

# Social well-being moderates behavioral therapy response for generalized anxiety disorder

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## ABSTRACT

**Introduction:** Identifying moderators of treatment outcome for depression and anxiety offers promise for personalizing treatment or providing novel intervention targets. Indices of social well-being have emerged as candidate moderators due to their robust impact on mental health and quality of life. Here, we examine whether measures of social support, isolation, and loneliness moderate outcomes to behavioral activation (BA) and exposure-based therapy (EXP) for individuals with GAD.

**Methods:** This secondary analysis of a randomized clinical trial included 69 participants (31 EXP, 38 BA). Participants completed the GAD-7, along with NIH PROMIS (Depression; Social Isolation; and Emotional, Instrumental, and Informational Support) and NIH Toolbox (Friendship; Loneliness) scales. Regularized factor analysis identified two factors: social support and isolation/loneliness.

**Results:** Social support ( $p < .001$ ,  $\eta^2 = 0.19$ ) and isolation/loneliness ( $p < .001$ ,  $\eta^2 = 0.33$ ) improved over time, regardless of treatment condition. Lower baseline social support related to more GAD-7 improvement to BA and less improvement to EXP ( $p = 0.030$ ,  $d = 0.17$ ). Greater baseline isolation/loneliness related to more PROMIS Depression improvement to BA and less improvement to EXP ( $p = 0.025$ ,  $d = 0.17$ ). Individuals reporting baseline isolation/loneliness  $\geq 0.22$  standard deviations above the sample mean exhibited no significant depression symptom reduction with EXP.

**Conclusions:** Measures of social well-being moderate treatment outcome to behavioral therapy for GAD, providing valuable information for personalized treatment. Results suggest, for individuals reporting low social support and/or high isolation and loneliness, exposure-based treatment outcomes may benefit from early or adjunctive intervention strategies targeting social well-being.

## 1. Introduction

Cognitive behavioral therapy (CBT) is often referred to as the current gold standard in psychotherapeutic treatment [1], with hundreds of clinical trials demonstrating its effectiveness [2,3]. However, as many as half of the people who receive CBT do not experience symptom remission [4–6]. Given the strong evidence supporting CBT as an effective

intervention for depression and anxiety (separately and co-morbidly) [3, 7–9], it is notable that long-term clinically-significant response rates may be as low as 50 % or less for anxiety disorders [4,5,10], and approximately 41–42 % for depression [3,6]. Troublingly, even these modest estimates may be inflated by the absence of standardized criteria for determining treatment response [10]. To increase the rate at which clients respond to treatment, researchers are increasingly focused on

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questions exploring which treatments are effective, for whom, why, and under what circumstances [11–13].

Personalized medicine seeks actionable answers to these questions, focusing on identifying which client characteristics are relevant when selecting treatments. Although there is a dearth of evidence-based guidance regarding personalized treatment in mental health at present, improved understanding of which factors influence treatment response could assist clinicians in selecting which treatment approach has the greatest likelihood of success for a specific client [13,14]. The field is currently exploring a wide range of personal characteristics, from demographic and clinical characteristics to neural correlates of treatment response, to identify which client characteristics reliably predict (i.e., predicting outcome regardless of treatment) or moderate (i.e., predicting outcome differentially between treatments) response to mental health treatments [12,15–17]. Although a greater proportion of the available literature for anxiety focuses on predictors rather than moderators [13,18], it has been recommended studies prioritize analyzing treatment moderators to better inform the personalized treatment of anxiety [13].

