Journal of Obesity and Chronic Diseases

https://doi.org/10.17756/jocd.2018-014

Research Article

Open Access

# Physical Activity and Blood Glucose Effects on Weight Gain Over 12 Years in Middle-Aged Adults

**Erin I. Walsh[1*], Richard Burns[1], Walter P. Abhayaratna[2], Kaarin J. Anstey[1,3] and Nicolas Cherbuin[1]**

[1]*Centre for Research on Ageing, Health and Wellbeing, Australian National University, Canberra, Australia*

[2]*College of Health and Medicine, The Australian National University, Canberra, Australia*

[3]*Neuroscience Research Australia (NeuRA), University of New South Wales, Sydney, Australia*

**[*]Correspondence to:**
Erin I. Walsh
Centre for Research on Ageing
Health and Wellbeing, 54 Mills Road
Australian National University, Canberra
ACT 2601, Australia
Tel: (612) 6125 8291
Fax: (612) 6125 1558
E-mail: erin.walsh@anu.edu.au

**Received:** February 08, 2018
**Accepted:** April 23, 2018
**Published:** April 25, 2018

**Citation:** Walsh EI, Burns R, Abhayaratna WP, Anstey KJ, Cherbuin N. 2018. Physical Activity and Blood Glucose Effects on Weight Gain Over 12 Years in Middle-Aged Adults. *J Obes Chronic Dis* 2(1): 20-25.



Published by United Scientific Group

## Abstract

**Background:** While high body weight and low levels of physical activity are established risk factors for type 2 diabetes, the associations between these risk factors and blood glucose levels in adults without diabetes are not well understood. We evaluated these associations in a cohort of adults studied over twelve years in a population-based sample.

**Methods:** Participants were 716 older adults from the Personality and Total Health (PATH) cohort study, followed over twelve years (2001-2013). Physical activity, height and weight were measured and converted to quartiles of metabolic equivalents (METs) and body mass index (BMI). Blood glucose (mmol/L) was obtained from venous blood samples. Mixed effects models were used to investigate the longitudinal association between METs, blood glucose, and BMI.

**Results:** Blood glucose was significantly associated with BMI (an increase of 1 mmol/L in glucose was associated with 0.33 additional unit increase in BMI). Higher METs were associated with less weight gain. A significant interaction between METs and blood glucose suggests that the most physically active participants were somewhat protected from the blood glucose/BMI association.

**Conclusion:** We conclude that blood glucose is associated with body weight even at non-clinical levels. This has implications for public health and prevention strategies targeting obesity, as it indicates that relationships between blood glucose, physical activity and body weight characterised in T2D diagnosis can be found in sub-clinical populations.

## Keywords

Blood glucose, Physical activity, Body mass index, Prevention

## Introduction

Obesity is amongst the most prevalent non-communicable diseases in Australia [1] and world-wide [2]. A body mass index (BMI) 25-30 (overweight) or > 30 (obese) is a risk factor for the development of Type 2 Diabetes (T2D) [3, 4], which is another of the most prevalent non-communicable diseases in Australia [5] and world-wide [3]. Chronically high blood glucose and T2D can contribute to fat deposition via mechanisms such as dehydration, lean body mass loss, and side-effects of insulin therapy [6, 7]. A lack of physical activity is a major risk factor for both obesity and T2D [8]. In 2012, approximately half of Australian adults fall short of World Health Organisation guidelines [9] .

Physical activity prevents weight gain and promotes weight maintenance [10-12] via several pathways, including increased net energy expenditure and

improved glycaemic regulation in normal weight through to obesity [13-15]. Poor glycaemic regulation, manifest in chronically high blood glucose levels, is a fundamental characteristic of T2D [16]. Another characteristic of T2D is weight gain arising from physiological and hormonal consequences of chronically high blood glucose, such as insulin insensitivity [17, 18]. There is growing recognition that blood glucose can impact health at pre-clinical levels, not just in T2D [19-22]. The possibility that blood glucose itself is associated with body weight and weight gain, particularly at pre-clinical levels, has implications for how public health and prevention strategies target blood glucose management.

