Model of energy balance predicts body weight and food intake in obesity/diabetes clinical trials
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Objectives: To develop a mathematical model of food intake (FI) that, along with an energy balance model, can be used to predict long-term body weight (BW) changes in response to various individual clinical pharmacotherapies trials and their combinations.

Methods: A differential equation model of energy balance and BW, which relates change in BW to the change in FI, was adapted from Chow and Hall [1]. Expanding on work in Göbel et al. [2], we incorporated a two-phase FI model, which describes the weight-loss and weight-regain stages of most anti-obesity clinical trials, into the energy balance model. The model captures the dose-dependent effects of individual drugs and their combinations on FI. We embed the combined FI/BW model in a two-level mixed effects statistical framework and fit it to BW data from published anti-obesity and diabetes clinical trials. In total, 80+ clinical trials containing 20+ various drugs were used for non-linear mixed effects model fitting and leave-p-out cross-validation.

Results: The model adequately captured BW changes across a majority of clinical trials. Identified proportionality and transition parameters allow for prediction of the magnitude of initial BW loss as well as its long-term durability. The model also identifies the changes in FI that ultimately lead to the predicted BW loss.

Conclusions: The longitudinal mixed effects model presented here provides an attractive approach to identifying a set of existing therapies that have the greatest potential for combination and to estimating their BW and FI effect sizes in the future. Additionally, the mechanistic model of FI and BW allows for prediction of long-term BW and FI dynamics based on the observed/predicted initial BW loss.

References: