Causal and bidirectional linkages over time between depression and diabetes regimen distress in adults with type 2 diabetes

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A B S T R A C T

Aims: Diabetes regimen distress (RD) and depression are related constructs, however the nature of their relationship has not been explored over time, leading to difficulties differentiating between RD and depression and for selection of programs of care. We examined longitudinal associations between RD and depression to explicate the direction and mechanism of operation between these two constructs.

Methods: 392 adults with type 2 diabetes participated in a randomized control trial (RCT) to reduce diabetes distress. Participants were assessed for RD and depression symptoms, using the PHQ-8, at baseline, and at 4 and 12 months. Latent growth curve models tested both predictive unidirectional and bidirectional longitudinal associations between changes in RD and depression.

Results: Changes in RD did not significantly predict changes in PHQ-8, nor did changes in PHQ-8 predict changes in RD. A significant bidirectional association was found (Coefficient Estimate = .081, p = .001), where decreases in RD were associated with decreases in PHQ-8. The association was strongest among those with high baseline RD or PHQ-8 scores.

Conclusions: In the context of an RCT to reduce distress, support was found for a covarying association, in which changes in RD and depression symptoms occurred in tandem over time. No support was found for a causative association. Findings point to RD and depression containing properties that may be related to a shared underlying dimension of emotional distress. Results suggest consideration of both RD and depression in clinical decision making, with interventions selected based on source of distress.

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1. Introduction

Both depression and regimen distress (RD) are common in patients with type 2 diabetes [1–3]. Depression, as measured by commonly used symptom scales, is not defined by the stressors that may have caused them, and reflects only the simple number of well-defined depression symptoms experienced over a specified period of time. In contrast, RD, a critical area of diabetes distress, is specifically diabetes-related and

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refers to the emotional distress associated with the daily management of diabetes [4]. These two constructs emerge from two distinct lines of clinical inquiry and they appear to be conceptually distinct: depression emerged from research on psychiatric diagnosis and psychopathology [5], whereas RD emerged from the literature on stress and coping and emotional regulation [6]. Practically, however, despite their differences in meaning and history, the two constructs share many similarities. RD and depression symptoms are moderately intercorrelated, with over two-thirds of patients reaching criteria for MDD also reporting at least moderate RD [1,7–9]. RD and depression also share modest relationships with glycemic control and disease management [7,10,11]. Despite this overlap, clearly differentiating between depression and RD has important implications for understanding the differences between depression and RD, and for guiding the selection of appropriate patient interventions for patients with diabetes.

We previously reported significant decreases in RD in a behavioral intervention designed to target distress [12]. Significant decreases, however, also occurred in depression symptoms as a result of the intervention, i.e. an intervention that targeted only RD significantly reduced both RD and depression symptoms [13]. It remains unclear, however, why changes in RD over time, as a result of a successful RD intervention, were linked to changes in depression symptoms over time. Clarifying this issue will help distinguish between the two constructs by identifying potential causal or interactive mechanisms that might explain why changes in one construct appear to be related to changes in the other. For example, if a causative or directional link occurs between RD and depression symptoms, including clinical depression, such that a reduction of RD “causes” a subsequent decrease in depression (or vice versa), an argument can be made for the relative independence of these two constructs. If, on the other hand, the two constructs co-vary closely together over time, their relative independence can be called into question such that each may be reflecting a significant part of the other or of a third variable. Clarifying this relationship has practical implications. For example, if changes in RD do not “cause” changes in depression, or vice versa, effective interventions may need to target each separately. In contrast, if RD and depression are part of the same construct or a shared underlying construct, single RD or depression interventions might be most effective and efficient for patients with both RD and depression.

This study explored how changes in RD are associated with changes in depression symptoms over time. In the context of a behavioral RCT to reduce diabetes distress among patients with type 2 diabetes, we tested two models: a directional or causal model whereby changes in RD were hypothesized to lead directly to changes in depression symptoms over time (and vice versa), and a bidirectional model in which changes in RD were hypothesized to co-vary with changes in depression symptoms over time. The impact of covariates was also explored.

