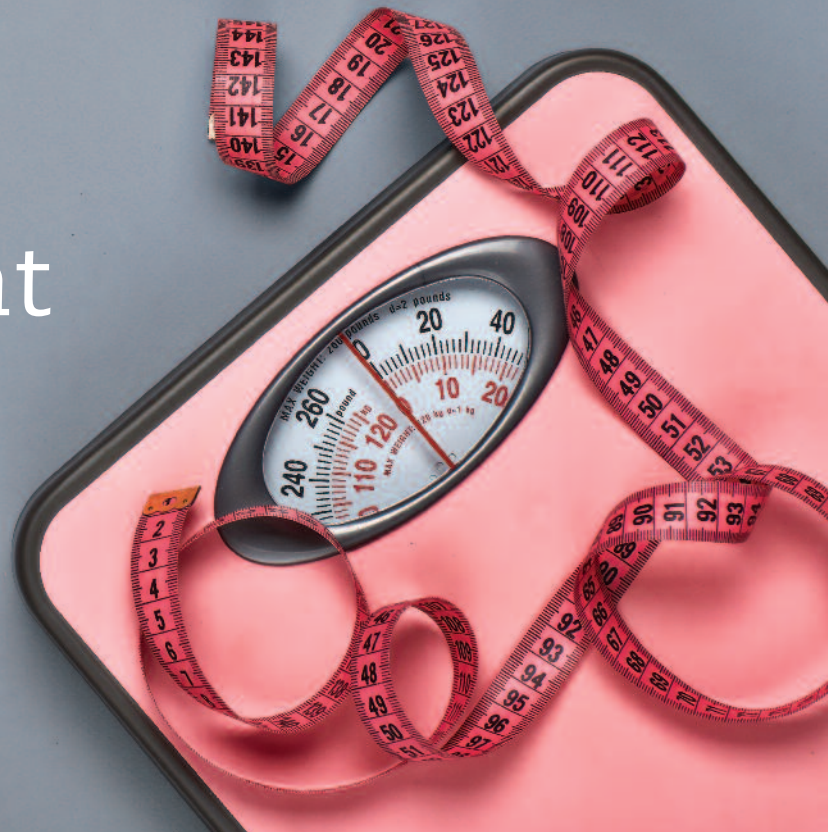


A gut feeling about body fat



TEAGASC research shows that loss of body fat causes the growth of the intestine and increases its capacity to absorb nutrients. This presents new approaches for weight management.

The intestine is a vital organ for sustaining life because it controls how much we eat and, of the nutrients ingested, how much are absorbed into the blood for delivery to target organs. Nutrient absorption is achieved by specific transporters expressed in the intestinal cells. The intestine also allows some nutrients to freely pass into the blood. Because the intestinal cells have to continuously divide to sustain these activities, there is a substantial energy usage by the tissue, which is known to be met by breaking down of some of the nutrients absorbed by the intestinal cells. While this coupling between the external nutrient supply and intestinal cellular activity is well known, and has been exploited to control the growth of the intestine by varying the diet, in this article we highlight an alternate, less well-known pathway that can also be used to control the growth of the intestine. Based on our recent work, published in the official journal of the World Obesity Federation (Nilaweera and Speakman, 2018), we propose that depletion of fat stores inside the body also causes the growth of the intestine, and that this occurs via a signalling mechanism involving the brain (**Figure 1D**).

