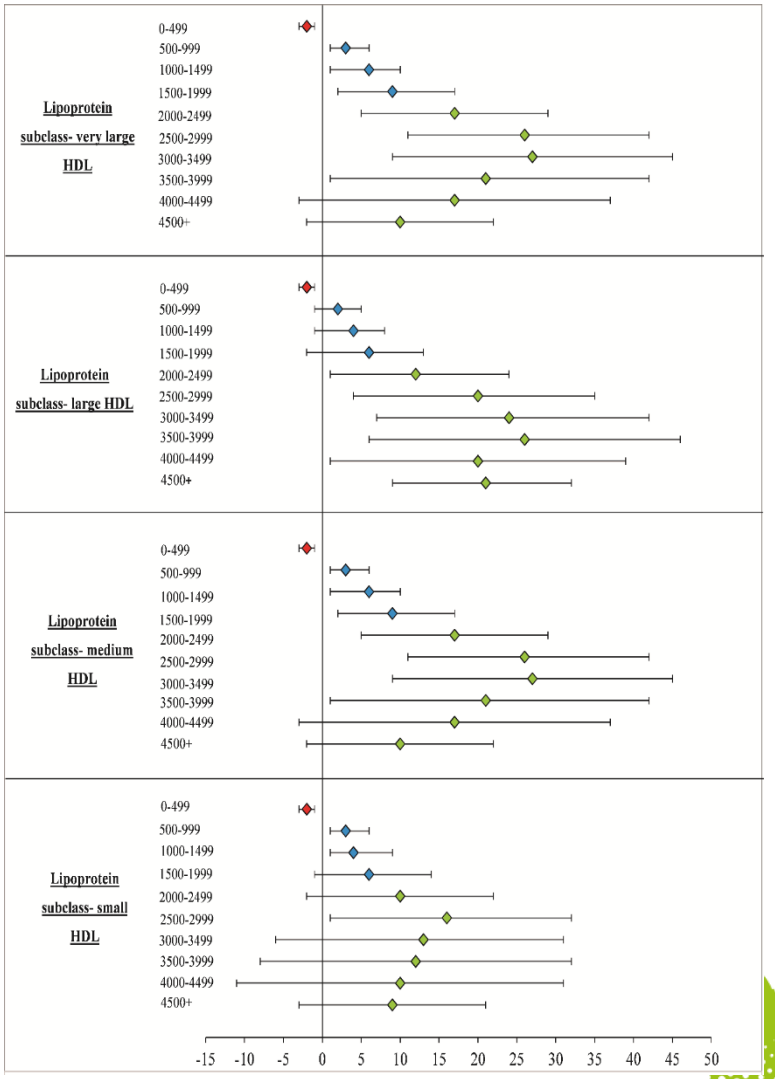


Association with lipid types

VLDL components



HDL components



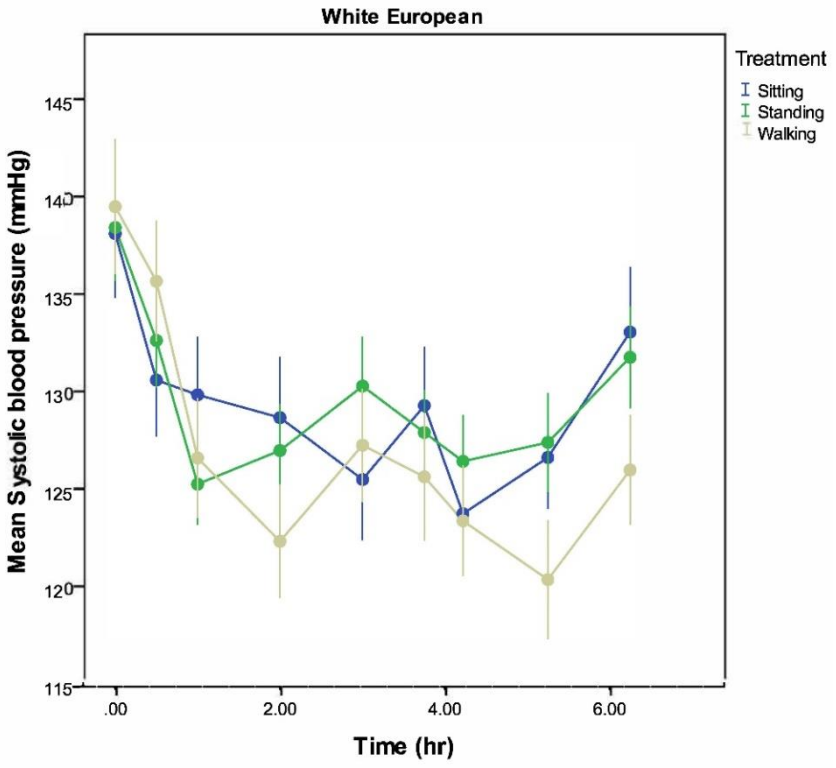
Changes to the Postprandial Lipidome

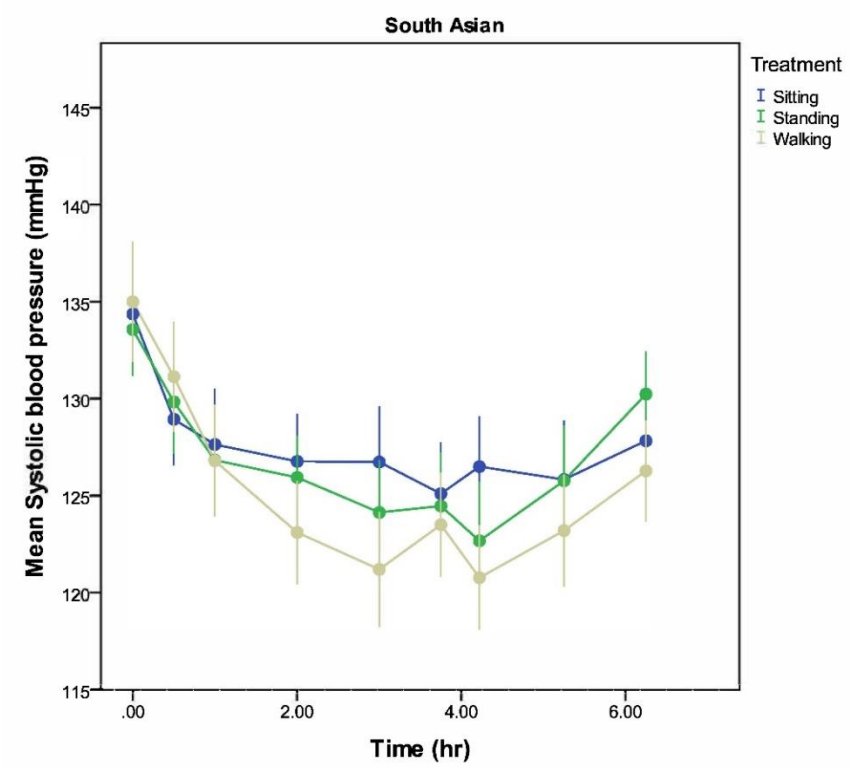
(Grace et al. 2017J Clin Endocrinol Metab)

Pathways	Key Lipid Class/Subclass	SIT	LW	SRA
Proinflammatory	Diacylglycerol	↑↑	↑	↑
	Triacylglycerol	↑↑	↑	↑
	Phosphatidylethanolamine	↑↑	↑	↑
Anti-inflammatory	Lysoalkylphosphatidylcholine	↓	↑/↔	↓
Antioxidant capacity	Alkenylphosphatidylcholine	↓	↑/↔	↔
Platelet activation	Phosphatidylserine	↓	↑	↓
	Phosphatidylethanolamine	↑↑	↑	↑
	Lysoalkylphosphatidylcholine	↓	↑/↔	↓

