

Changing Sedentary Behaviour in the Prevention and Management of Chronic Diseases – Triangulating on Mechanisms

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Acknowledgements



Bronwyn Kingwell



Paddy Dempsey



Neville Owen



Megan Grace



Robyn Larsen



Genevieve Healy



Outline

- **The building blocks of an integrated research program addressing the health consequences of prolonged sitting**
 - *Insights from triangulation: observational, experimental and intervention research cross-talk – NHMRC Centre of Research Excellence on Sitting Time and Chronic Disease Prevention*
- **Developing deeper insights on the mechanistic underpinnings linking prolonged sitting to elevated health risks**
 - Evidence from acute studies – metabolic and vascular impacts
 - Next steps and unanswered questions

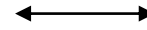
National Health & Medical Research Council Centre of Research Excellence on Sitting Time & Chronic Disease Prevention



Theme 1 Measurement



Theme 2 Mechanisms



Theme 3 Interventions



Healy



Trost



Kingwell



Dunstan



Salmon



Eakin



Winkler



Lambert



Timperio



Neville Owen

+ a number of International & National Associate Investigators



Identifying and addressing sedentary behaviour targets



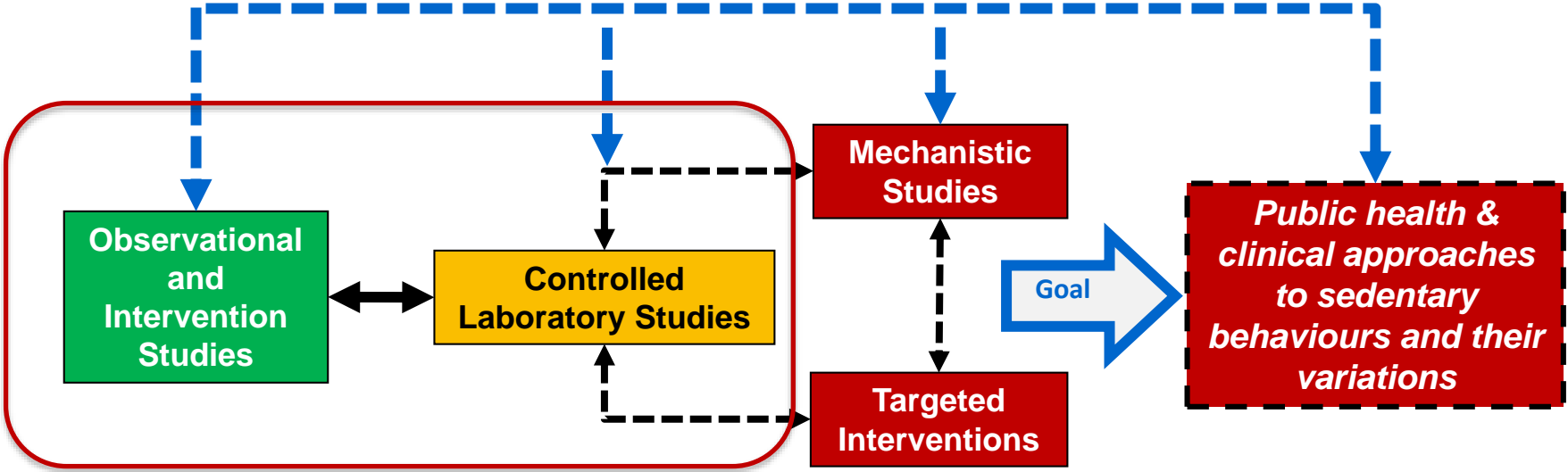
Strengthening evidence base



Modest evidence base



Limited evidence base

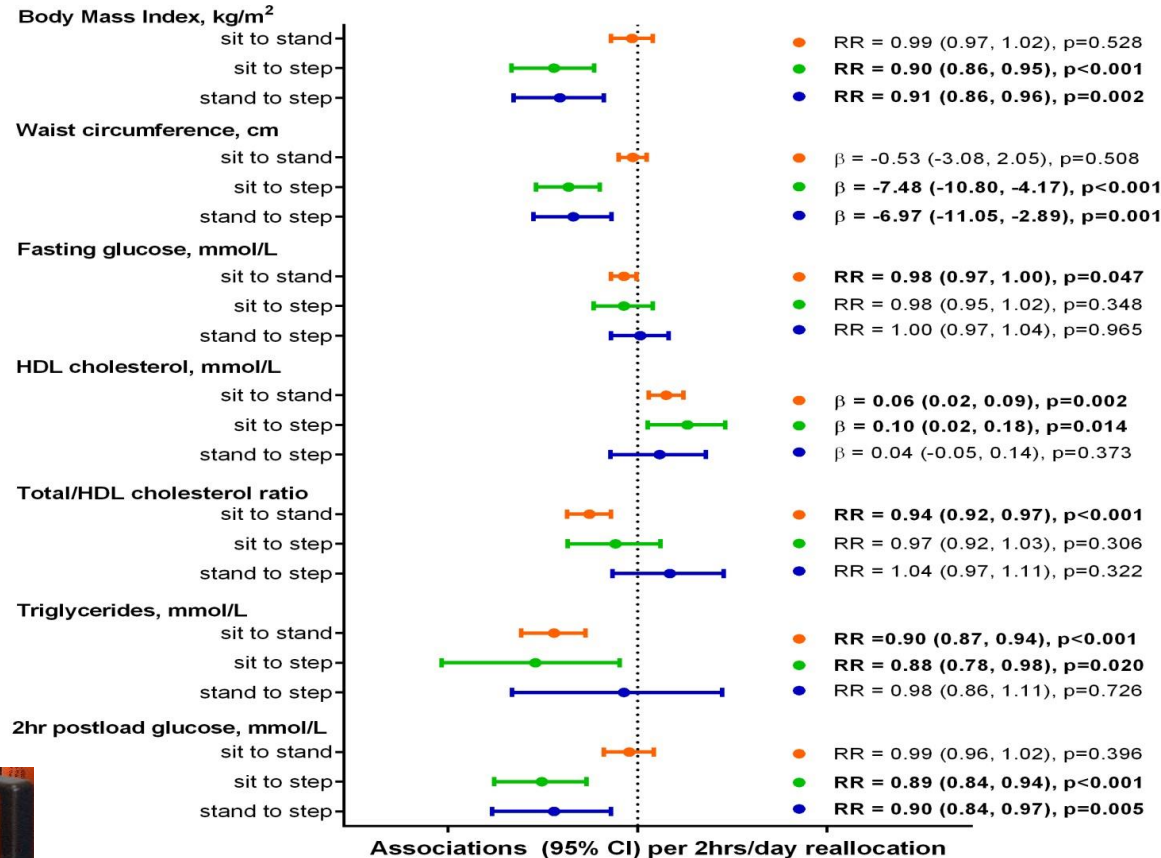


‘Scoping & Hypothesis Generation’

‘Strengthening Causal Inference, Dose-Response, Biological Plausibility & Specificity’

‘Communication, Engagement & Translation’

Observational: Informing behaviour change interventions



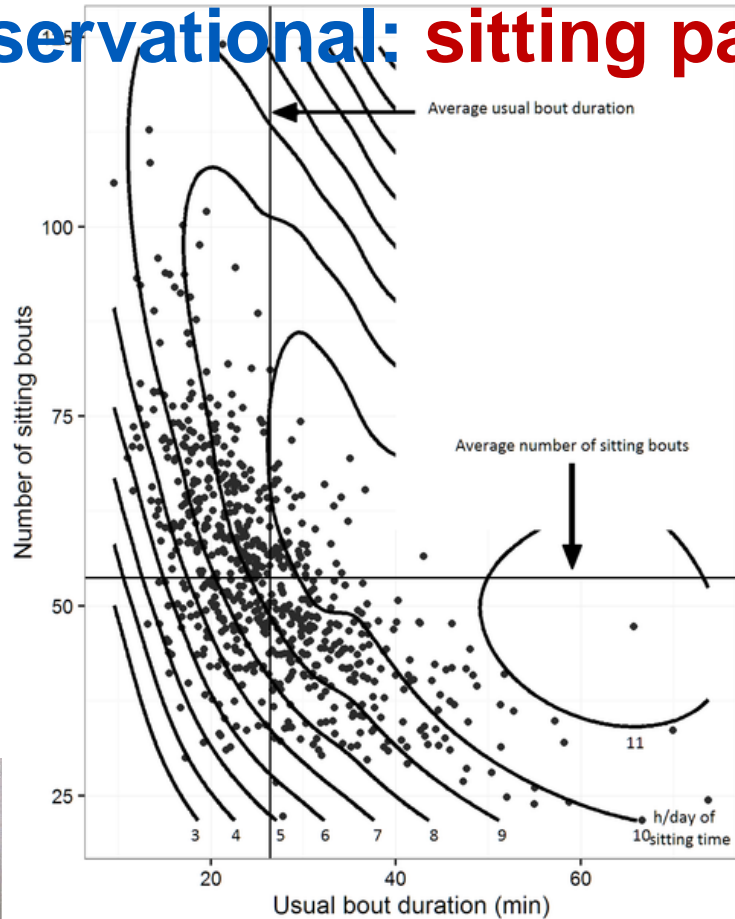
Sitting to standing – benefits for fasting glucose, HDL-C, triglycerides