The interplay between blood glucose across the full range, physical activity at levels present in a general population, and the full range of body weights is unclear. This is in part because the literature tends to focus on clinical groups, such as the obese, and interventions, where participants behaviour is manipulated (e.g. they engage in unusually high levels of physical activity). Understanding these factors in a general population is particularly important in middle-age (40-60 years) where incidence of both T2D and obesity peaks [23-25], and amount of physical activity declines [10, 26]. This study will explore the association between BMI, fasting blood glucose and physical activity in a large population sample of community-living middle-aged and elderly adults followed longitudinally over twelve years.

## Materials and Methods

### Study population

The PATH Through Life project is a longitudinal study of ageing in the Canberra and Queanbeyan region beginning in 2001, collecting data at four year intervals across four waves of data collection (follow-up in 2013, to date) [27]. This study sampled participants from the two older cohorts (aged 40-44 and 60-64 at baseline) who provided blood glucose measures (see supplementary materials for details on sample section), resulting in a final sample of 716 (40s $n$ = 349, 60s $n$ = 367). All participants provided written informed consent. This study was approved by the Australian National University Human Research Ethics Committee.

### Measures

Blood glucose was available on three occasions: waves 2, 3, and 4 for the 40s cohort, and waves 1, 2, and 4 for the 60s cohort. BMI, physical activity, blood glucose and all other measures (except total caloric intake) were available for all four waves of data collection. Blood glucose was measured from venous blood collected after a skipped breakfast, using an LX20 analyser by an oxygen rate method (Beckman-Coulter, Fullerton, CA, USA). Two outlier values (> 16 mmol/L) were removed.

Body weight, height, and weekly average number of hours and minutes engaged in mild (e.g. walking, weeding), moderate (e.g. dancing, cycling) and vigorous (e.g. running, squash) physical activity were provided by self-report. BMI was computed with the formula weight (kg)/height x height ($m^2$) based on self-reported weight and height. Because a BMI of 0 is impossible, BMI was centred on the boundary between underweight and normal weight (18.5). Metabolic Equivalents (METs) is a measure that encapsulates the vigorousness and duration of physical activity into a single measure relative to a resting metabolic rate, expressed here as total METs expended during physical activity per week (henceforth METs) [28, 29]. METs were calculated from self-report of hours per week spent engaging in physical activity with the formula (hours mild intensity physical activity×3)+(hours moderate intensity physical activity×6)+(hours vigorous intensity physical activity×9) [28, 29], a ratio reflecting Jette et al., exploration of METs at varying degrees of physical activity [30]. To account for zero-bounding and extreme positive skew, METs were split into quartiles [0, 16.5], (16.5, 33], (33, 57] and (57, 345]. Covariates including demographic and dietary information were measured primarily via self-report (see supplementary materials).

Gender, age, years of education, smoking status and depression [31], were assessed by self-report. Age effects were separated into cohort (age group) and time (age – age at baseline) effects. The log of depression was taken to correct for skewness. Participants were considered hypertensive based on medication use, or two seated blood pressure measures exceeding 140/90 mmHg [32]. Total caloric intake at baseline was measured using the CSIRO Food Frequency Questionnaire [33], and converted to z scores. As in Walsh et al. [34], individuals were categorised into three diabetic groups depending on two or more blood glucose measures and self-report; type 2 diabetes (T2D; > 7 mmol/L, or self-reported diabetes diagnosis), impaired fasting glucose (IFG; also known as prediabetes [35], 5.6-6.9 mmol/L and not T2D) and normal fasting glucose (NFG; < 5.6 and not IFG or T2D).

### Statistical analysis

A series of multi-level models examined cross-sectional associations between BMI, METs and blood glucose levels across the full glycaemic range, and whether longitudinal within-subject changes in either METs or blood glucose levels were associated with changes in BMI over time. Analyses were carried out in R v 3.2.0, using the lme4 package [36]. Fixed effect significance was ascertained via 95% confidence intervals, and random effect significance via $\chi^2$ model comparison tests for random effects. Pseudo-$R^2$ was calculated using the MuMIn R package [37]. All models adjusted for cohort (40s or 60s), time (time in study, years from baseline), gender, education, depression, smoking, hypertension, energy intake, and diabetes status. Alpha was set at 0.05.