Blood pressure

Yates et al J Gerontol A-Biol in press



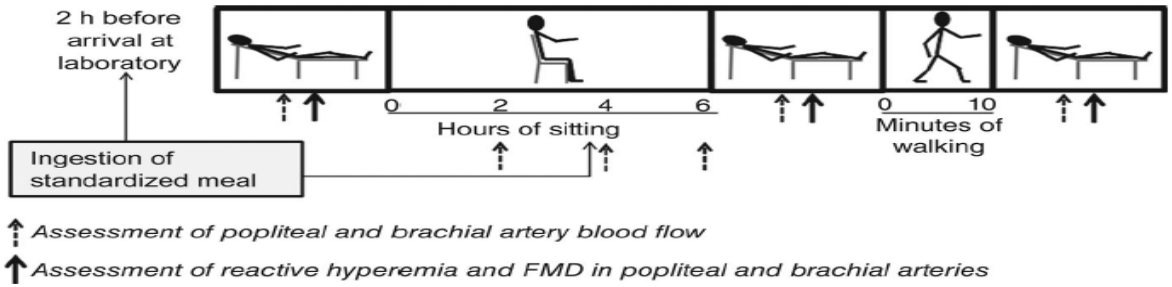


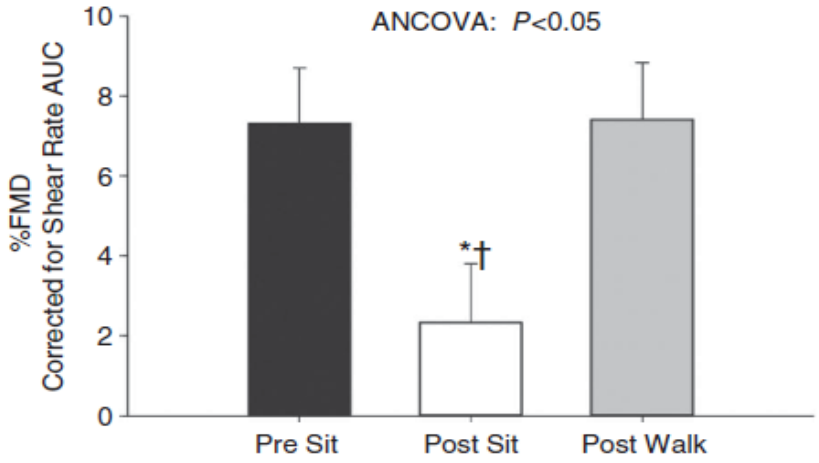
Average reduction = 4 (2, 6) mmHg

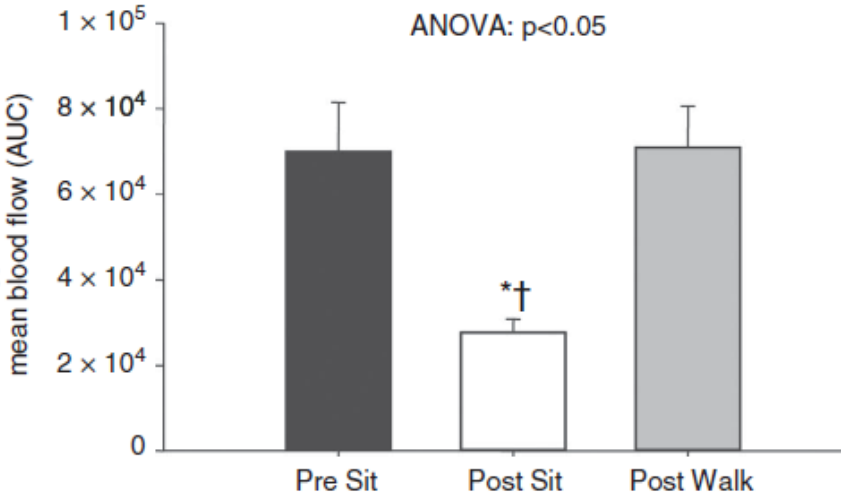
Equivalent to 6% difference in the risk of cardiovascular mortality

Vascular function

Restaino et al. 2015 Exp Physiol



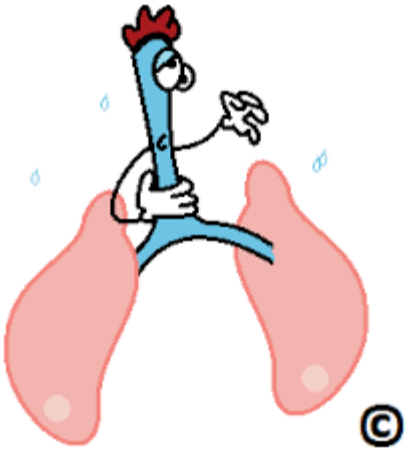


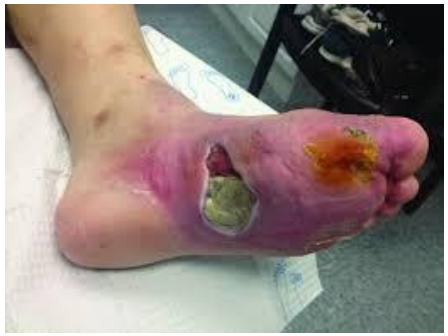


Future Directions: New disease areas

Example

- Can breaking prolonged sitting with light movement be used as a therapy to promote health in
  - Breathlessness
  - Diabetic foot





Future Directions – Ecological validity

Example

- Breaking sedentary behaviour with light walking or light resistance exercise according to the legal rest requirements for Lorry Drivers

Future Directions – chronic exposures

Conclusion

- Experiential evidence shows that regularly breaking sitting with light-intensity movement acutely improves metabolic health
- Those with low fitness, of South Asian ethnicity, older age and greater BMI may benefit the most
- Breaking prolonged sitting with light walking may also improve endothelial function and vascular health

Acknowledgments

UNIVERSITY OF LEICESTER

NHS
National Institute for Health Research

NIHR Leicester BRC

Thank you

www.leicesterdiabetescentre.org.uk

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