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Not frozen in time: the past matters to the relationship between body weight and insulin

Insulin is a hormone which regulates how your food fuels your body. The food you eat is digested and converted into glucose, which then travels through your blood to reach all of the organs and tissues in your body which rely on glucose for fuel. Our bodies and brains need a constant supply of this glucose, but too much can be harmful. If blood glucose remains too high for too long, it can actually cause damage to the body and lead to the development of type 2 diabetes. One of the key reasons this doesn't happen to everyone is insulin.

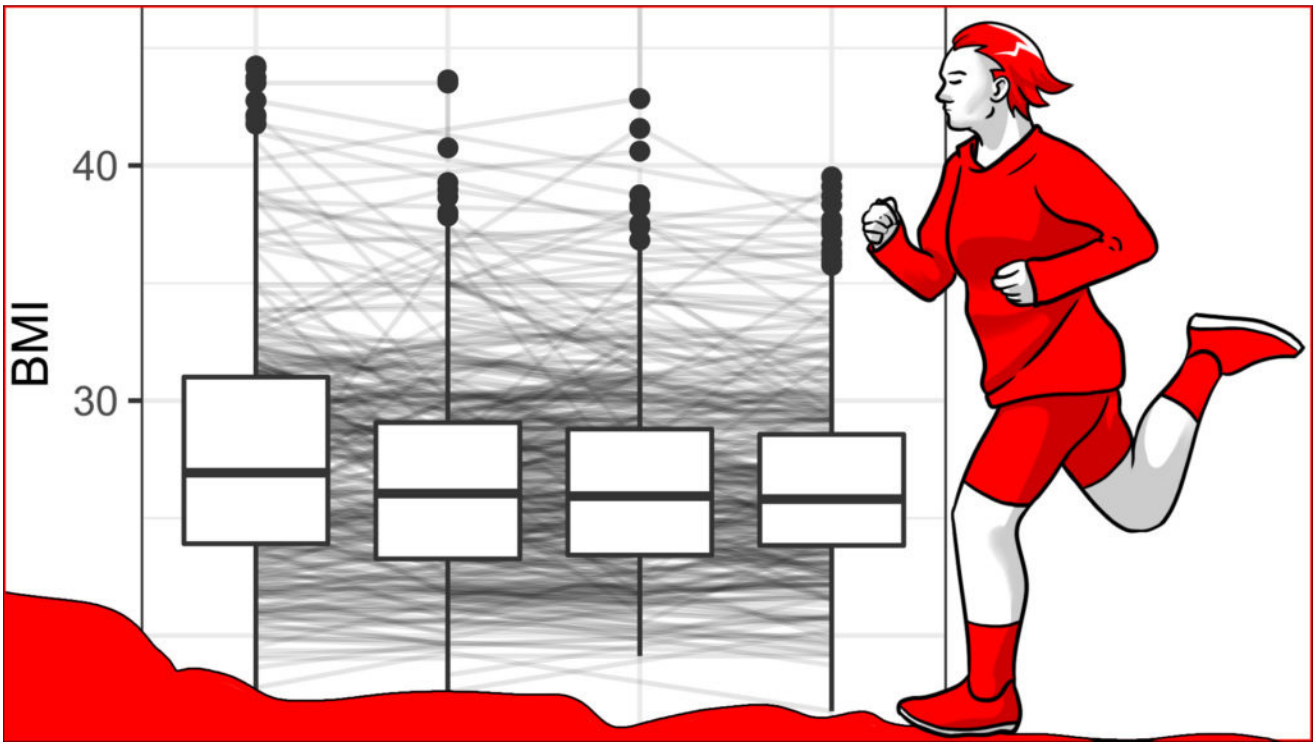

Fig. 1. Graphical abstract artistically representing the active role of insulin (running figure) in managing blood glucose (ground) in the presence of BMI and BMI change (background figure).

In a healthy metabolism, when blood glucose levels are high, insulin is secreted to allow the tissues that need fuel to take the glucose they need. When blood glucose levels are low, insulin secretion is inhibited. Even if the amount of glucose from food stays constant, the amount hanging around in the blood can reach damaging levels if insulin metabolism isn't working properly. This is why it is important to understand what might impair the production of the insulin, or reduce the sensitivity of insulin receptors.

It is widely established that body fat is associated with blood glucose levels, insulin resistance, and the risk of developing diabetes. We know this mostly from large studies comparing the insulin metabolism of people who have a normal body weight against those who are underweight, overweight, and obese. There is also

evidence from studies following the same people over several years, which show that weight loss can improve insulin metabolism, while weight gain can impair it. But, unlike other areas of health, there aren't many studies that look at how these changes in weight, and weight at a snapshot in time, might be associated with glucose metabolism.

Imagine two people: one weighs 80 kilograms and has been consistently losing weight for several years, the other weighs 60 kilograms but has been consistently gaining weight. Evidence indicates that know that the individual with the higher body weight is more of a risk for impaired insulin metabolism. But at the same time, there is evidence that weight loss is protective for insulin function. So, who is likely to have the poorest insulin metabolism?

In this study we investigated the impact of previous body weight change alongside current body weight on insulin metabolism. Participants were 512 people aged over 40, sampled from the Personality and Total Health (PATH) Through Life study, a large longitudinal study investigating ageing, health, cognition and other individual characteristics over the course of twelve years. We measured body weight as Body Mass Index, from the with the formula weight (in kilograms) over height (in meters) squared. We also measured blood glucose and insulin from blood samples, as plasma glucose, plasma insulin, and derived insulin measures of insulin production and sensitivity. Our analyses also took into account other relevant factors like blood pressure, diabetes diagnosis, and physical activity.

Our results supported the conclusion that high body weight is associated with elevated blood glucose levels and impaired insulin function. We also found that weight loss was associated with lower blood glucose levels and improved insulin function, though people in our study never became underweight, so we can only say weight loss was beneficial in people who started out overweight. Most importantly, we showed that measuring body weight at one point in time only gives us half the story when it comes to insulin metabolism: it also really matters if someone is losing or gaining weight.

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Publication

Trajectories of BMI change impact glucose and insulin metabolism.
Walsh EI, Shaw J, Cherbuin N
Nutr Metab Cardiovasc Dis. 2018 Mar