Sitting to stepping – benefits for BMI, waist circumference, triglycerides, 2hr glucose

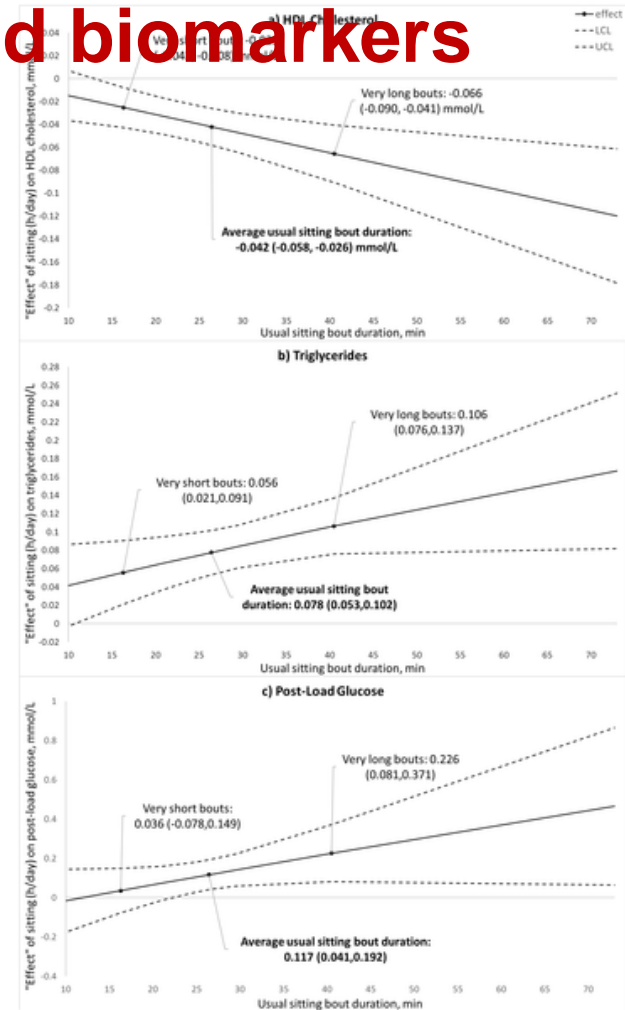


Source: Healy et al. *Eur Heart J* 2015 36: 2643-2649

Observational: sitting patterns and biomarkers



Source: Bellettiere J, Winkler EAH, Chastin SFM, Kerr J, Owen N, *et al.* (2017) Associations of sitting accumulation patterns with cardio-metabolic risk biomarkers in Australian adults. *PLOS ONE* 12(6): e0180119



Experimental: cross-talk with observational findings

IDLE Breaks: Brief walking breaks at moderate and light intensity: acute responses

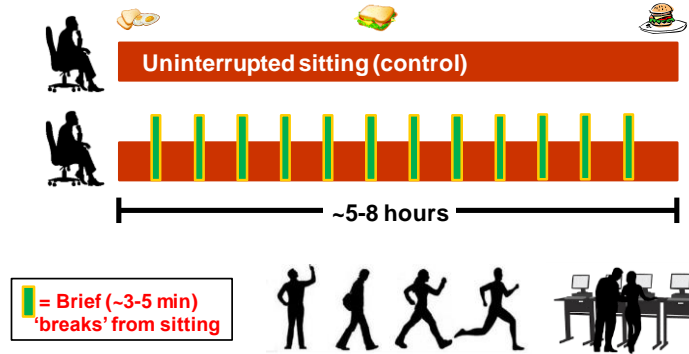
ABLE Breaks: Brief walking at moderate and light intensity: cumulative responses

Sit Or Stand (SOS): Standing-only breaks over 5 days

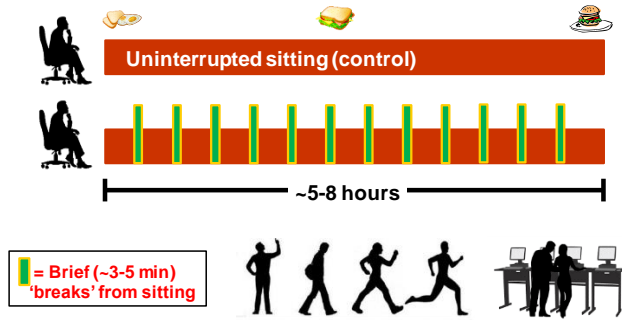
REWARD: Walking and simple resistance breaks in T2D

Active Ads: Breaking up sitting after a high-energy evening meal while watching TV

Brain Breaks: Interacting effects of acute exercise with breaks in sitting on cognitive function in older adults



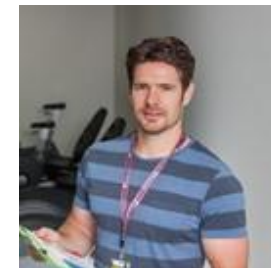
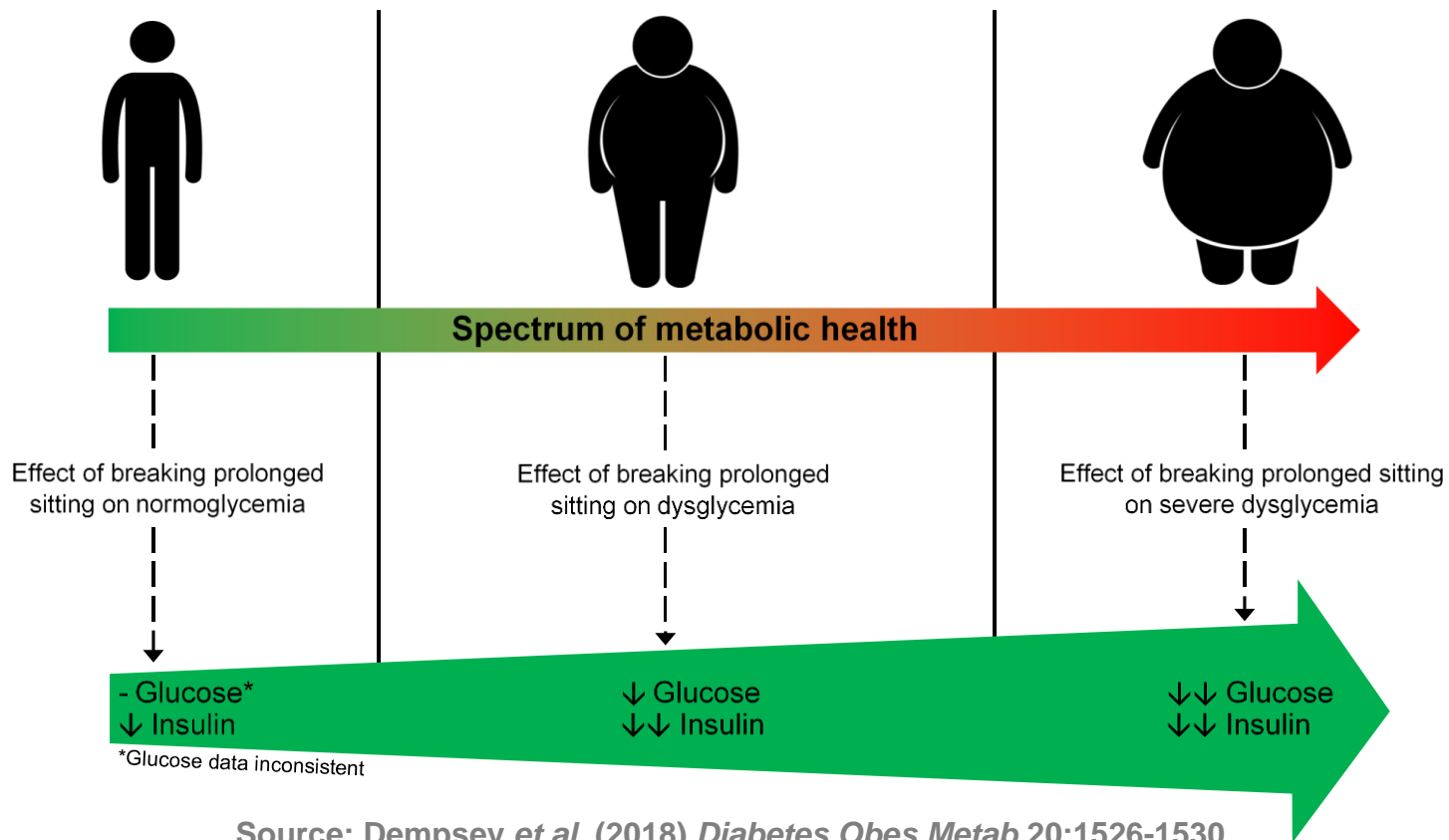
Experimental: interruptions and biomarkers



- ✓ Postprandial glucose and insulin responses
- ✓ Blood pressure
- ✓ Lipids
- ✓ Haemostatic markers

At least in the short-term (< 5 days)

Key Observation: Glycaemic benefits appear to be proportional to degree of metabolic impairment



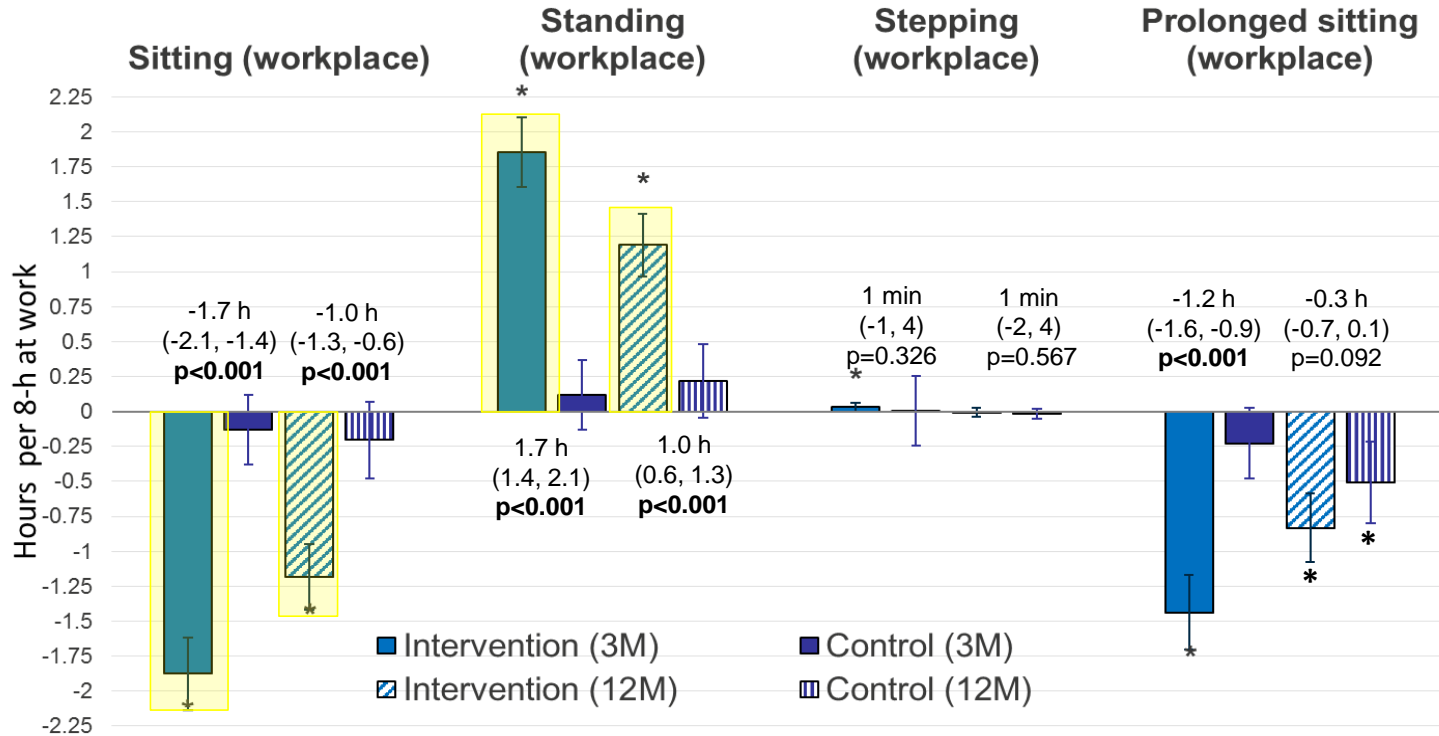
Paddy Dempsey



Ashleigh Homer

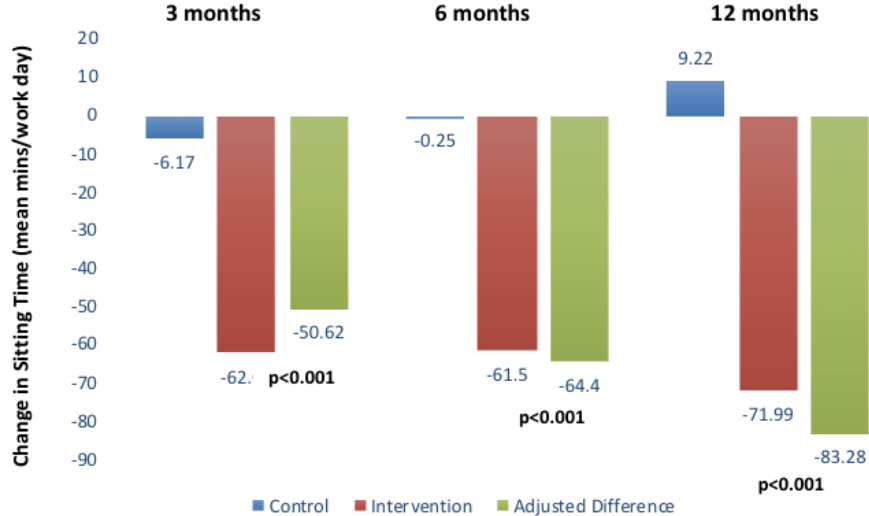
Source: Dempsey *et al.* (2018) *Diabetes Obes Metab* 20:1526-1530

Intervention: Large changes in workplace sitting

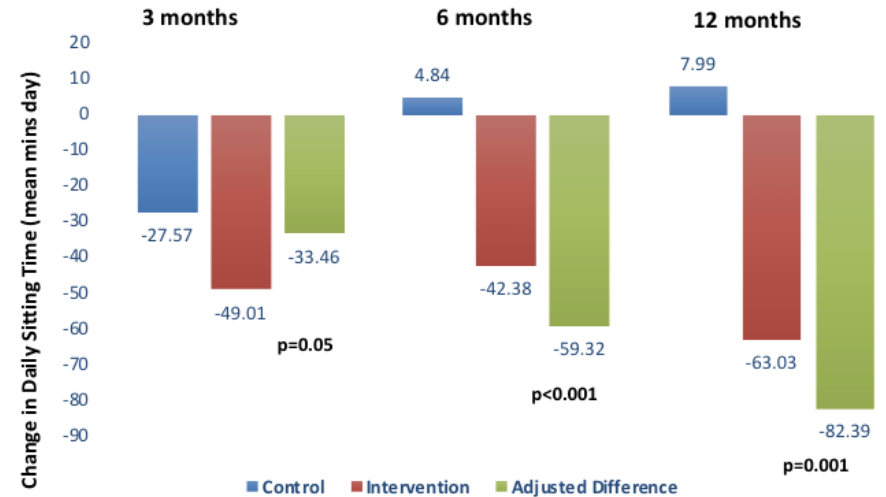


Intervention: Large changes in workplace sitting

Workplace sitting



Total sitting



Source: Edwardson C *et al.* *BMJ* 2018



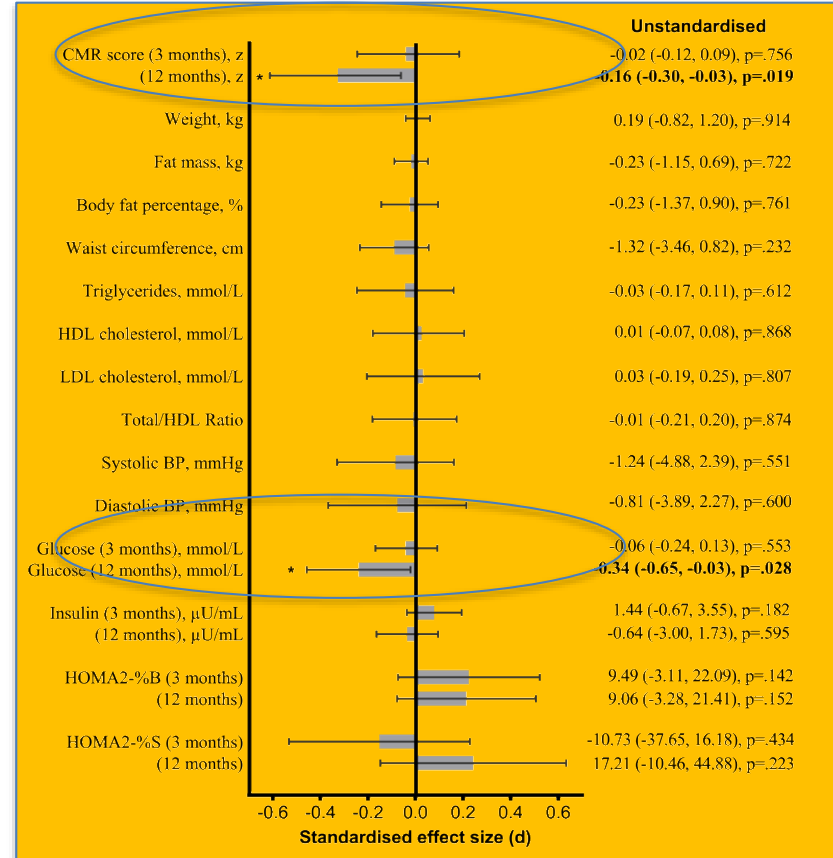
G Healy



EPIDEMIOLOGY

A Cluster RCT to Reduce Workers' Sitting Time: Impact on Cardiometabolic Biomarkers

