SUPPLEMENTARY INFORMATION

Methods

Confounding

Confounding arises when a spurious association is seen between an exposure and an outcome due to a third variable (Supplemental Figure 1A). Confounding occurs when three conditions are met:

1. The confounder is associated with the exposure (novel predictor)
2. The confounder is associated with the outcome in the absence of exposure
3. The confounder is not on the biological (causal) pathway from the exposure to the outcome

In the example depicted in Supplemental Figure 1B, diabetes is positively associated with preoperative BMI (patients with a higher preoperative BMI are more likely to have diabetes, making the direction of this relationship positive “+”). In this example, preoperative BMI is also positively associated with number of pounds lost (patients with a higher preoperative BMI are more likely to achieve a large number of pounds lost). Because of these associations, the association between diabetes (novel predictor) and number of pounds lost (outcome) will be artificially inflated by preoperative BMI (confounder). In the extreme circumstance, if there is truly no association between diabetes and pounds lost, there will appear to be a positive association between diabetes and pounds lost solely because of the association between diabetes and preoperative BMI. Diabetes will, in essence, “pick up” the association between preoperative BMI and pounds lost.
If even one of the three properties of confounding does not hold, confounding will not occur. In the example above, this means that in order to prevent confounding by preoperative BMI, one of the following would have to be false:

1. Preoperative BMI is not associated with diabetes
2. Preoperative BMI is not associated with pounds lost
3. Diabetes causes a higher/lower preoperative BMI, which then in turn causes greater weight loss (in this case, preoperative BMI would be a mediator of the relationship between diabetes in weight loss, rather than a confounder)

Whether preoperative BMI is a mediator of the relationship between a potential novel predictor and the outcome (i.e., is on the causal pathway) is a biological question that will need to be answered for each potential predictor that is examined. Similarly, whether a relationship between the novel predictor and preoperative BMI exists will need to be tested for each potential predictor. Therefore, the easiest way to eliminate confounding by preoperative BMI for all potential predictors is to eliminate the relationship between preoperative BMI and the weight loss metric used.
Supplemental Figure 1

A. Novel Predictor → Weight Loss Metric
   pBMI

B. Diabetes → %EBWL
   pBMI
   +
   −