TRAJECTORIES OF WEIGHT CHANGE, BMI, AND THEIR IMPACT ON GLUCOSE AND INSULIN METABOLISM

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INTRODUCTION

High body weight and weight gain are associated with elevated blood glucose levels and insulin resistance, and increases the risk of developing type 2 diabetes[1-5].

Weight loss can help control blood glucose levels and insulin sensitivity, even in individuals without diabetes [6, 7].

Body weight measured at any given point in time (momentary body weight) and preceding weight change can have simultaneous, independent effects on cardiovascular risk outcomes[8], hypertension[9], and insulin and glucose metabolism[10-12].

This study investigated the extent to which momentary body weight and preceding weight change is associated with blood glucose and insulin metabolism in ageing.

METHOD

Participants were 667 community-living adults from the Australian cities of Canberra and Queanbeyan, drawn from the Personality and Total Health (PATH) Through Life study[13]. It includes four waves of data collection, with measures every four years over twelve year period.

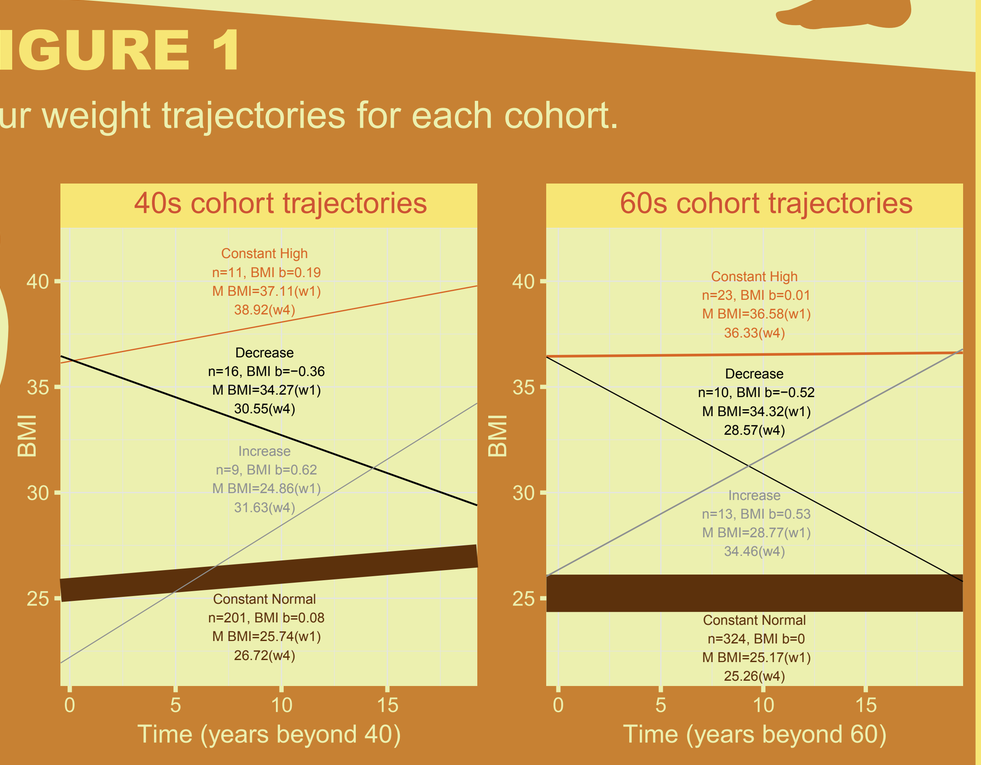
We focussed on cohorts aged 40-44 (40s ●) and 60-65 (60s ▲) at baseline. This sample included underweight, normal weight, overweight and obese individuals, and individuals with and without diabetes.

Body Mass Index (BMI,kg/m^2) was calculated from self-reported height and weight measured over the study duration. We used latent class analysis to establish weight change trajectories (figure 1).

Plasma insulin (μIU/ml), plasma glucose (mmol/L), HOMA2 insulin resistance, sensitivity, and beta cell function were assessed from venous blood samples taken at follow-up.

FIGURE 1

Four weight trajectories for each cohort.



All analyses were carried out in R version 3.2.0. A latent class model was used to estimate mutually exclusive classes of BMI change over time. Exploratory modelling and the Bootstrap Likelihood Ratio Test (BLRT) were used to establish the appropriate number of classes (2, 3, 4, or 5) and link function (linear, or beta), using the packages mclust (v 5.2) and lcmm (v1.7.5).

RESULTS

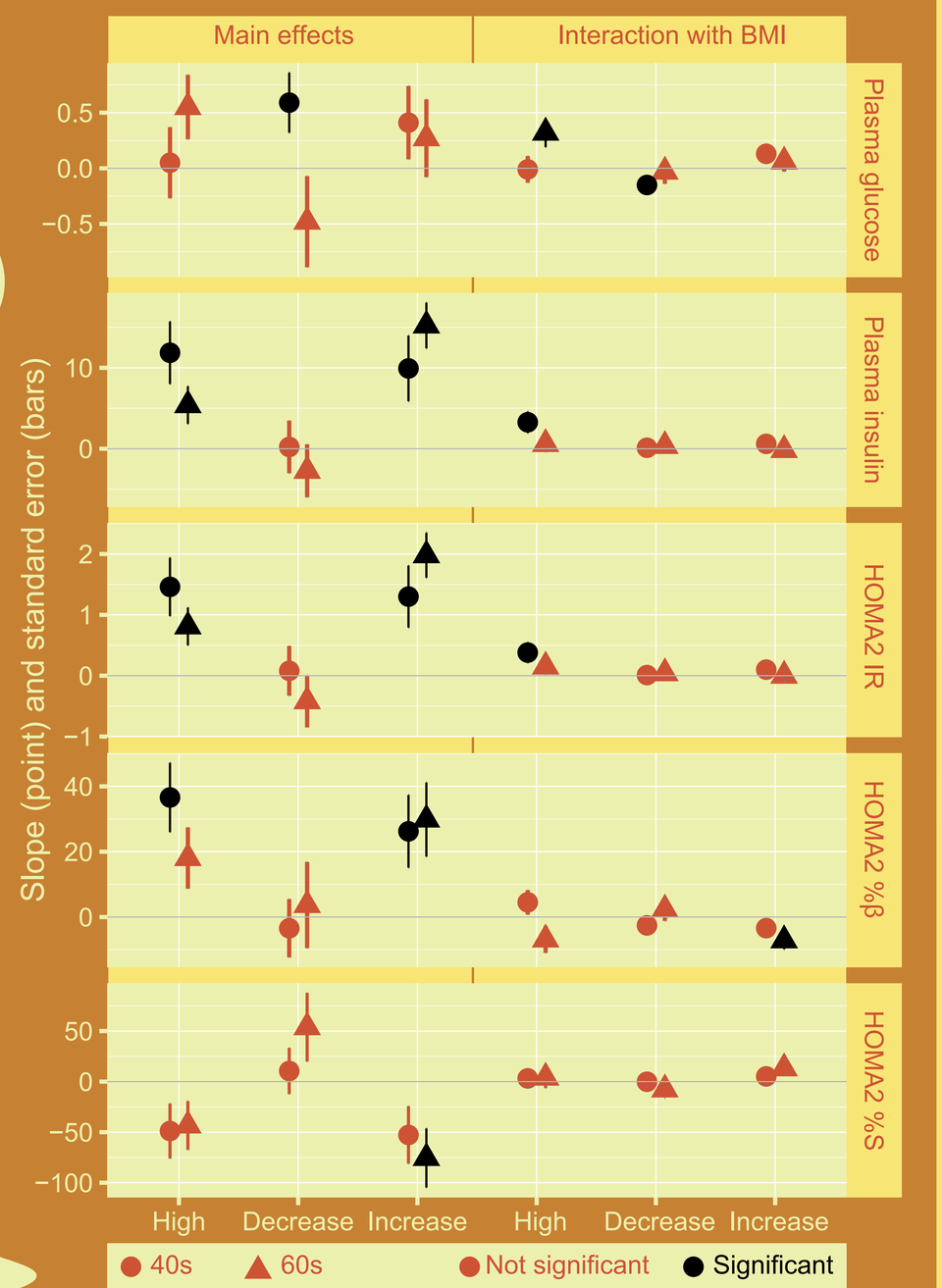
The four trajectories were increase, decrease, constant normal, and constant high. As summarised in figure 2, compared with individuals with a constant normal trajectory, individuals in the decrease trajectory did not significantly differ on any outcome.

Individuals with an increase or a constant high trajectory had significantly higher HOMA2-%β and HOMA2-IR at follow-up.

Significant interactions between trajectory and BMI at follow-up suggested that weight trajectories modulate the association between BMI and glucose metabolism at any given time point.

FIGURE 2

Multivariate generalised linear model coefficients



All models control for hypertension, type 2 diabetes, physical activity, gender, and age. Participants were considered hypertensive based on self-reported medication use, or the average of two seated blood pressure measures exceeding 140 mmHg systolic and 90 mmHg diastolic. Participants were placed in categories of type 2 diabetes (self-reported, or two or more measurement occasions where blood glucose levels >7mmol/L), IFG (not type 2 diabetes and two or more blood glucose measures >5.6mmol/L), or NFG (not type 2 diabetes or IFG, and two or more blood glucose measures <5.6). Physical activity was measured in term of Metabolic Equivalents (METs), from self-reported hours spent engaging physical using the formula (hours mild PA×3)+(hours moderate PA×6)+(hours vigorous PA×9).

Multivariate generalised linear models were applied to account relatedness between the outcome measures. Plasma glucose, plasma insulin, HOMA2-IR, HOMA2-%β and HOMA2-%S were specified as outcome variables, and follow-up BMI, BMI class, and covariates were specified as predictors. If multivariate significance (indicated by F-statistic derived from the Pillai-Bartlett Trace) was achieved, general linear models for each outcome were computed. Three models were fit: (1) the impact of BMI (at wave 4) on outcomes, (2) the impact of trajectory on plasma glucose, insulin, HOMA2-IR, HOMA2-%β and HOMA2-%S, then (3) the interaction between BMI (at wave 4) and trajectory on plasma glucose, insulin, HOMA2-IR, HOMA2-%β and HOMA2-%S. Values only shown if multivariate Pillai's trace was significant (hence empty space for interactions in 60s). Points indicate slope in fully controlled post-hoc linear model, with grey line indicating zero (so points below line indicate negative association, points above line indicate positive association). Error bars represent standard error from the same model. Significance is at $\alpha < 0.05$.

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CONCLUSIONS

High and increasing body weight was associated with higher insulin resistance and decreased insulin sensitivity.

Preceding change in weight has a simultaneous, independent effect on blood glucose metabolism.