GENEVIEVE N. HEALY^{1,2,3}, ELISABETH A. H. WINKLER¹, ELIZABETH G. EAKIN¹, NEVILLE OWEN^{1,2,4,5,6}, ANTHONY D. LAMONTAGNE⁷, MARJ MOODIE⁷, and DAVID W. DUNSTAN^{1,2,5,6,8}



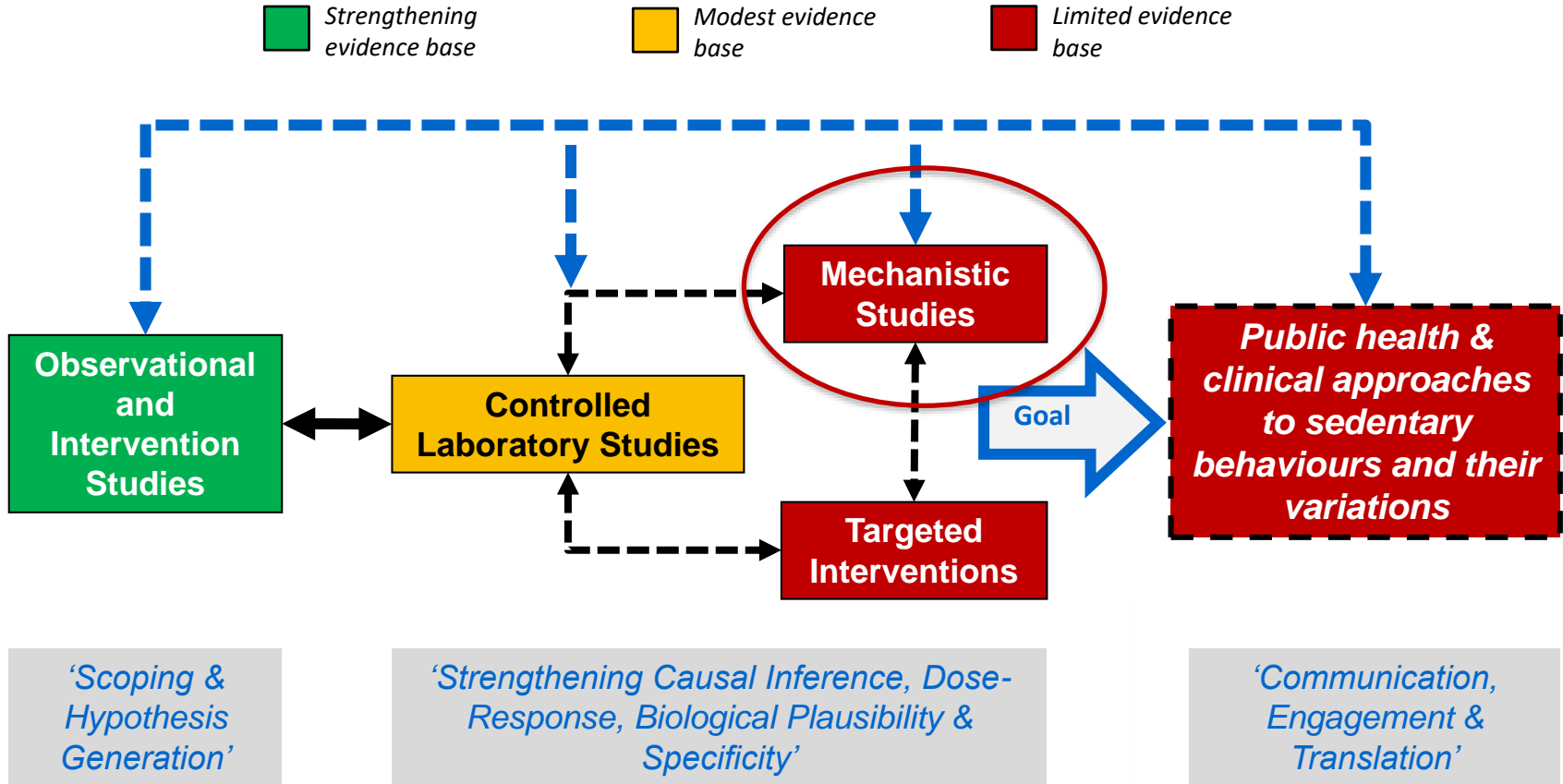
Source: Healy G et al. (2017) Med Sci Sports Exerc 49: 2032-2039



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Prolonged sitting: elucidating the mechanisms



Understanding the acute mechanistic impacts of prolonged sitting



Vascular

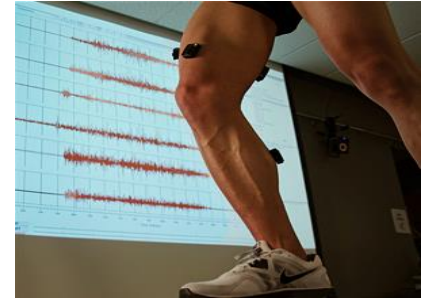
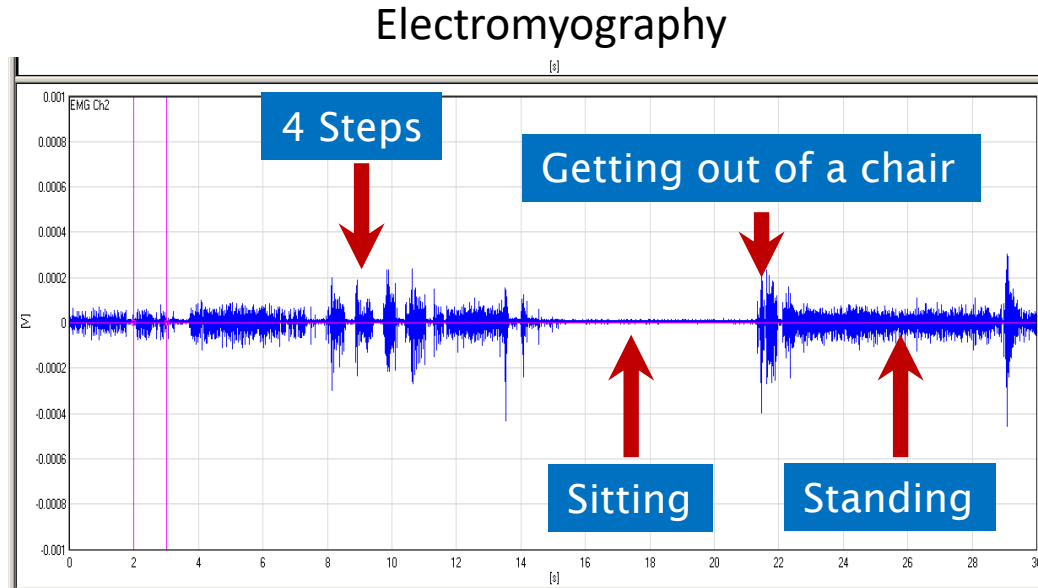
- ↓ Conduit artery flow
- ↓ Capillary recruitment
- ↓ Endothelial function
 - ↓ shear stress
 - ↓ vasodilatation
 - ↑ leukocyte adhesion
- ↑ Haemostasis

Metabolic

- ↓ muscular contractile activity
- ↓ ATP production
 - ↓ glucose uptake and metabolism
 - ↓ lipolysis, FFA uptake, fat oxidation

Source: Dempsey PC & Thyfault JP Physiological responses to sedentary behavior. In: Leitzman MF, Jochem C, Schmid D (eds) *Sedentary behavior epidemiology* 2018 Springer International Publishing