2. Methods

2.1. Subjects

Patients with type 2 diabetes were recruited from the patient registries of several community medical groups and diabetes education centers. The primary inclusion criterion was a mean score of $\geq 1.5$ on the two-item Diabetes Distress Screener [14] (confirmed later by the full scale). Response options for the two items ranged from 1 “not a problem” to 6 “very serious problem” with a response of 2 defined as “a little problem”, thus including individuals with at least a modest level of diabetes distress [15]. Additional inclusion criteria included: a registry-recorded diagnosis of type 2 diabetes $\geq 12$ months; age $\geq 21$ years; ability to read and speak English; at least moderate computer use ability; easy availability of a computer with Internet access; and self-reported problems with adherence to diabetes management (healthy eating or exercise plan not followed in 3 of 4 days during the previous week, or medications not taken 2 or more days during the previous week based on the Summary of Diabetes Self-Care Activities [16]. Exclusion criteria included depression symptoms (Patient Health Questionnaire-8 score $\geq 15$) [17] and severe diabetes complications or functional deficits (e.g., dialysis, blindness). Thus, the sample included patients who had at least modest distress and some behavioral management difficulties so that change in one or more of these variables could be observed over time.

2.2. Procedures

A description of the study protocol and the intervention program have been previously published [12]. Patients received a letter from their health-care facility informing them of the Reducing Distress and Enhancing Effective Management (REDEEM) study. During a subsequent phone call, the project was explained, patients were screened, and eligible patients were invited to a meeting where eligibility requirements were confirmed, informed consent was obtained, and a 1.5 h baseline assessment was completed. The assessment included: height and weight, questionnaires, brief interview, and visit to a community laboratory for collection of biological data. Patients were then randomized to one of the three interventions, using a computer-generated algorithm, and an intervention visit was scheduled. In keeping with a pragmatic design and comparative effectiveness research [18], no usual care condition was included because of concerns about maintaining distressed patients in a non-interventional study arm. The interventions, as described previously [12], were: (a) Computer-Assisted Self-Management (CASM), which featured a 40 min, previously validated, web-based, diabetes self-management improvement program that addressed diet, physical activity and medication adherence [19,20], (b) CASM plus problem-solving therapy (CAPS) [20,21], an eight-step CBT-based intervention that targeted RD directly, and (c) a minimal intervention that featured a 20 min, computer-delivered health risk appraisal and provided written diabetes education (Leap Ahead) [22]. In all conditions, patients received a live supplemental booster session at month 5, which included a repeated health risk appraisal for Leap Ahead patients and an automated program to reduce negative behavioral practices for patients in CASM and CAPS. Patients in all conditions also received the same sequence of eight live 15 min phone calls (at weeks 2, 4, 7, 12, 24, 28, 36, and 44) to check progress and provide encouragement. Assessments were repeated at 4 and 12 months after
initiation of the intervention. The UCSF IRB and the committees of collaborating institutions approved this study. Data were collected between 2008 and 2011, and analyzed in 2012–2013.

2.3. Measures

Patient demographic variables included age, gender, ethnicity/race (dichotomized as white and non-white), and education (trichotomized as less than college, technical school, college). Diabetes status included use of insulin (yes/no), years since diagnosis, and total number of comorbidities (e.g., asthma, rheumatoid arthritis) and complications (e.g., kidney problems, stroke) from a list of 22.

Regimen distress was assessed by the five-item Regimen Distress (RD) subscale ($\alpha = .90$) from the diabetes distress scale (DDS, 24). The RD subscale was selected for the current study as it was the area of diabetes distress directly targeted by the interventions. In addition, RD is the area of diabetes distress with the highest prevalence, and it displays the highest correlation with the DDS total sale score [12].

The modified Patient Health Questionnaire-8 is a measure of depression symptoms linked to DSM diagnostic criteria for MDD, but excludes the suicide item [24]. The PHQ is widely used in primary care practice as a screener and outcome measure of depression symptoms.