## Results

Participant characteristics can be seen in table 1. The association between blood glucose, METs and BMI are summarised in figure 1. The distributions of glucose, BMI and METs were similar across cohorts (supplementary figure 1). Interaction terms were used to clarify whether cohorts should be analysed separately or in the same model (supplementary table 1). The lack of significant interaction terms between cohort and glucose, or cohort and METs in predicting BMI indicated that analysis could proceed with combined cohorts to maximise power.

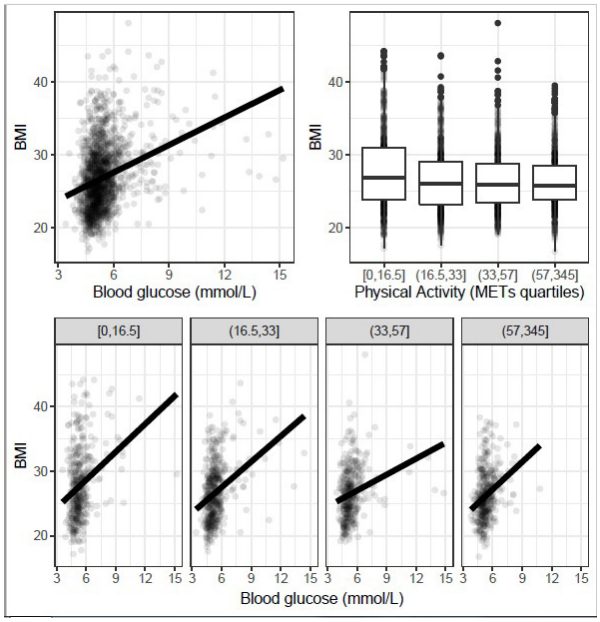


**Figure 1:** The association between blood glucose, METs and BMI.

**Caption.** Faint points individual measurements for individual participants, pooled over time. Thick black lines are illustrative indications of unadjusted bivariate associations between BMI and blood glucose. The upper left panel depicts the positive association between BMI and blood glucose. The upper right panel shows that BMI is largely similar across METs quartiles, but more kurtosed and slightly higher for the most sedentary group. The bottom panel shows the association between BMI and blood glucose across METs quartiles. This figure depicts data with outliers included, as was the case in the main analyses. However, note that associations remained consistent when more extreme values of blood glucose were removed by exclusion of individuals with T2D (supplementary figure 3).

**Table 1:** Participant demographic information at baseline.

| | **Baseline** |
|---|---|
| Age | M=55.38 (SD=8.04) |
| Gender (female) | N=358 (50%) |
| Blood glucose (mmol/L) | M=5.38 (SD=0.95) |
| IFG | N=121 (16.90%) |
| T2D | N=83 (11.59%) |
| METs | M=38.69 (SD=34.49) |
| (16.5,33] | N=188 (26.26%) |
| (33,57] | N=156 (21.79%) |
| (57,345] | N=144 (20.11%) |
| BMI | M=26.73 (SD=4.44) |
| Overweight | N=285 (42.22%) |
| Obese | N=127 (18.81%) |

*Note:* NFG = Normal fasting glucose, IFG = Impaired Fasting Glucose, T2D = type 2 diabetes mellitus. Continuous METs, sedentary and adequate exercise, and number of overweight/obesity is presented for context, and is not present in statistical analysis. Note that METs quartiles were calculated across all time points and all participants (to reflect possible change in physical exercise, this allowed participants to change quartiles over time), so quartile membership will not sum perfectly to 25% per category at any given time point. Participant characteristic by cohort can be seen in supplementary table 1.

## Fixed effects

Mixed effects models are presented in table 2. Blood glucose was significantly positively associated with BMI (model 1). Each 1mmol/L in blood glucose was significantly associated with an additional 0.33 units BMI (model 1). There was no significant interaction between glucose and METs in predicting BMI (model 2). While BMI increased by an average of 0.19 over the course of the study, those undertaking some (METs 16.5-33) or a lot (METs > 57) of exercise experienced significantly less weight gain per year (~0.1 BMI units less per year) when compared with the most sedentary individuals (METS < 16.5) (model 3). There was no significant three-way interactions between glucose, METs and time (model 4).