Prolonged Sitting Diminishes Skeletal Muscle Contractile function



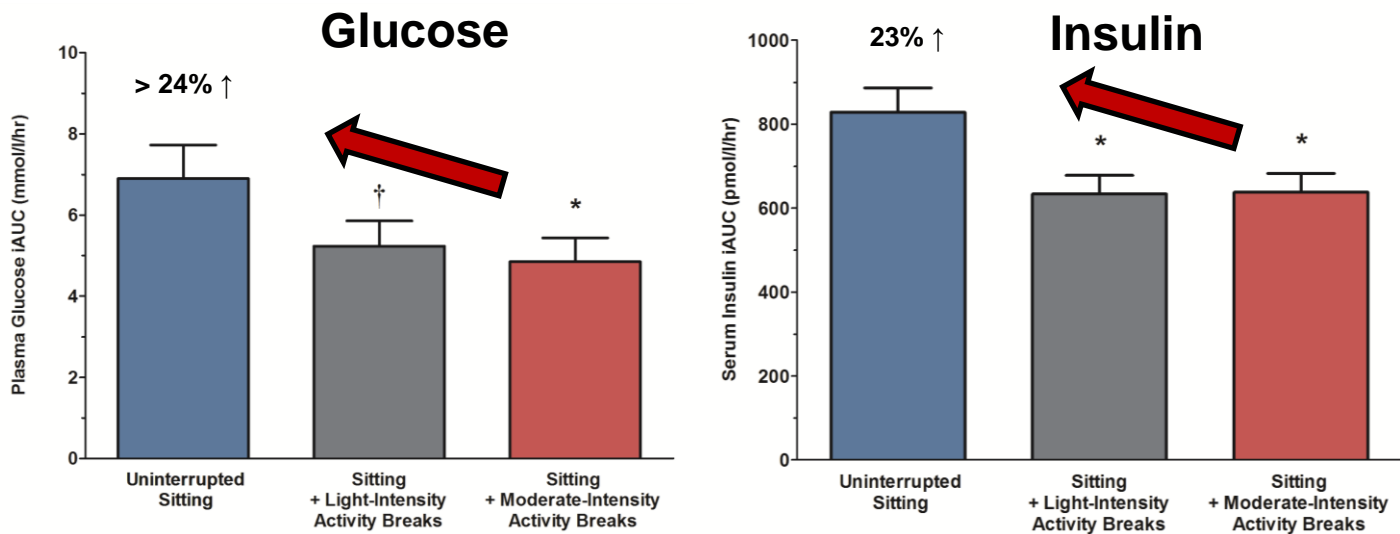
Source: Hamilton M *et al. Diabetes*, 2007

Prolonged sitting impairs glycemic control

PARTICIPANTS (n=19)

Age: 45-65 years

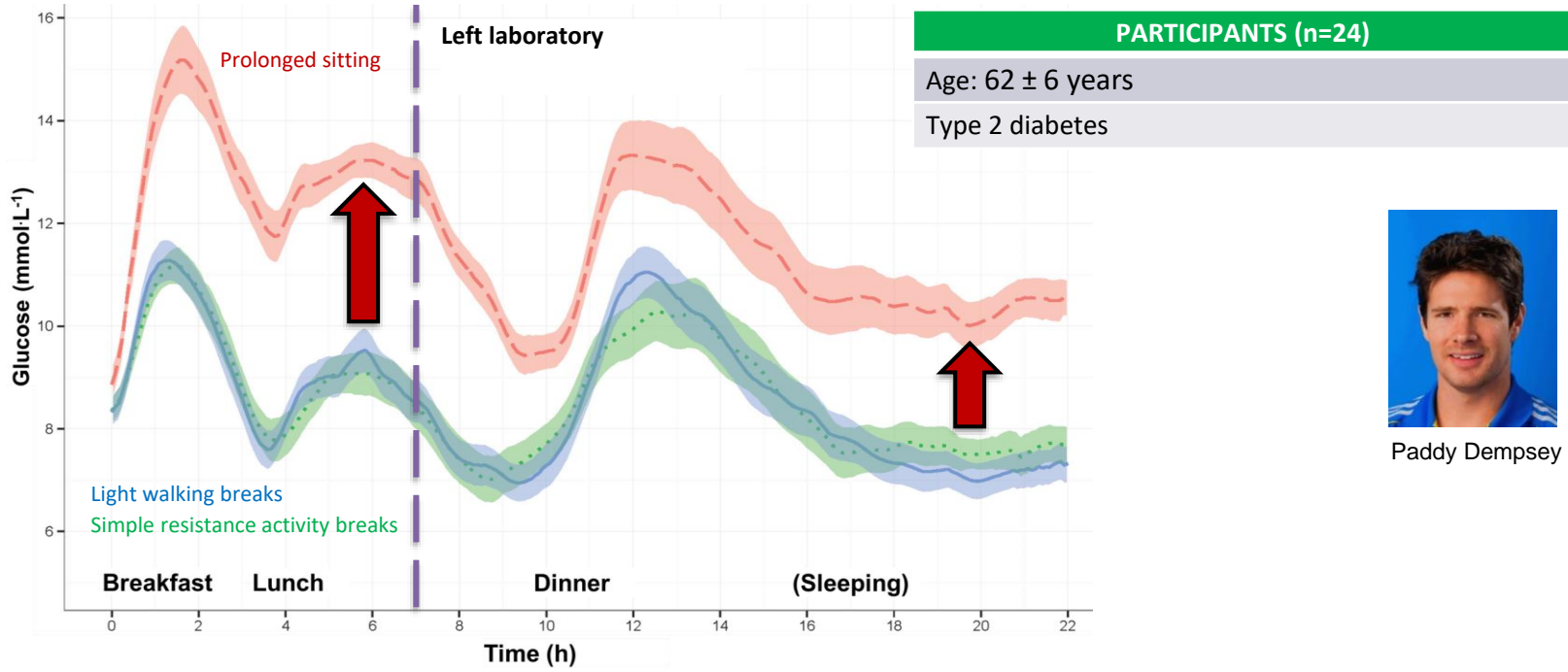
Overweight/obese: BMI > 25 ≤ 45 kg/m²



Meal challenge: 75g CHO/50g fat (Calogen: Nutricia Aust)

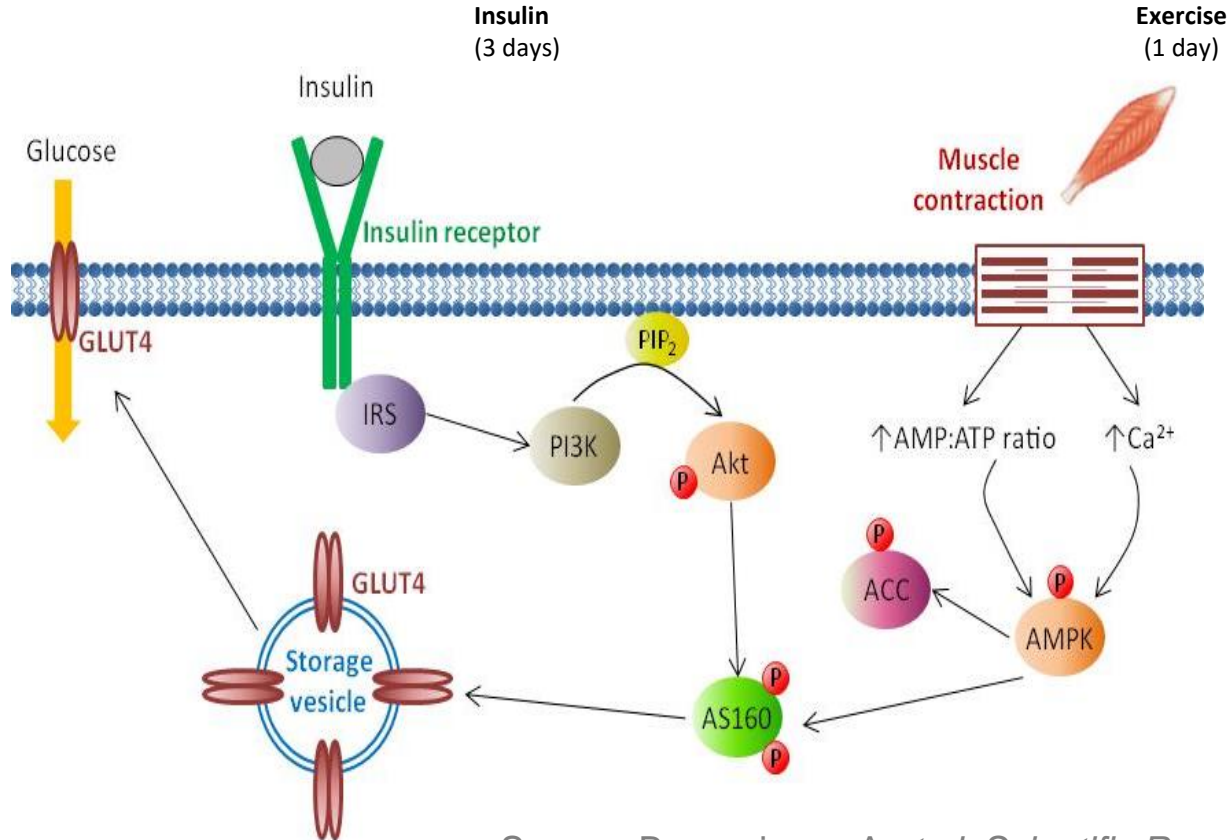
Source: Dunstan DW *et al.* (2012) *Diabetes Care* 35: 976-983