2.4. Data analysis

Missing data were imputed with multiple imputation procedures using NORM version 2 software [25] (RE. NORM imputes data through the expectation-maximization algorithm). Associative latent growth models (LGMs) examined the correlations between RD and PHQ-8 scores across time [26]. First, each measure was modeled separately to determine whether it increased, decreased, or remained constant over time both within and across study arms. Because the RD and PHQ-8 slopes were expected to be negative, to make interpretation of effects more straightforward, loadings for the slopes were set at baseline = 0, 4 months = −1, and 12 months = −3. Once successfully modeled separately, they were modeled simultaneously in two ways: to examine the predictive effect of change in RD on change in PHQ-8 over time and vice versa (unidirectional regression model), and to determine whether change in RD and change in PHQ-8 significantly co-varied together over time (bidirectional regression model). For both models, predictors previously shown to be related to each were included: age, current use of antidepressant medication, sex, white/non-white ethnicity, education, years with diabetes diagnosis, number of comorbidities/complications, and insulin use. Treatment condition also was included as a covariate to assess for differential effects by study arm. Analyses were conducted in Mplus 6.0 software using maximum likelihood estimation.

3. Results

3.1. Sample characteristics

Of 2606 patients identified from registries, 658 were eligible and 436 agreed to participate (66.6%). Of these, 392 (89.5%) participants completed baseline assessment and intervention: 150 were randomized to CASM, 146 to CAPS and 96 to Leap Ahead (Table 1). No differences were found between eligible patients who screened positive for the study and participated, and those who screened positive but refused to participate. Attrition was 13.8% from baseline to 4 months, 5.7% from 4 to 12 months, and 18.7% from baseline to 12 months. Only 8.4% of patients missed both 4- and 12-month assessments. There were no significant between-group differences in attrition across either time period on any key study variable. There were no significant baseline differences among the three study groups on any key demographic or diabetes status variable (Table 1) nor were there any differences on key variables based on recruitment source (community group vs. diabetes education center). The diverse sample had a mean age of 56 years (SD = 9.6), 53.8% of the sample were female, 8.7% of patients had ≤12 years of education, and mean baseline HbA1c was 7.4% (SD = 1.6) [57.0 mmol/mol (17.6)].

3.2. Changes in RD and depression symptoms over time

Separate latent growth models indicated that there was significant change in both RD and PHQ-8 from baseline to 12 months within the entire REDEEM sample, both when covariates were included and excluded. Mean slopes were significant (and negative) for both PHQ-8 (mean slope = .298, $p < .001$) and RD (mean slope = .222, $p < .001$) across the 12-month period. On average, participants started at a covariate-adjusted RD level of 2.972 and decreased .222–.750 by 4 months, then decreased another .444 to reach 2.306 at 12 months. For PHQ-8, the mean covariate-adjusted intercept was 4.535 ($p < .001$). On average, participants started at a covariate-adjusted PHQ-8 level of 4.535 and decreased .298–4.237 by 4 months, then decreased another .596 to reach 3.641 at 12 months. Thus, the RD intervention led to significant reductions in both RD and PHQ-8 over time across the entire sample with no between-treatment group differences.

3.3. Models of associations between regimen distress and depression symptoms

Two latent growth models were specified, each representing a reasonable fit to the data: $\chi^2(25) = 100.51; p < .0001; CFI = .89$; root mean square error of approximation = .09, and standardized root mean square residual = .031. The first model examined the predictive, potentially causative, effect of change in RD, the target of the interventions, on change in PHQ-8 (unidirectional regression model). Change in RD did not significantly predict change in PHQ-8 over time. Likewise, a unidirectional model that examined the predictive effect of change in PHQ-8 on change in RD also did not reach significance.

The second model examined the bidirectional association between change in RD and change in PHQ-8 over time, and for this model the relationship between the two slopes was allowed to co-vary freely. As shown in Table 2 and Fig. 1, change in RD and change in PHQ-8 significantly and positively co-varied (Coefficient Estimate = .081, $p = .001$), indicating that change in these two variables occurred in tandem over time. In addition, the RD intercept predicted both the RD Slope...
Table 1 - Baseline characteristics of participants randomized across three conditions (N = 392).