In recent years, indices of social well-being—such as social isolation (absence of social interactions), loneliness (perceived distress at unmet social needs), and social support (resources/support provided by others)—have emerged as candidate moderators of anxiety treatment outcome warranting further investigation, due to their well-documented association with physical and mental health [19–22]. Growing evidence demonstrates that disruptions in these indices of social well-being have critical policy and public health implications [23–25], increasing the risk of cardiovascular disease, stroke, and all-cause mortality to a degree comparable with obesity and smoking [26–28]. Underscoring the clinical relevance for mental health, the prevalence of loneliness and isolation is considerably higher in clinical samples (five to eleven times higher with anxiety, ten times higher with depression) when compared with the general population [19]. Further, loneliness, isolation, and low social support have been associated with increased severity and risk of onset of depression [29–31], general and social anxiety [32–35], and self-harm [20,25,36]. These relationships are bi-directional, as rising depression [30] and anxiety [37,38] predict worsening social support and isolation/loneliness, which in turn bias cognition and behavior in ways that promote anxiety and depression [31,39,40], creating a cycle of deteriorating mental health and social well-being.

Poor perceptions of social support and increased isolation and loneliness have also been demonstrated to predict, in general, worse outcomes in the treatment of depression and anxiety treatment [22]; with preliminary evidence suggesting these factors impact treatment through influencing the working alliance between clients and therapists [41,42]. It is unclear, however, whether specific treatment approaches are more or less effective for those experiencing disruptions in various aspects of social well-being [22]. Two behavioral therapies frequently utilized in the treatment of GAD and co-occurring depression are exposure-based therapy (EXP) and behavioral activation (BA). While both approaches utilize behavioral intervention techniques, EXP seeks to reduce behavioral avoidance and worry through repeated therapeutic exposure to feared situations, while BA focuses on increasing approach behavior and opportunities for positive reinforcement through scheduling rewarding and valued activities. Both EXP and BA have the potential to improve social functioning, through reducing avoidance of social situations related to anxiety or enhancing approach towards rewarding social interactions, respectively. However, although social engagement is not an explicit target of treatment, the focus on engaging in meaningful and value-driven activities in BA often involves scheduling activities related to increasing social engagement [43–45]. It is possible this emphasis on value-driven approach behaviors may mitigate the deleterious effects of loneliness and deficits in social support on treatment outcomes [22].

In the present study, we explore whether isolation, loneliness and social support moderate treatment response to behavioral therapy (BA

or EXP) for GAD in a community sample. Data were collected as part of a clinical trial assessing neural predictors of treatment response for GAD. The primary aim of this study was to explore whether varying degrees of perceived social support, isolation, and loneliness at baseline differentially predict treatment response between BA and EXP, with the hypothesis that poorer perceived social support and higher levels of loneliness and isolation would predict (1) worse anxiety and depression symptom severity outcomes for EXP (as loneliness and lack of social support may reduce one's ability to benefit from psychotherapy in general [22]), and (2) improved anxiety and depression outcomes for BA (given the focus of BA on engaging in reinforcing activities consistent with their goals and values may better target isolation and loneliness). We also explored whether BA and EXP differentially impacted pre- to post-treatment changes in isolation, loneliness and perceived social support, with the hypothesis that participants in BA would exhibit greater improvements over time. Given prior studies demonstrating indices of social well-being may impact the quality of the social relationship between clients and therapists (i.e., working alliance) [46,47], and the possibility that social well-being could impact clinical outcomes through influencing the therapeutic relationship [41,42], our exploratory third and final aim was to assess whether baseline perceived social support, isolation, and loneliness predict changes in working alliance throughout therapy.

## 2. Method

Although a summary of the present study's method is provided here, study procedures are also detailed fully [48] and summarized [49] elsewhere. The clinical trial was registered with ClinicalTrials.gov (identifier NCT02807480); primary symptom outcome results and results concerning neural predictors of treatment outcome have been previously published [49,50].