Sustained nocturnal impairment of glycemic control by prolonged daytime sitting



Source: Dempsey P *et al.*, *Diabetologia* 2017. 60(3):499-507

Prolonged sitting impairs dual pathways for skeletal muscle glucose uptake



Audrey Bergouignan

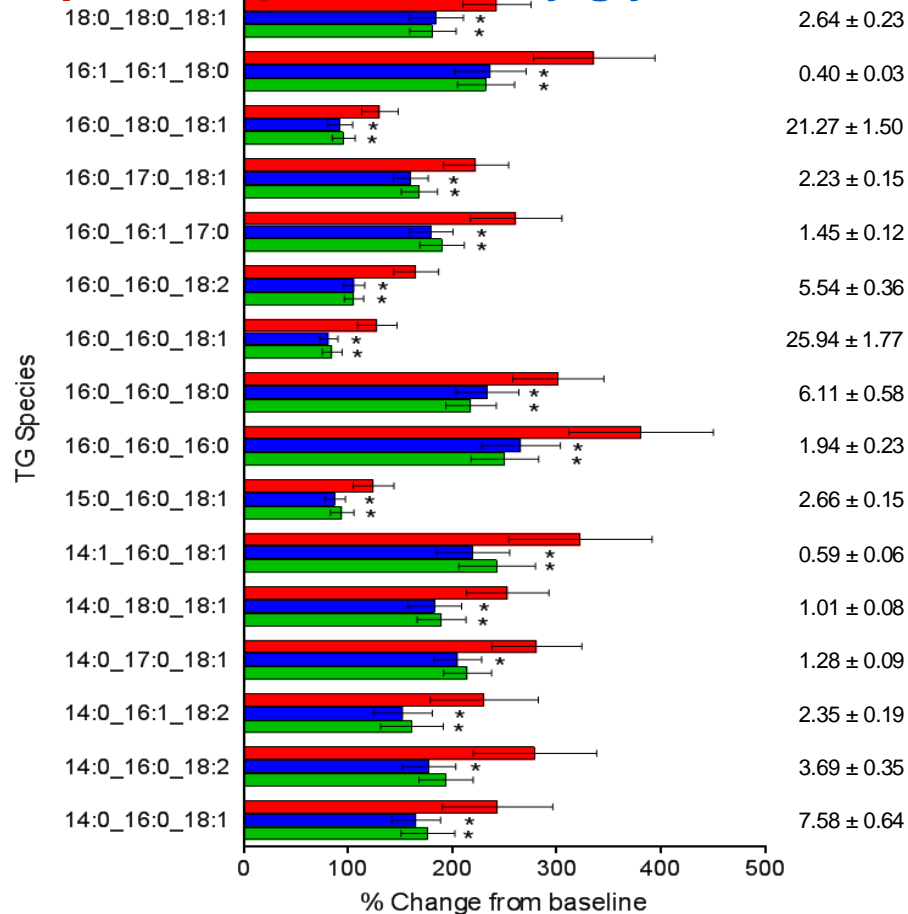


Source: Bergouignan A *et al.* *Scientific Reports*, 2016



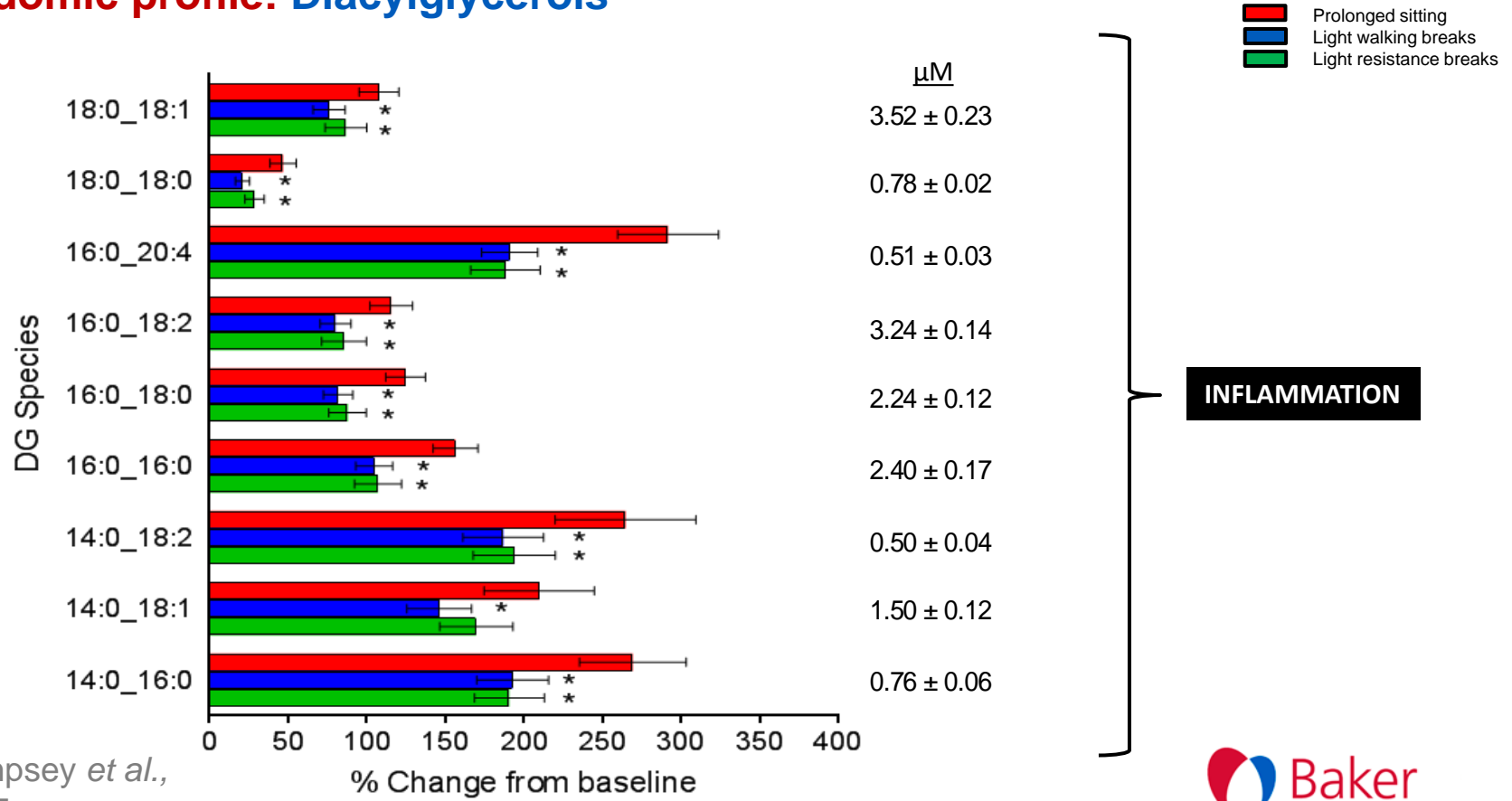
Liquid chromatography,
electrospray ionisation-tandem
mass spectrometry

Prolonged sitting modulates the post-prandial plasma lipidomic profile: Triacylglycerols μM