<table>
<thead>
<tr>
<th>Characteristic or variable</th>
<th>All M (SD) or % N = 392</th>
<th>Leap Ahead M (SD) or % n = 96</th>
<th>CASM M (SD) or % n = 150</th>
<th>CAPS M (SD) or % n = 146</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>56.11 (9.55)</td>
<td>55.23 (10.88)</td>
<td>56.96 (8.78)</td>
<td>55.82 (9.36)</td>
<td>.34</td>
</tr>
<tr>
<td>Female</td>
<td>53.8%</td>
<td>59.4%</td>
<td>48.0%</td>
<td>56.2%</td>
<td>.17</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>.64</td>
</tr>
<tr>
<td>Amer Indian/Alaska Native</td>
<td>0.8%</td>
<td>0%</td>
<td>1.3%</td>
<td>0.7%</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>19.4%</td>
<td>18.8%</td>
<td>22.0%</td>
<td>17.1%</td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>16.6%</td>
<td>24.0%</td>
<td>11.3%</td>
<td>17.1%</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>11.2%</td>
<td>10.4%</td>
<td>12.7%</td>
<td>10.3%</td>
<td></td>
</tr>
<tr>
<td>Pacific Islander</td>
<td>1.8%</td>
<td>1.0%</td>
<td>1.3%</td>
<td>2.7%</td>
<td></td>
</tr>
<tr>
<td>White, non-Hispanic</td>
<td>40.1%</td>
<td>35.4%</td>
<td>41.3%</td>
<td>41.8%</td>
<td></td>
</tr>
<tr>
<td>Multiple ethnicities</td>
<td>5.9%</td>
<td>6.3%</td>
<td>4.7%</td>
<td>6.8%</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>4.3%</td>
<td>4.2%</td>
<td>5.3%</td>
<td>3.4%</td>
<td></td>
</tr>
<tr>
<td>Income</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>.44</td>
</tr>
<tr>
<td>Less than $49,999</td>
<td>31.3%</td>
<td>34.3%</td>
<td>32.0%</td>
<td>28.8%</td>
<td></td>
</tr>
<tr>
<td>$50,000-$100,000</td>
<td>40.3%</td>
<td>44.8%</td>
<td>38.7%</td>
<td>39.0%</td>
<td></td>
</tr>
<tr>
<td>More than $100,000</td>
<td>28.3%</td>
<td>20.8%</td>
<td>29.3%</td>
<td>32.2%</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>.93</td>
</tr>
<tr>
<td>High school or less</td>
<td>8.7%</td>
<td>10.4%</td>
<td>8.0%</td>
<td>8.2%</td>
<td></td>
</tr>
<tr>
<td>Technical school</td>
<td>30.4%</td>
<td>28.1%</td>
<td>30.0%</td>
<td>32.2%</td>
<td></td>
</tr>
<tr>
<td>College</td>
<td>61.0%</td>
<td>61.5%</td>
<td>62.0%</td>
<td>59.6%</td>
<td></td>
</tr>
<tr>
<td>% Take insulin</td>
<td>17.9%</td>
<td>19.8%</td>
<td>15.3%</td>
<td>19.2%</td>
<td>.59</td>
</tr>
<tr>
<td>Years since diag. diagnosis</td>
<td>6.90 (5.93)</td>
<td>7.60 (6.44)</td>
<td>6.89 (6.04)</td>
<td>6.46 (5.46)</td>
<td>.34</td>
</tr>
<tr>
<td># comorb./complications</td>
<td>3.35 (2.58)</td>
<td>3.55 (2.75)</td>
<td>3.35 (2.62)</td>
<td>3.21 (2.43)</td>
<td>.61</td>
</tr>
<tr>
<td>% take depression meds</td>
<td>21.4%</td>
<td>23.2%</td>
<td>20.7%</td>
<td>21.0%</td>
<td>.89</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>33.07 (7.78)</td>
<td>33.25 (8.41)</td>
<td>32.13 (7.17)</td>
<td>33.93 (7.90)</td>
<td>.13</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>7.41 (1.61)</td>
<td>7.45 (1.71)</td>
<td>7.45 (1.53)</td>
<td>7.34 (1.62)</td>
<td>.81</td>
</tr>
</tbody>
</table>

* One-way analysis of variance or chi-square test, as appropriate.