## Random effects

The intra-class correlation coefficient for BMI was 0.87 (bootstrapped 95% CI [.86, .88]), indicating high between-subject variability. This justifies mixed effect models with a random intercept for individuals. This random intercept reflected the wide range of BMI in analyses (≈18 units of BMI across all models). Model fit was significantly improved with addition of a random slope for glucose ($\chi^2 = 23.18$, $p < 0.01$). This allowed the association between blood glucose and BMI to randomly vary within individuals, to the magnitude of ≈0.5 units BMI. Pseudo $R^2$ indicated each model explained around 88% of variability in BMI, with much of this explanatory power lying in random effects (marginal $R^2 \approx 0.17$, conditional $R^2 \approx 0.88$; table 2).

## Sensitivity analysis

The significant association between glucose and BMI held even when individuals with T2D were excluded from analysis ($b = 0.59$, 95% CI [0.23, 0.79]). This step removed possible blood glucose outliers (as extremal values of blood glucose were limited to T2D diagnoses; see supplementary figures 2 and 3), indicating the primary association was not driven by outliers. Models were re-run with a random intercept only (supplementary table 2). While the magnitude and significance of fixed effects for glucose remained largely unaffected, some fixed effects for METs reached significance, notably a significant interaction between METs and glucose indicating that, compared with the most sedentary group, individual in the (16.5,33] METs group experienced significantly less weight gain associated with glucose (glucose $b = 0.53$, 95% CI (0.11, 0.47); interaction $b = -0.41$ 95% CI (-0.72, -0.10), therefore each unit of glucose was only associated with an increase in BMI of 0.12, rather than 0.53, in this group). A random effect for METs (as a continuous variable due to model convergence problems with quartiles) was not significant ($\chi^2 = 2.7$, $p = 0.09$), indicating the impact of METs on BMI did not significantly vary within individuals over time. Self-report and pharmaceutical benefits scheme data search for medication corresponding to ATC code A10A (Insulin's and analogues) indicated no participants in the current sample were on insulin therapy, thus associations between BMI and T2D were not due to weight gain from insulin treatment of diabetes.

## Discussion

This study explored the longitudinal association between physical activity and blood glucose and body weight in a sample