INFLAMMATION

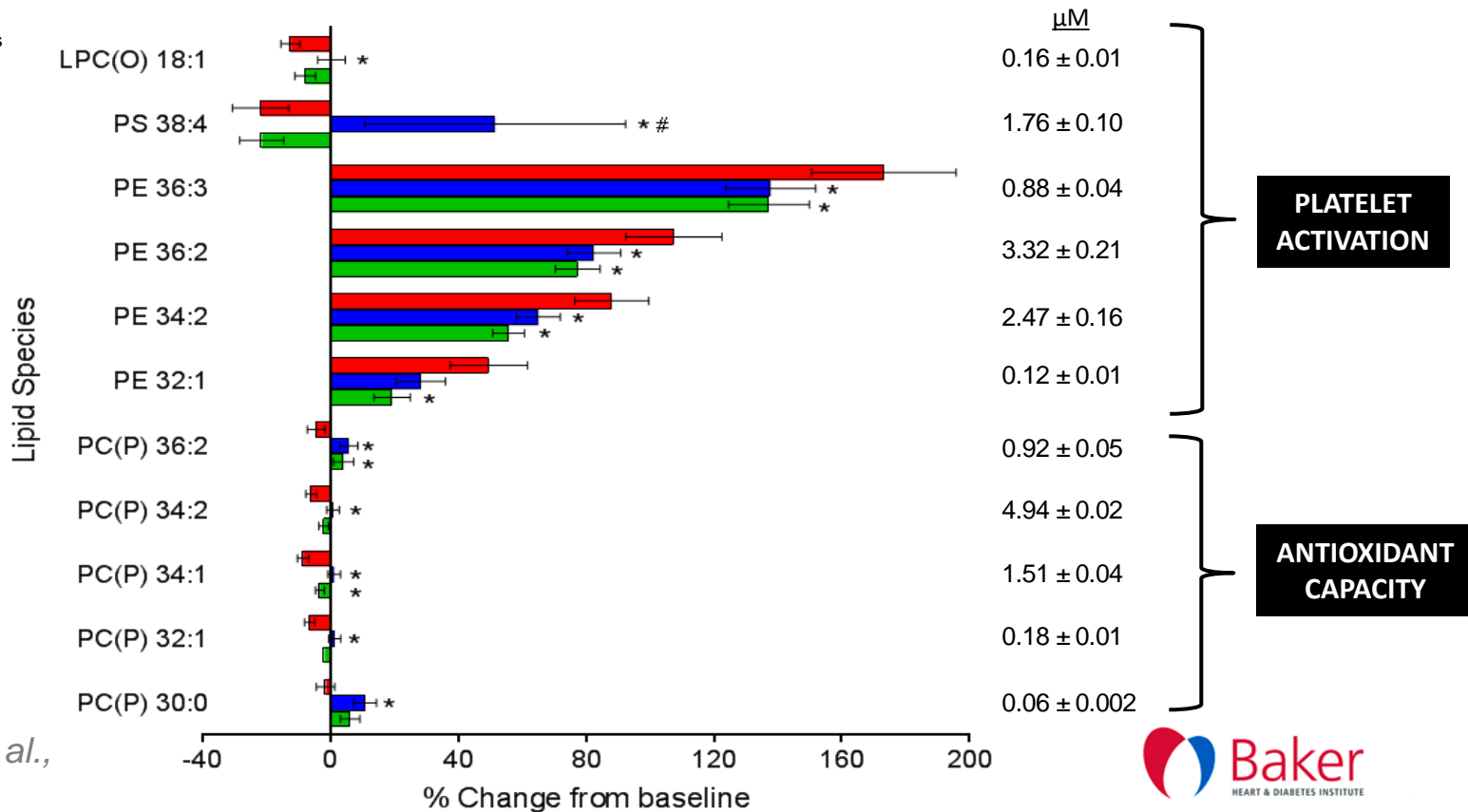
Prolonged sitting modulates the post-prandial plasma lipidomic profile: Diacylglycerols



Grace, Dempsey *et al.*,
JCEM, 2017

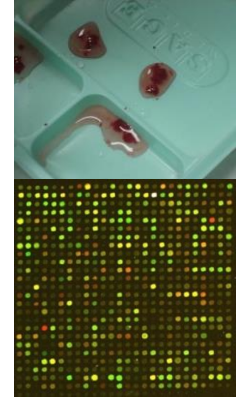
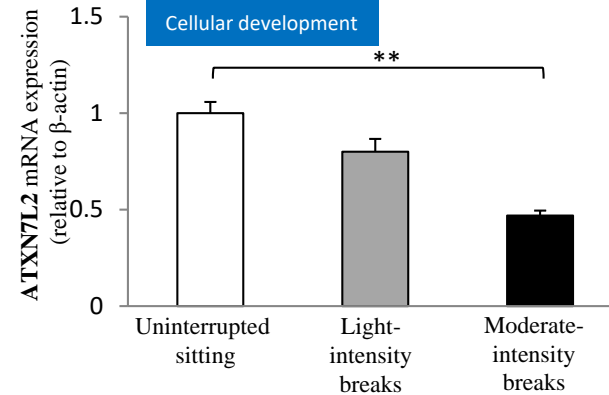
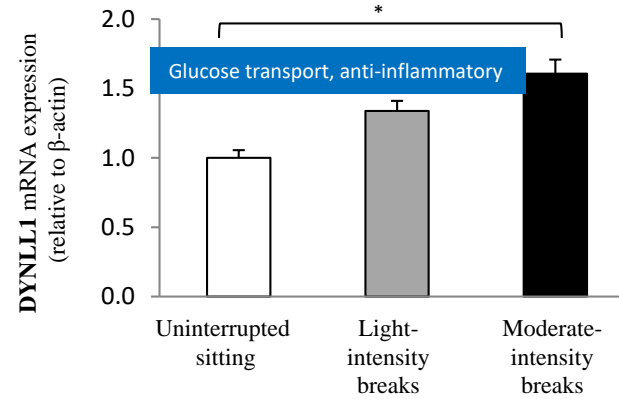
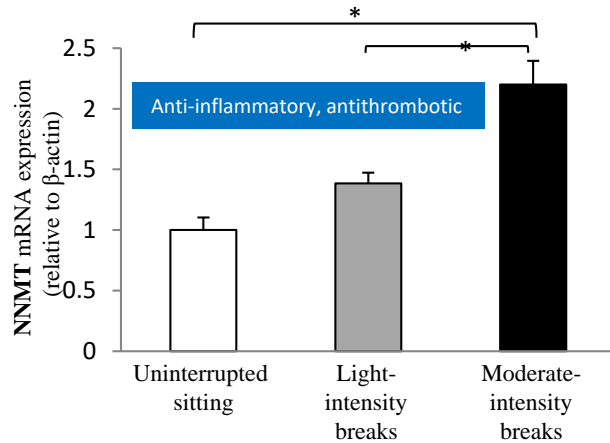
Prolonged sitting modulates the post-prandial plasma lipidomic profile: Other Lipid Species

- Prolonged sitting
- Light walking breaks
- Light resistance breaks



Prolonged sitting modulates multiple skeletal muscle gene expression pathways

75 differentially expressed genes
-18 cellular development
-21 cellular growth & proliferation
-16 small-molecule biochemistry
-10 carbohydrate metabolism



Understanding the acute mechanistic impacts of prolonged sitting



Vascular

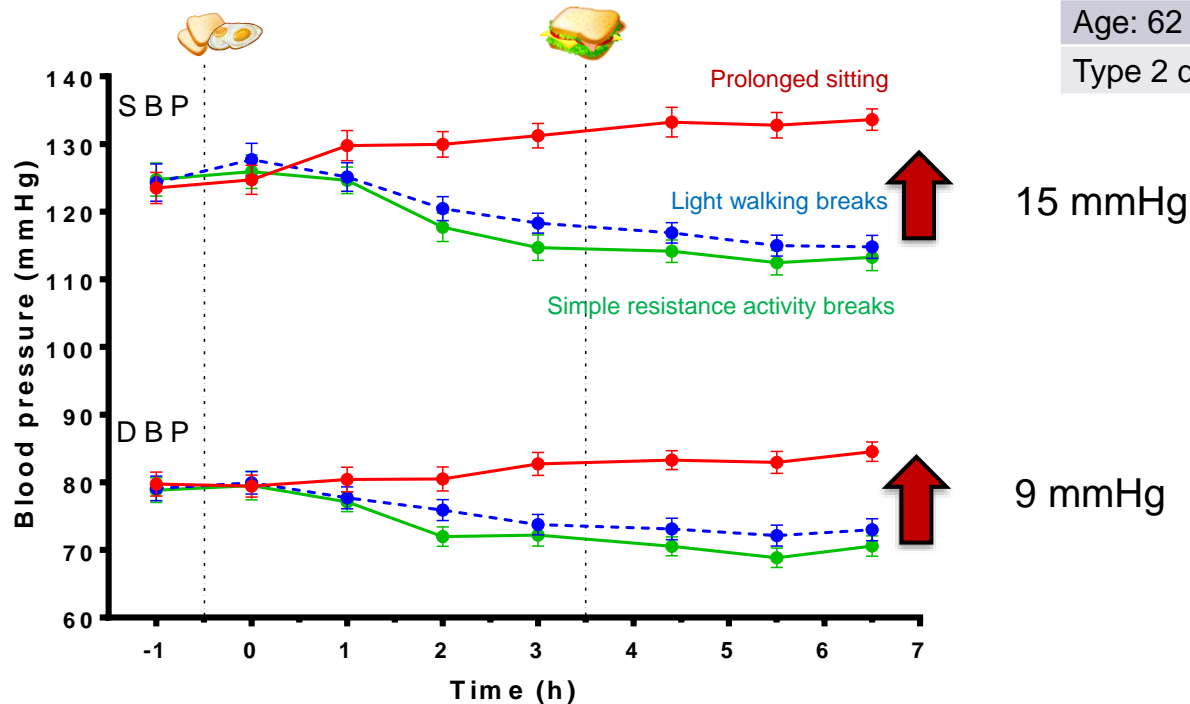
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Source: Dempsey PC & Thyfault JP Physiological responses to sedentary behavior. In: Leitzman MF, Jochem C, Schmid D (eds) *Sedentary behavior epidemiology* 2018. Springer International Publishing

