SUPPLEMENTARY MATERIAL

Fig. S1. Motivation items based on DiClemente and Prochaska [1].

For each of the 3 categories (weight, exercise, and diet) below, please choose the one statement that describes you best today.

1. Weight
   □ I have not thought about losing weight in the past 6 months.
   □ I have thought about losing weight, but I have not yet taken any action to lose weight. I plan to make a change in the next 6 months.
   □ I have thought about losing weight, but I have not yet taken any action to lose weight. I plan to make a change in the next 30 days.
   □ I have thought about losing weight and am currently beginning to take action to lose weight.
   □ I have made changes to lose weight and have been doing so for at least 6 months.

2. Exercise
   □ I have not exercised in the past 6 months.
   □ I have not exercised, but I intend to start an exercise regimen in the next 6 months.
   □ I have not exercised, but I intend to start an exercise regimen in the next 30 days.
   □ I have been exercising regularly for less than 6 months.
   □ I have been exercising regularly for more than 6 months.

3. Diet
   □ I have not followed my diet in the past 6 months.
   □ I have not followed my diet, but I intend to start following my diet in the next 6 months.
   □ I have not followed my diet, but I intend to start following my diet in the next 30 days.
   □ I have been following my diet for less than 6 months.
   □ I have been following my diet for more than 6 months.
Appendix 1. Development of trajectories for changes in body mass index.

Our goal was to be able to create categories that could be applied to other populations rather than simply describing the 1900 trial subjects. In order to create categories that could be generalized to other studies and clinical practice, we needed to define the categories based on their overall shape, rather than specific measurements at individual time points. This strategy would allow, for example, different durations of follow-up or schedules of data collection.

Our approach was based on an observation across the canagliflozin Phase 3 program showing that weight loss is associated with increasing satisfaction with weight, although this relationship varies across individuals. The amount of weight loss required to produce an improvement in weight satisfaction was person-specific and also depended on how weight was changing; for example, a slow and steady weight loss was more closely related to weight satisfaction improvement than a bigger initial loss followed by a partial regain.

To elucidate these patterns, we sorted individual weight trajectories into clusters based on the rate of weight change between weight measurements. We used a fuzzy clustering method [2-4] similar to k-means to produce data-driven patterns of weight from baseline through 52 weeks. Common choices for the number of clusters are five or nine; we chose nine clusters in an effort to avoid missing infrequent but distinct and important patterns of weight change. The individual patterns are shown in panel A. Interestingly, most of the clusters were not “flat,” but showed discernible patterns of weight gain and loss.

We split the data set into a model development set and a validation set, and used a regression spline model to capture the essential shape of the categories for the model development set. We then applied this technique to the validation set, assigning each observation to the closest spline pattern. We found that the spline categorization matched the initial category assigned by the clustering algorithm exactly for 89% of the subjects in the validation set. The essential shapes described by the spline model are shown in panel B.
Some of the trajectories were visually similar, so we combined patterns based on weight gain and weight loss in the first and second half of the study period. Pooling the data in this way effectively imposes the assumption that periods of weight gain and periods of weight loss will be reflected differently in patient-reported outcome measures [5].
This categorization into four groups based on gains and losses was related to baseline variables, including race and gender. But even after adjustment for these variables in a logistic regression model, improvement in weight satisfaction was similar in the groups collapsed into the four categories, but different across the categories. The odds ratios for improvement in weight satisfaction at week 52 (compared to group 4) were 2.79 for group 1 (95% confidence interval [CI] 1.81, 4.32), 1.92 for group 2 (95% CI 1.26, 2.92), and 1.65 for group 3 (95% CI 0.99, 2.74). Results were similar for other patient-reported outcome components, such as satisfaction with level of energy.

We wanted to apply these trajectories to a trial that was independent of the model development to examine whether these were generalizable. The trial comparing canagliflozin versus glimepiride [6,7] was selected because it was a good opportunity to apply these patterns in the context of the current research objectives. We initially used the regression spline model to assign trajectories, which produced the following results:

| Weight trajectory (spline model assignment) | Pattern 1 (N = 376) | Pattern 2 (N = 501) | Pattern 3 (N = 163) | Pattern 4 (N = 147) | P value |
|-------------------------------------------|---------------------|---------------------|---------------------|---------------------|---------|
| Starting or continuing to take Action at week 36* | 1.98 (1.26, 3.12) | 1.52 (0.99, 2.33) | 1.27 (0.76, 2.12) | 1 (ref) | 0.020* |
| - To lose weight                          | 2.25 (1.37, 3.70) | 1.47 (0.93, 2.33) | 1.34 (0.76, 2.34) | 1 (ref) | 0.008* |
| - To follow diet                          | 2.10 (1.31, 3.37) | 1.50 (0.96, 2.35) | 1.41 (0.82, 2.45) | 1 (ref) | 0.015* |

*MID improvement in IWQoL-Lite total score* 1.71 (1.13, 2.58) | 1.20 (0.80, 1.78) | 0.99 (0.60, 1.64) | 1 (ref) | 0.015* |

*Denotes statistically significant.

We were concerned that these elaborate methods might detract from the focus of this paper so an alternative specification was tested. We assigned the groups based on weight gain or loss in the first 18 weeks and in the second 18 weeks, which produced the (remarkably similar) results in this manuscript. An advantage of the more heuristic model is that the pattern definitions in our manuscript can be replicated in other studies without the need to calculate fitted values for each subject.
References

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