**Table 2:** Mixed effect model coefficients.

| | Model 1 | Model 2 | Model 3 | Model 4 |
|---|---|---|---|---|
| **Fixed effects** | | | | |
| Time | 0.02 | 0.02 | 0.19* | 0.24 |
| | [-<0.01, 0.05] | [-<0.01, 0.05] | [0.03, 0.35] | [-0.10, 0.59] |
| Glucose | 0.33* | 0.42* | 0.48* | 0.61* |
| | [0.09, 0.56] | [0.06, 0.77] | [0.16, 0.79] | [0.08, 1.13] |
| METs (16.5,33] | 0.08 | 1.18 | 0.66* | 2.27 |
| | [-0.26, 0.43] | [-0.72, 3.07] | [0.10, 1.23] | [-1.29, 5.83] |
| METs (33,57] | -0.07 | 0.5 | 0.2 | 0.49 |
| | [-0.46, 0.31] | [-1.77, 2.77] | [-0.41, 0.81] | [-3.65, 4.63] |
| METs (57,345] | -0.38 | -0.62 | 0.33 | 0.74 |
| | [-0.80, 0.04] | [-3.52, 2.27] | [-0.31, 0.97] | [-4.02, 5.49] |
| Glucose x METs (16.5,33] | | -0.2 | | -0.3 |
| | | [-0.55, 0.14] | | [-0.96, 0.36] |
| Glucose x METs (33,57] | | -0.11 | | -0.05 |
| | | [-0.53, 0.31] | | [-0.81, 0.71] |
| Glucose x METs (57,345] | | 0.05 | | -0.07 |
| | | [-0.50, 0.59] | | [-0.96, 0.82] |
| Time x Glucose | | | -0.02 | -0.03 |
| | | | [-0.05, 0.01] | [-0.09, 0.03] |
| Time x METS_ med (16.5,33] | | | -0.09* | -0.18 |
| | | | [-0.16, -0.02] | [-0.63, 0.28] |
| Time x METS_ med (33,57] | | | -0.04 | -0.03 |
| | | | [-0.11, 0.04] | [-0.55, 0.49] |
| Time x METS_ med (57,345] | | | -0.10* | -0.25 |
| | | | [-0.17, -0.03] | [-0.81, 0.32] |
| Time x Glucose x METs (16.5,33] | | | | 0.02 |
| | | | | [-0.07, 0.10] |
| Time x Glucose x METs (33,57] | | | | -0.002 |
| | | | | [-0.10, 0.09] |
| Time x Glucose x METs (57,345] | | | | 0.03 |
| | | | | [-0.08, 0.13] |
| Constant | 8.67* | 8.20* | 7.41* | 6.73* |
| | [6.20, 11.14] | [5.38, 11.03] | [4.69, 10.14] | [3.22, 10.24] |
| Random effects (Variance) | | | | |
| Intercept (individual) | 16.93 | 18.00 | 17.53 | 18.51 |
| Slope (glucose) | 0.50 | 0.52 | 0.51 | 0.54 |
| Correlation | -0.60 | -0.61 | -0.62 | -0.64 |
| Residual | 2.07 | 2.06 | 2.04 | 2.05 |
| Variance explained | | | | |
| Marginal $R^2$ | 0.17 | 0.17 | 0.17 | 0.17 |
| Conditional $R^2$ | 0.89 | 0.88 | 0.89 | 0.89 |
| Model fit | | | | |
| Log Likelihood | -2,652.61 | -2,653.81 | -2,657.66 | -2,665.07 |
| Akaike Inf. Crit. | 5,343.21 | 5,351.61 | 5,361.32 | 5,388.14 |

*Note:* * indicates significance at $\alpha < 0.05$. Numbers in brackets denote 95% confidence intervals. All models control for gender, years of education, depression, and smoking measured at each wave, hypertension and diabetes status throughout the study, and total caloric intake at baseline. Coefficients without a random slope for glucose can be seen in supplementary table 2.

of middle-aged and elderly adults, spanning the full range of blood glucose, physical activity, and body weight found in a non-clinical population over twelve years of measurement. Our key finding was that higher blood glucose was associated with higher BMI. This remained significant even when individuals with T2D were excluded from analysis. Physical exercise was associated with significantly less weight gain, with those who engaged in physical activity that expended 57 or more METs per week experiencing approximately 1.08 fewer units of BMI gain over the course of the study. This is builds on meta-analyses finding that physical exercise is inversely associated with T2D incidence risk, and that this effect is partially mediated by adiposity [38], by demonstrating this pattern extends to effects in blood glucose before the T2D range.

Higher blood glucose was significantly associated with higher body weight; every 1 mmol/L of glucose was associated with 0.33 units higher BMI (0.59 if individuals with T2D were excluded from analysis). This further emphasises that high blood glucose in the sub-clinical range can be associated with adverse health outcomes [19-21]. Importantly, this association varied substantially across individuals. Not only did the intercept for BMI vary by up to 18 units across individuals, but the magnitude of the association between glucose and BMI varied by half a unit of BMI. This impacted the group-level association between blood glucose and physical activity; the most physically active participants appeared to experience 0.12 (rather than 0.53 in the least physically active) units increase in BMI associated with each 1 mmol/L higher blood glucose, though this effect lost significance once blood glucose was allowed to randomly vary within individuals. While broadly aligned with the wider literature on the benefits of physical activity for managing blood glucose levels [13-15], this indicates that individual-rather than group-level processes underlie the longitudinal association between blood glucose and body weight. Further research should pursue the possibility of a random slope interaction between blood glucose and physical activity, possibly using purposive sampling to maximise variability in both physical activity and blood glucose levels to improve the likelihood of model convergence.