Prolonged sitting increases blood pressure



PARTICIPANTS (n=24)

Age: 62 ± 6 years

Type 2 diabetes

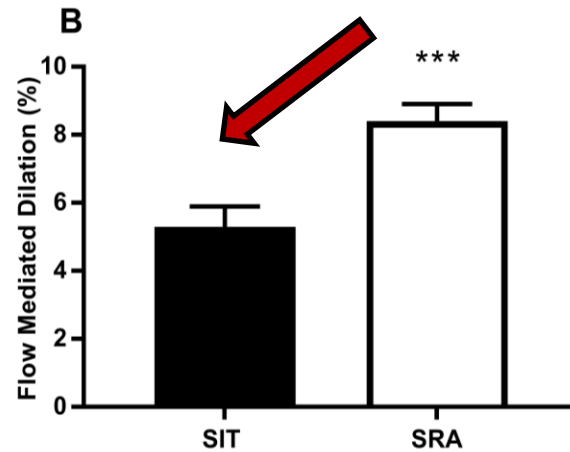
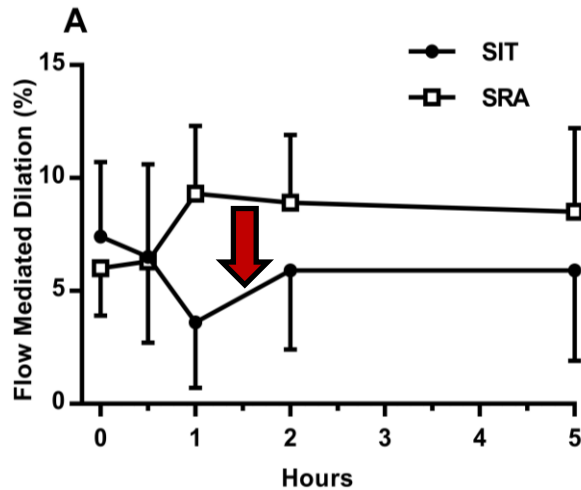
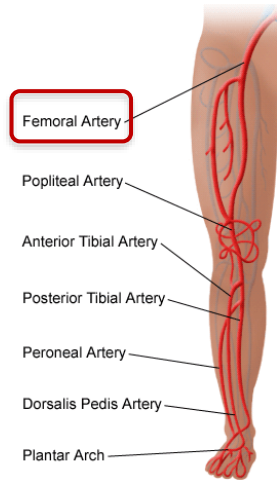
15 mmHg

9 mmHg

Source: Dempsey PC, et al. (2016) *J Hypertens.* 34: 2376-2382

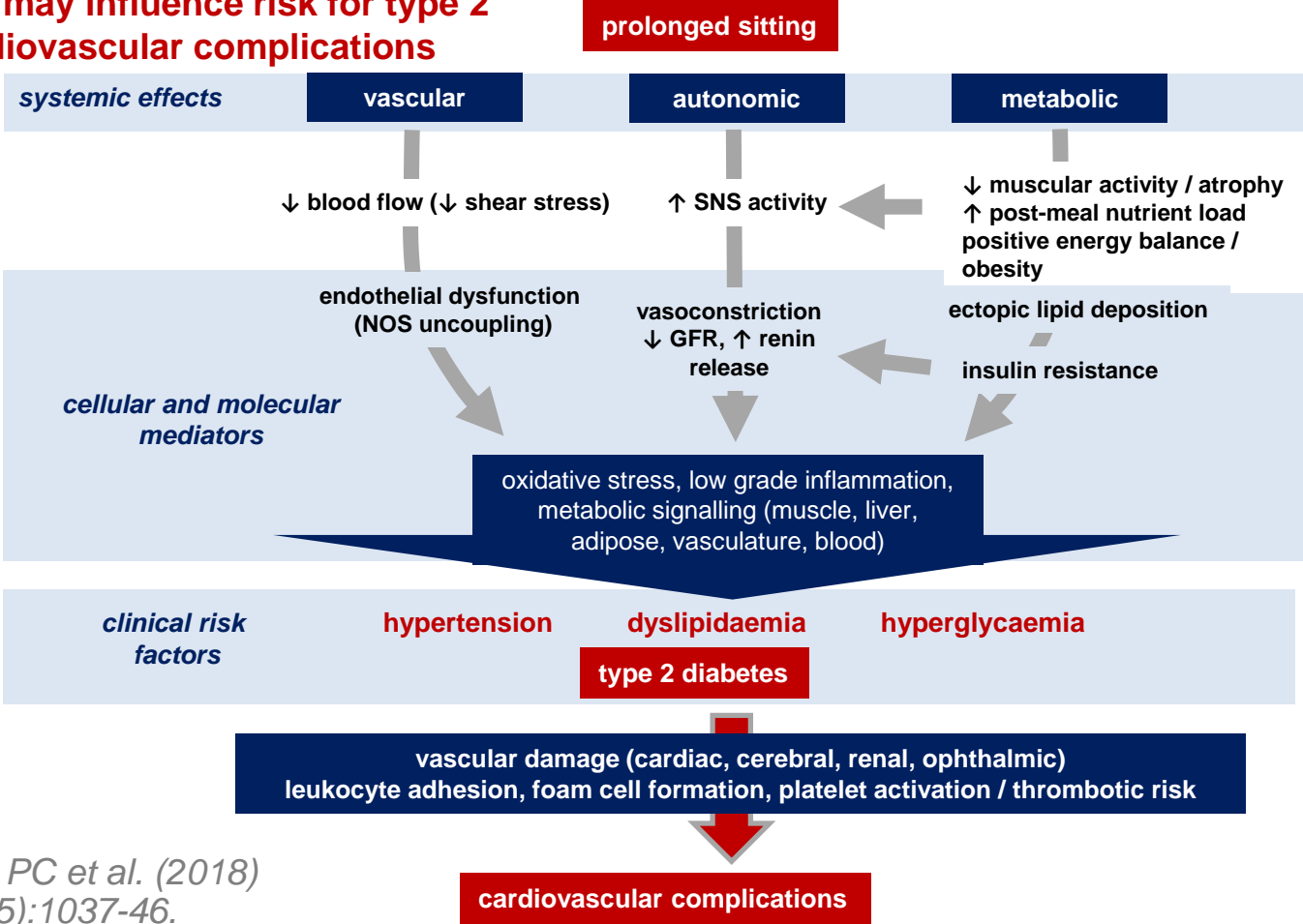
Prolonged sitting reduces femoral FMD

Compared to simple resistance exercises



Source: Climie R et al. (2018) *J Appl Physiol*; Sep 6 2018 [Epub ahead of print]

Mapping the mechanisms by which longer-term prolonged sitting may influence risk for type 2 diabetes and cardiovascular complications



Source: Dempsey PC et al. (2018) Hypertension. 72(5):1037-46.



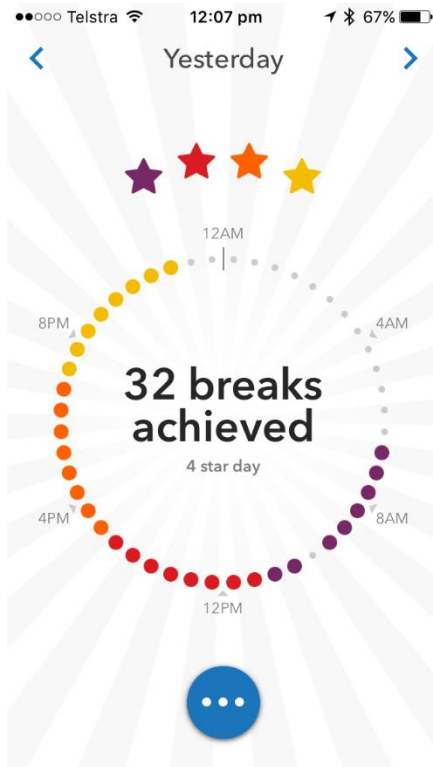
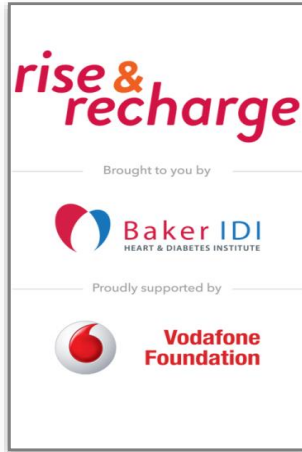
Unanswered questions

Which mechanism(s) can be most effectively altered by sustained reductions in prolonged sitting?

What are the temporal and dose-response relationships between biological mechanisms and different modalities, frequencies and interruptions to prolonged sitting time?

What are the cellular and molecular underpinnings of risk factor improvement resulting from sustained change in prolonged sitting?

Thank You For Listening



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Baker Heart & Diabetes Institute
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