Figure S1. Notes to Figure 1

(a) The dichotomous predictors in each panel represent the presence/absence of the condition. The first-order terms in the upper left portion of each panel are global predictors of effects involving Diabetes or Heart Failure, while the interaction term reveals the additional effect when both conditions co-occur. If we drop the three predictors that tap the diagnosis subgroup, estimates will be across the entire panel sample rather than within the targeted subgroup (see subsection 4.2. "The Derived Protocol").

(b) The MIMIC model in each panel reflects endorsement of the items Depressed (CES-D ≥ 11) and Talked Less (CES-D ≥ 11) that can be attributed to co-occurring Diabetes and Heart Failure (Path 2), after adjusting for endorsement that can be attributed instead to the overall level of the latent trait of Depression in these conditions (Paths 1 and 3).

I considered an optional set of pathways to test for suppressor effects by predicting the formative (causal) indicator of each of the four non-traditional items by the predictors comprising the exogenous diagnosis subgroup (see Discussion subsection "The derived protocol"). The formative indicators now become a set of mediators, which causes them to switch from being exogenous to endogenous during model estimation. However, this set of pathways is not an option in panel (b) since it would require estimation of all possible regression effects, which does not result in an estimable MIMIC model. This option is valid only when specifying some, and not all, formative indicators, such as those for the four non-traditional CES-D items reported in Table 2 (a).

In panel (b), Path 1 is dropped during the first part of sequential estimation (see Discussion subsection "The derived protocol") when all remaining reflective indicators are estimated. The second part of sequential estimation retains Path 1 and drops the pathways to all of these remaining reflective indicators, in order to estimate the effect of the latent trait (Depression).

(c) Sixteen of the 20 CES-D items are traditional symptoms of depression. The final representation of items in each panel, *Each* of 4 *Non-Traditional* CES-D Items (Fearful, Lonely, People Unfriendly, People Disliked Me), comprises the four non-traditional symptoms in the CES-D scale [these items are named with a '1' in panel (b)]. Although direct effects from Diabetes, Heart Failure, and their interaction are specified to all 20 CES-D items, to keep each panel clear and simple, they are only drawn (Path 2) to the first two CES-D items: Depressed (CES-D ≥ 11) and Talked Less (CES-D ≥ 11) in panel (a) and Depressed 2 (CES-D ≥ 0) and Talked Less 2 (CES-D ≥ 0) in panel (b). Also, arrows are not drawn to reflect the error term from the latent trait and the measurement error terms from each of the CES-D items in order to minimize distracting complexity within the figure.

(d) Although each of the four non-traditional items (Lonely, Fearful, People Unfriendly, and People Disliked Me) contributes to the sensitivity and specificity of the CES-D scale in detecting real <u>cases</u> of subsequently confirmed clinical depression, they are not standard <u>symptoms</u> of depression. Corresponding instrumental variables (when CES-D ≥ 0) are specified to predict virtually all of

the variation within each of these four non-traditional items (when CES-D ≥ 11) because unpredicted residual variation within any of them may confound direct estimates (Path 2) to any of the remaining 16 standard (traditional) items of depression. In addition, at least one of these instrumental variables is needed to resolve the problem of estimation indeterminacy that would otherwise result due to there being one too few degrees of freedom for estimation of a MIMIC model in which every direct effect is specified.

(e) The last predictor box shown in panel (a), *Each* of 4 *Non-Traditional* CES-D Items (Fearful, Lonely, People Unfriendly, People Disliked Me; CES-D ≥ 0) is added 1) to account for unique variation from each of these non-traditional CES-D items (CES-D ≥ 11; Path 4); and 2) to permit estimation of the bidirectional effects of each of these non-traditional items (CES-D ≥ 11) by using two versions (i.e., continuous and ordinal) of the variable (bi-directional Paths 5). Because each of these non-traditional items (CES-D ≥ 11) is a subset of a broader variable when CES-D ≥ 0, the latter accounts for virtually all of the remaining variation in each non-traditional item (CES-D ≥ 11), which prevents confounding of direct paths to other items (Path 2).

(f) Let us use the item Lonely to illustrate the instrumental variables for the 4 non-traditional CES-D items in panel (a). Part of the overall variation in Lonely (CES-D ≥ 11) attributed to pre-existing lonely feelings predicts the latent trait of Depression. Part of the overall variation in Lonely (CES-D ≥ 11) manifests as an item from the measurement model portion of the MIMIC (i.e., in both of the bidirectional Paths labeled as 5, the right path is an effect indicator with factor loading parameter λ), reflecting lonely feelings that manifest as a component of the latent factor for depression.

To prevent confounding of direct effects to the traditional symptoms of depression, the same type of specification used with the Lonely item is used with each of the remaining three non-traditional CES-D depression items [i.e. Fearful (CES-D ≥ 11), People were Unfriendly (CES-D ≥ 11), and People Disliked Me (CES-D ≥ 11)]. In the same way that Lonely–Continuous (CES-D ≥ 11) is predicted by its instrumental variable [i.e., Lonely regardless of Depression (CES-D ≥ 0)], each of these three items is predicted by its corresponding instrumental variable when CES-D ≥ 0. In panel (a), all four items are estimated with bidirectional effects (the paths labeled as 5), and in panel (b), all twenty items are estimated with bidirectional effects (the paths labeled as 4) to prevent confounding of their direct effects.

(g) An instrumental variable must be highly correlated with the original variable, but cannot be correlated with the residual term when it is regressed on the instrumental variable: $Y = b(I) + U$, where Y is the original variable, I is the instrumental variable, and U is the residual term. [38] In the instrumental variable approach in panel (a), the original variable for a particular CES-D item, Y, only reflects when the item occurs as part of subthreshold or clinically significant depression (the original responses for participants with residual depression are set to zero), which form the basis as well for the estimated reflective indicators. In contrast, the instrumental variable, I, includes the original responses for all participants regardless whether they present with residual, subthreshold, or clinically significant depression. The identical values for Y and I in participants with subthreshold or clinically

significant depression results in U values equal to zero, resulting in a low correlation in these participants between the instrumental variable (I) and the residual term (U).