Supporting evidence

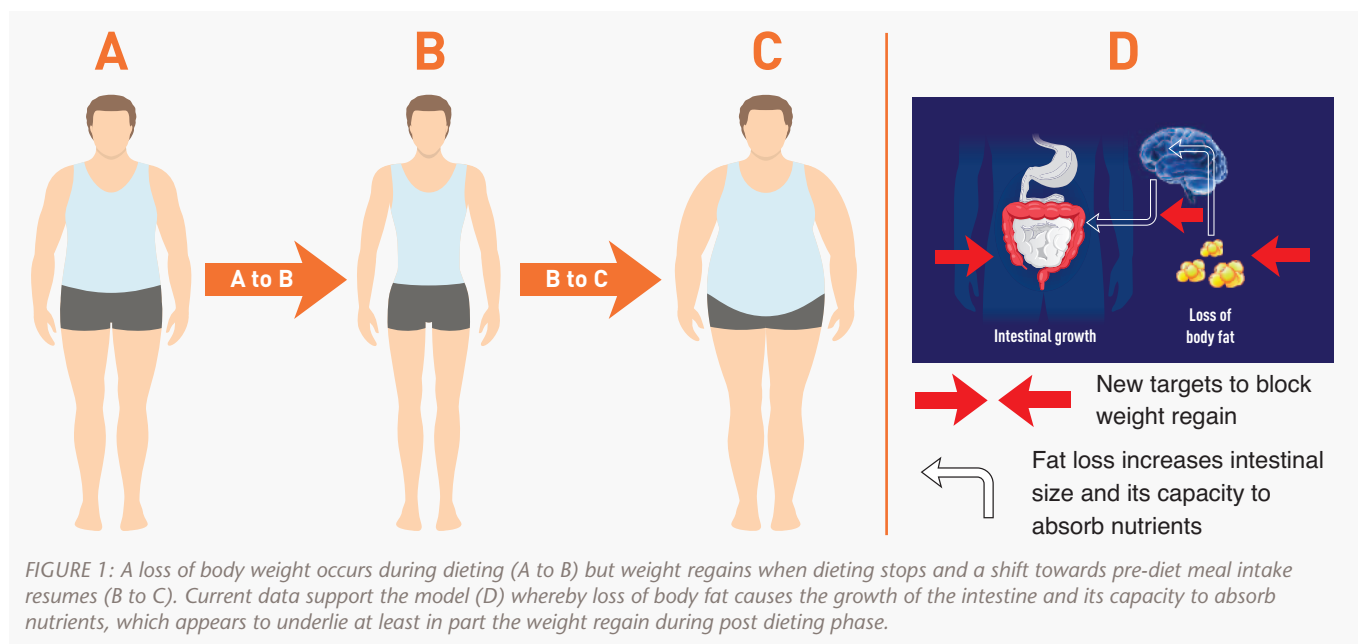
Our body weight varies constantly, sometimes daily, but more noticeably over long periods following intake of high-energy diets coupled with reduced physical activity. While this would increase body weight, a reduced calorie intake and/or increased physical activity would have an opposite response. The change in body weight arises largely due to corresponding variation in fat stores in the body. As part of our ongoing research to understand the

mechanisms controlling body weight, we wanted to know how this variation in fat stores impacts on other organs in the body. To this end, we looked at data from interventions that cause fat loss: dietary whey protein intake; calorie restriction (or dieting); cold exposure; lactation; and, bariatric surgery (where surgical changes to the gastrointestinal tract cause reduced food intake, and fat loss) (Nilaweera and Speakman, 2018). We extended this review of data to include different animals such as mammals, birds and reptiles. By going through our own data related to some of these interventions, and those of others, it became clear that there is a link between loss of body fat and the growth of the intestine, involving changes in the brain.

We proposed that animals, including humans, have evolved this internal mechanism (fat-brain-intestine pathway) to control the growth of the intestine to survive periods of food shortage, where loss of fat would signal to increase the size of the intestine. The enlarged intestine would then be able to absorb nutrients efficiently upon ingestion of a meal consumed during the period of food scarcity, and use the energy in the food to survive this challenging period and replenish the depleting fat stores.

Relevance to society, policy makers and industry

The UN has declared a “Decade of Action on Nutrition, 2016-2025” in recognition of the need to eliminate all forms of malnutrition, specifically over-nutrition and under-nutrition. Developing interventions that can control the growth of the intestine may provide a way to address these grand challenges.



Over-nutrition

The world is experiencing an obesity epidemic arising from over-consumption of high-energy, palatable foods. While dieting is a popular way to lose weight and body fat, maintaining the lost body weight is a difficult task when dieting stops and a shift to pre-diet meal intake resumes. The link between fat loss and intestinal growth proposed by us provides an understanding of why the change in the diet post weight loss enhances weight gain so quickly (Figure 1). Is there a way then to sustain lost body weight?

Our recent work shows that intake of whey protein isolate (WPI) in sufficient quantities causes the gut to shrink (McAllan *et al.*, 2015), as well as affecting the mechanisms involved in nutrient absorption in the intestine, including the gut microbiota (Nilaweera *et al.*, 2017). This work will pave the way for the creation of better weight loss/weight maintenance interventions.

Under-nutrition

Alongside the obesity epidemic, which affected 600 million adults worldwide in 2014, there were 462 million underweight individuals resulting from poor nutrition (WHO records). This could arise because of physical inability to consume food (for instance in old age), chronic illness (cachexia), or psychological reasons (anorexia).

For these affected individuals, the solution is not simply giving access to more food. Thus, by targeting key components of the fat-brain-intestine signalling pathway that are sensitive to nutrients (Nilaweera and Speakman, 2018), it would be possible to promote the growth of the intestine and increase its capacity to absorb nutrients in underweight individuals with limited desire to consume nutrients (Figure 1).

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