The second and fourth METs quartiles (16.5-33 and 57>) were associated with significantly less weight gain over time, though the third quartile (33-57) was not, a perplexing pattern similar to findings elsewhere of a positive association between visceral adipose tissue and moderate (but not light or vigorous) physical activity [26]. This may be due to different pathways between comparatively light and vigorous physical exercise. More METs can be achieved in less time by increased intensity of physical activity, hence mild physical activity can be particularly protective by displacing time spent being sedentary [11, 12, 39]. Alternatively, some types of physical activity which are inherently vigorous, such as running, are particularly associated with effective weight loss [39].

This study has some limitations and some significant strengths. The major strength was the longitudinal sampling of narrow middle and older age bands, and inclusion of non-clinical body weight and blood glucose levels. The primary limitation was the use of self-report. Although reported

overweight and obesity was close to national averages [40], over three quarters of the current sample met or surpassed WHO guidelines for physical activity, far more than would be expected from national physical activity estimates [2, 9]. This could reflect a genuinely active sample, as recent surveys indicate Canberra is the most physically active city in Australia [41], or more likely be due to well-documented over-reporting bias of physical activity [10]. Regardless, this may have contributed to the lack of a cross-sectional significant association between physical activity and body weight, widely reported elsewhere [10-12]. However, the use of quartiles preserves the relative amount of exercise undertaken within the sample, and was sufficiently sensitive to reveal a longitudinal protective effect.

## Conclusion

This study was the first exploration of how physical activity and blood glucose are simultaneously longitudinally associated with body weight in a non-clinical sample of middle-aged and elderly adults. We conclude that the effects of physical activity are seen most clearly in terms of weight change over time that blood glucose is associated with body weight even before diabetes sets in, and that longitudinal within-subject variation in blood glucose over time is particularly important. This has implications for public health and prevention strategies targeting obesity, as it indicates that relationships between blood glucose, physical activity and body weight characterised in T2D diagnosis can be found in sub-clinical populations.

## Disclosures/Competing Interests

The authors declare that they have no conflict of interest.

## Acknowledgements

The authors are grateful to Anthony Jorm, Helen Christensen, Peter Butterworth, Chantal Réglade-Meslin, Simon Easteal, Andrew McKinnon, Kristine Koh, Patricia Jacomb, Karen Maxwell, and the PATH project interviewers.

This work was supported by NHMRC [grant numbers 973302, 179805, 157125, 1002160, 1063907] and ARC [grant number 130101705]. Nicolas Cherbuin and Kaarin Anstey's Research Fellowship are funded by ARC [grant number 120100227] and NHMRC [grant number 1002560].

All authors were involved in conception and planning of the work that led to the manuscript and/or analysis and interpretation of the data; all contributed to the drafting and critical revision of the manuscript; and all approve this final submitted version of the manuscript.

Approval for the study was obtained from the human research ethics committees of the Australian National University (protocol number: wave 1 M9807; wave 2 2002 / 189; wave 3 2006/314; wave 4 2010/542) and the University of New South Wales (protocol number HREC 00149). All participants provided written, informed consent.