Table 2 - Results from two models comparing change in PHQ and regimen distress.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Bidirectional regression model</th>
<th>Regimen distress slope</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PHQ slope</td>
<td>Regimen distress slope</td>
</tr>
<tr>
<td></td>
<td>Estimate (SE)</td>
<td>p</td>
</tr>
<tr>
<td>RD slope</td>
<td>.081 (.025)</td>
<td>.001</td>
</tr>
<tr>
<td>PHQ intercept</td>
<td>–.021 (.357)</td>
<td>.952</td>
</tr>
<tr>
<td>RD intercept</td>
<td>.154 (.069)</td>
<td>.025</td>
</tr>
<tr>
<td>Age</td>
<td>.007 (.007)</td>
<td>.308</td>
</tr>
<tr>
<td>Depression meds</td>
<td>-.286 (.367)</td>
<td>.088</td>
</tr>
<tr>
<td>Sex</td>
<td>.243 (.133)</td>
<td>.069</td>
</tr>
<tr>
<td>White/non-white</td>
<td>.107 (.141)</td>
<td>.447</td>
</tr>
<tr>
<td>Education</td>
<td>-.067 (.104)</td>
<td>.521</td>
</tr>
<tr>
<td>Years with diagnosis</td>
<td>-.006 (.012)</td>
<td>.620</td>
</tr>
<tr>
<td>Comorbs/complications</td>
<td>.058 (.027)</td>
<td>.035</td>
</tr>
<tr>
<td>Insulin</td>
<td>.049 (.172)</td>
<td>.773</td>
</tr>
<tr>
<td>Treatment group</td>
<td>-.063 (.085)</td>
<td>.460</td>
</tr>
</tbody>
</table>

(Coefficient Estimate = .090, p = .002) and the PHQ-8 slope (Coefficient Estimate = .154, p = .025). The PHQ-8 intercept significantly predicted the RD slope (Coefficient Estimate = .184, p = .002), but was unrelated to change in PHQ-8. These findings indicated that higher baseline RD was significantly associated with greater improvement in both RD and PHQ-8, and that higher baseline PHQ-8 scores were significantly related to greater improvement in RD, further supporting the bi-directional relationship. Participant age was negatively related to change in RD, with younger participants displaying less improvement in RD over time than older participants (Coefficient Estimate = –.007, p = .001). comorbidities/complications was positively related to change in both RD (Coefficient Estimate = .020, p = .012) and PHQ-8 (Coefficient Estimate = .058, p = .035), with patients having fewer comorbidities/complications improving more in both than patients with more comorbidities/complications.

Because higher initial RD had been related to greater improvement in distress over time [12] the bidirectional model was further tested with subsets of participants to determine whether the co-variation between RD and PHQ-8 was consistent across the full range of scores. Using median splits of RD and PHQ-8, four additional bidirectional models were tested. Results indicated that the bi-directionality observed between
RD and PHQ-8 in the entire sample also occurred across all patient subgroups, although the relationship was strongest among those with higher initial RD (Coefficient Estimate = .076, \( p = .033 \)) or PHQ-8 (Coefficient Estimate = .080, \( p = .036 \)). These subgroup findings demonstrated that change in RD was significantly associated with change in PHQ-8 across the entire distribution of scores, regardless of initial RD or PHQ-8 levels.

4. Discussion

Regarding our primary research question, we find that in the context of an intervention trial, reductions in RD do not “cause” similar reductions in depression symptoms over time. Likewise, reversing the order, reductions in depression symptoms do not “cause” significant reductions in RD over time. Consequently, we find no support for a causative model that accounts for the observed relationships between these two constructs.

In contrast, support for a bidirectional model of co-variation was observed: RD and depression symptoms significantly co-varied together over time, and this co-variation occurred across the full distribution of scores, although the largest changes occurred for participants who began the study with the highest RD or PHQ-8 levels. Furthermore, younger adult participants displayed less change in both RD and PHQ-8 than older participants, and those with fewer complications/comorbidities evidenced greater change in both RD and PHQ-8 than those with more complications/comorbidities. The parallel findings for both RD and PHQ-8 regarding change based on initial levels, age and complications/comorbidities provide additional support for the bidirectional model.

What are the theoretical and practical implications of an associational, bi-directional, non-causal relationship between changes in depression and RD? Conceptually, the parallel changes in these constructs in response to a single RD intervention are consistent with other non-experimental studies that have shown similar kinds of overlap [8]. Together, these findings suggest that RD and depression symptoms contain properties that may be related to a single, shared, underlying dimension of ‘emotional distress’. Emotional distress is a core construct that forms the foundation for most life distress and psychopathology [9]. Given the significant, parallel relationships between RD and depression symptoms with respect to measures of self-management [7,27], diabetes complications and mortality risk [28,29], emotional distress may best be considered a continuous, scalable psychological characteristic rather than a discrete co-morbid clinical condition.

Although RD and depression symptoms may commonly reflect emotional distress, they may do so in different ways. We suggest that emotional distress among people with diabetes has two major, independent characteristics that are differentially reflected by RD and depression symptoms: the content or source of the distress, in this case specific aspects of diabetes and its management (RD), and the severity of the distress, in this case the number and intensity of depression symptoms (PHQ-8). Thus, what we may be observing in the significant bidirectional model reported here is that RD reflects one major characteristic, the content or source of emotional distress, whereas depression symptoms reflects the other, the severity of emotional distress. The benefit of including the concept of emotional distress is that, along with severity, it places the emotional experience of diabetes within a life context by also considering its source or cause, thus adding to clinical understanding and directing appropriate interventions. We restrict the use of the terms ‘depression’ and MDD only to criteria that match DSM guidelines – depression, by definition, implies psychopathology, and our data suggest that people with...
diabetes who are upset and stressed about their disease and its management are not necessarily experiencing a psycho-pathological reaction, unless their reaction is sufficiently high on the severity scale and meet DSM criteria for clinical depression.

This framework has practical, clinical implications. The literatures on depression and RD within the diabetes arena have been plagued by inconsistencies and contradictions because of problems with definition and measurement [4,9,30]. An applied approach that follows from a bidirectional, non-causal model identifies RD and depression as two characteristics of the same underlying phenomenon, ‘emotional distress’, and not as competing constructs or conditions. This requires that clinicians incorporate both into clinical decision making. For example, a patient who reaches a high level of severity of emotional distress, perhaps by reaching a positive screen on the PHQ-8, may require a clinical intervention. The kind of intervention, however, should be dictated by the source of the distress, which is not identified or defined by depression scales alone. A patient who reports being overwhelmed by their diabetes treatment regimen and who experiences feelings of failure with self-management may benefit from an intervention that targets these diabetes-specific stressors. Patients with high severity and other sources of distress may benefit from different interventions, following appropriate guidelines, including the prescription of antidepressant medication and/or psychotherapy. Different interventions with relevance to both source and severity can occur across the continuum of emotional distress, as supported by the results of our subgroup analysis, but both characteristics need to be assessed and considered carefully to inform the kind and intensity of intervention. Thus, a bidirectional model provides a practical framework for assessing and addressing the full spectrum of emotional distress in diabetes care.

Several study limitations are noteworthy. First, the study design included only three time periods for analysis. Multiple time periods for a growth curve analysis would have been preferred. Second, patients with diabetes and a PHQ-8 score of ≥15 were excluded, so the consistency of the bidirectional findings at the upper range of depression symptoms was not studied. However, data suggest that diabetes patients with major depressive disorder (MDD) are as equally likely to endorse diabetes as a source for their depression symptoms as those who do not meet diagnostic criteria for MDD [31]. Third, the subgroup analyses forced a partition of the sample and, therefore, reduced statistical power. Although the results were consistent in all analyses, confirmation with a larger sample would be helpful.

In conclusion, this study explored the unidirectional and bidirectional relationships over time between change in RD and change in depression symptoms as part of a diabetes distress reduction intervention. We find no support for a ‘causative’ relationship between change in RD and change in depression symptoms, but significant support for a bidirectional relationship over time in both overall and subgroup analyses. Along with other studies, these findings lead us to propose that RD and depression symptoms serve as two characteristics of an underlying third variable of emotional distress, with the former reflecting the source or content of the distress and the latter reflecting the severity of the distress. Both are crucial for informing the type and intensity of clinical intervention among patients with diabetes.

**Conflict of interest**

No potential conflicts of interest relevant to this article were reported.

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Dr. Danielle Hessler is the guarantor of this work, and, as such, had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. DH and LF reviewed the research data and wrote the manuscript, LS, PA, and VB reviewed and edited the manuscript, and LS conducted the data analyses and wrote the Data Analysis section. Appreciation is expressed to Jeffrey Gonzales for his valued assistance, and to the following medical groups and diabetes education centers for their collaboration: Alta Bates Diabetes Education Center, Brown and Toland Medical Group, California Pacific Medical Center Diabetes Education Center, Hill Physicians Medical Group, and UCSF Lakeshore Medical Group.

**References**