## References

1. Buchmueller TC, Johar M. 2015. Obesity and health expenditures: evidence from Australia. *Econ Hum Biol* 17: 42-58. https://doi.org/10.1016/j.ehb.2015.01.001
2. World Health Organisation. 2018. Obesity and Overweight.
3. Seidell JC. 2000. Obesity, insulin resistance and diabetes—a worldwide epidemic. *Br J Nutr* 83(S1): S5-S8. https://doi.org/10.1017/S000711450000088X
4. World Health Organization. 2000. Obesity: preventing and managing the global epidemic.
5. Australian Bureau of Statistics. 2011. 4820.0.55.001 - Diabetes in Australia: a snapshot, 2007-08.
6. Cichosz SL, Lundby-Christensen L, Johansen MD, Tarnow L, Almdal TP, et al. 2017. Prediction of excessive weight gain in insulin treated patients with type 2 diabetes. *J Diabetes* 9(4): 325-331. https://doi.org/10.1111/1753-0407.12418
7. Jacob AN, Salinas K, Adams-Huet B, Raskin P. 2007. Weight gain in type 2 diabetes mellitus. *Diabetes Obes Metab* 9(3): 386-393. https://doi.org/10.1111/j.1463-1326.2006.00622.x
8. World Health Organization. 2010. Global recommendations on physical activity for health.
9. Australian Bureau of Statistics. 2013. 4364.0.55.004 - Australian health survey: physical activity, 2011-12.
10. Tucker JM, Welk GJ, Beyler NK. 2011. Physical activity in US adults: compliance with the physical activity guidelines for Americans. *Am J Prev Med* 40(4): 454-461. https://doi.org/10.1016/j.amepre.2010.12.016
11. Rao DP, Orpana H, Krewski D. 2016. Physical activity and non-movement behaviours: their independent and combined associations with metabolic syndrome. *International Journal of Behavioral Nutrition and Physical Activity* 13: 26. https://doi.org/10.1186/s12966-016-0350-5
12. Healy GN, Wijndaele K, Dunstan DW, Shaw JE, Salmon J, et al. 2008. Objectively measured sedentary time, physical activity, and metabolic risk. *Diabetes Care* 31(2): 369-371. https://doi.org/10.2337/dc07-1795
13. Ivy JL. 1997. Role of exercise training in the prevention and treatment of insulin resistance and non-insulin-dependent diabetes mellitus. *Sports Med* 24(5): 321-336.
14. Fogelholm M, Kukkonen-Harjula K. 2000. Does physical activity prevent weight gain–a systematic review. *Obesity Reviews* 1(2): 95-111. https://doi.org/10.1046/j.1467-789x.2000.00016.x
15. Mainous AG, Tanner RJ, Anton SD, Jo A, Luetke MC. 2017. Physical activity and abnormal blood glucose among healthy weight adults. *Am J Prev Med* 53(1): 42-47. https://doi.org/10.1016/j.amepre.2016.11.027
16. Astrup A, Finer N. 2000. Redefining type 2 diabetes: 'diabesity' or 'obesity dependent diabetes mellitus'? *Obes Rev* 1(2): 57-59. https://doi.org/10.1046/j.1467-789x.2000.00013.x
17. Brown A, Guess N, Dornhorst A, Taheri S, Frost G. 2017. Insulin-associated weight gain in obese type 2 diabetes mellitus patients–what can be done? *Diabetes Obes Metab* 19(12): 1655-1668. https://doi.org/10.1111/dom.13009
18. Chen W, Balland E, Cowley MA. 2017. Hypothalamic insulin resistance in obesity: effects on glucose homeostasis. *Neuroendocrinology* 104(4): 364-381. https://doi.org/10.1159/000455865
19. Nilsen T, Vatten LJ. 2001. Prospective study of colorectal cancer risk and physical activity, diabetes, blood glucose and BMI: exploring the hyperinsulinaemia hypothesis. *Br J Cancer* 84(3): 417-422. https://doi.org/10.1054/bjoc.2000.1582
20. Collaboration ERF, Sarwar N, Gao P, Seshasai SR, Gobin R, et al. 2010. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. *Lancet* 375(9733): 2215-2222. https://doi.org/10.1016/S0140-6736(10)60484-9

21. Mortby ME, Janke AL, Anstey KJ, Sachdev PS, Cherbuin N. 2013. High "normal" blood glucose is associated with decreased brain volume and cognitive performance in the 60s: the PATH through life study. *PLoS One* 8(9): e73697. https://doi.org/10.1371/journal.pone.0073697
22. Walsh EI, Shaw M, Sachdev P, Anstey KJ, Cherbuin N. 2018. Brain atrophy in ageing: estimating effects of blood glucose levels vs. other type 2 diabetes effects. *Diabetes Metab* 44(1): 80-83. https://doi.org/10.1016/j.diabet.2017.06.004
23. Hughes VA, Frontera WR, Roubenoff R, Evans WJ, Singh MA. 2002. Longitudinal changes in body composition in older men and women: role of body weight change and physical activity. *Am J Clin Nutr* 76(2): 473-481. https://doi.org/10.1093/ajcn/76.2.473
24. Newman AB, Lee JS, Visser M, Goodpaster BH, Kritchevsky SB, et al. 2005. Weight change and the conservation of lean mass in old age: the health, aging and body composition study. *Am J Clin Nutr* 82(4): 872-878. https://doi.org/10.1093/ajcn/82.4.872
25. Centers for Disease Control and Prevention. 2013. Distribution of age at diagnosis of diabetes among adult incident cases aged 18–79 years, United States, 2011.
26. Keating SE, Parker HM, Pavey TG, Baker MK, Caterson ID, et al. 2016. Objectively quantified physical activity and sedentary behavior in predicting visceral adiposity and liver fat. *Journal of Obesity*: 2719014. http://dx.doi.org/10.1155/2016/2719014
27. Anstey KJ, Christensen H, Butterworth P, Easteal S, Mackinnon A, et al. 2012. Cohort profile: the PATH through life project. *Int J Epidemiol* 41(4): 951-960. https://doi.org/10.1093/ije/dyr025
28. Jette M, Sidney K, Blümchen G. 1990. Metabolic equivalents (METS) in exercise testing, exercise prescription, and evaluation of functional capacity. *Clin Cardiol* 13(8): 555-565. https://doi.org/10.1002/clc.4960130809
29. Pate RR, Pratt M, Blair SN, Haskell WL, Macera CA, et al. 1995. Physical activity and public health: a recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. *JAMA* 273(5): 402-407. https://doi.org/10.1001/jama.1995.03520290054029
30. Jette M, Sidney K, Blumchen G. 1990. Metabolic equivalents (METS) in exercise testing, exercise prescription, and evaluation of functional capacity. *Clin Cardiol* 13(8): 555-565. https://doi.org/10.1002/clc.4960130809
31. Goldberg D, Bridges K, Duncan-Jones P, Grayson D. 1988. Detecting anxiety and depression in general medical settings. *BMJ* 297(6653): 897-899.
32. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA* 311(5): 507-520. https://doi.org/10.1001/jama.2013.284427
33. Lassale C, Guilbert C, Keogh J, Syrette J, Lange K, et al. 2009. Estimating food intakes in Australia: validation of the Commonwealth Scientific and Industrial Research Organisation (CSIRO) food frequency questionnaire against weighed dietary intakes. *J Hum Nutr Diet* 22(6): 559-566. https://doi.org/10.1111/j.1365-277X.2009.00990.x
34. Walsh EI, Jacka FN, Butterworth P, Anstey KJ, Cherbuin N. 2017. The association between Western and Prudent dietary patterns and fasting blood glucose levels in type 2 diabetes and normal glucose metabolism in older Australian adults. *Heliyon* 3(6): e00315. https://doi.org/10.1016/j.heliyon.2017.e00315
35. Jeong SM, Yoo B, Kim YJ, Oh B, Kang HC. 2017. Associations between trends in aging, physical activity, central obesity and body mass index with diabetes prevalence in Korea: a series of cross-sectional studies from the 1st to 5th Korean National Health and Nutrition Examination Survey (1998-2012). *Korean J Fam Pract* 7(2): 195-201. https://doi.org/10.21215/kjfp.2017.7.2.195
36. Bates D, Mächler M, Bolker B, Walker S. 2015. Fitting linear mixed-effects models using lme4. *Journal of Statistical Software* 67(1): 1-47. https://doi.org/10.18637/jss.v067.i01
37. Bartoń K. 2018. MuMIn: Multi-model inference. R package version. 1.9. 13. 2013.
38. Aune D, Norat T, Leitzmann M, Tonstad S, Vatten LJ. 2015. Physical activity and the risk of type 2 diabetes: a systematic review and dose–response meta-analysis. *Eur J Epidemiol* 30(7): 529-542. https://doi.org/10.1007/s10654-015-0056-z
39. Wewege M, Berg R, Ward RE, Keech A. 2017. The effects of high-intensity interval training vs. moderate-intensity continuous training on body composition in overweight and obese adults: a systematic review and meta-analysis. *Obes Rev* 18(6): 635-646. https://doi.org/10.1111/obr.12532
40. Australian Bureau of Statistics. 2008. 4719.0 - Overweight and obesity in adults, Australia, 2004-05.
41. Australian Sports Commission. 2016. AusPlay Summary of Key National Findings October 2015 to September 2016 data.