### 2.1. Procedure

Ethical approval was received prior to data collection, participants provided written informed consent and were compensated for participation, and procedures were performed in accordance with the Declaration of Helsinki. Data were collected as part of a single-center (Tulsa, OK), randomized clinical trial (two-condition) investigating multilevel predictors of response to EXP versus BA for GAD. Both psychotherapeutic interventions were delivered in a manualized in-person group format with group randomization (in blocks of 4) for 80 % of participants. Following the onset of the COVID-19 pandemic (March, 2020), both treatment arms transitioned to individual virtual therapy with individual randomization (20 % of participants). The content of both manuals (BA and EXP) utilized for individual therapy was identical to that of the group-based therapies, except modified to allow for more individualized discussion for the individual clients' experiences. Participants in group therapy were assigned to closed treatment groups of 8–10 participants prior to group randomization. Participants were blinded to group assignment until after all baseline assessments were completed. Participants and providers were not blinded during weekly and post-treatment assessment.

Secondary data analyzed for this study were gathered as part of a larger battery of outcome and process measures (for additional details, see [supplemental materials](#)). Consistent with previous clinical trials for GAD, the primary outcome was the GAD-7 [51]. NIH Patient-Reported Outcomes Measurement Information System (PROMIS) and NIH Toolbox measures were used to assess depression symptom severity as a secondary outcome (PROMIS Depression scale [52]), as well as facets of social well-being including loneliness, isolation, and social support (PROMIS Emotional Support, Instrumental Support, Informational Support, and Social Isolation [53]; NIH Toolbox Friendship, and Loneliness [54]). Participant perception of working alliance was assessed using the Working Alliance Inventory – Short Form [55] (WAI).

Research Electronic Data Capture (REDCap) was used to collect self-report data electronically (see Figure S1 for an illustrative timeline). All participants completed initial screening assessments to confirm exclusion and inclusion criteria, as well as baseline assessment for variables of interest (GAD-7; PROMIS Depression, Emotional Support, Instrumental Support, Informational Support, and Social Isolation; NIH Toolbox Friendship, and Loneliness). Throughout treatment participants completed weekly self-report symptom measures (GAD-7, PROMIS Depression), with working alliance assessed at weeks three, six, and nine (WAI). Following treatment, participants completed all assessments conducted at baseline.

## 2.2. Participants

As part of the larger study mentioned above [48–50], 121 treatment-seeking individuals were consented over a period of 5 years (April 2016–April 2021), and recruitment was stopped once the planned number of participants were randomized to treatment ( $n = 101$ ); of these, 94 participants started treatment and 69 participants completed treatment (31 EXP, 38 BA; 73.4 %). Treatment completion was defined as participation in at least 7 therapy sessions (for a participant flow diagram, please see Fig. S3). Researchers used electronic and print advertisements to recruit participants from local mental health clinics and the general population.

Participants ranged in age from 18 to 55 years old, were fluent in English, without severe depression (i.e., excluded if PHQ-9 total score > 17), without acute suicidal ideation (with intent or plan) and met criteria for GAD per the Mini International Neuropsychiatric Interview (MINI, version 6.0.0 for DSM-IV-TR or version 7.0.2 for DSM-5) [56]. Participants reporting current use of selective serotonin re-uptake inhibitors (SSRIs) were included if dosage was stable for at least 6 weeks prior to enrollment. Supplemental materials include a full description of exclusion criteria. Baseline characteristics and MINI-assessed psychiatric comorbidities are summarized in Table 1.

## 2.3. Interventions

Both EXP and BA interventions were delivered in a manualized format across ten sessions. To isolate mechanisms of behavior techniques for the primary study's purpose of investigating positive and negative valence systems, both treatments were adapted to exclude cognitive techniques and centered on behavioral intervention techniques only. Group interventions were delivered in 90-minute, weekly sessions led by two co-therapists; participants who received individual therapy due to protocol changes made in response to the onset of the COVID-19 pandemic received 50-minute, weekly sessions delivered by a single therapist. Study therapists received extensive training in both treatment-arms and included licensed clinicians (doctoral- and/or master's-level), clinical psychology postdoctoral fellows, and clinical psychology graduate students. Experts in each intervention (and their trainees) performed fidelity ratings of select therapy session recordings, which indicated acceptable fidelity to each treatment-arm (see original study for details [49]). Study therapists attended weekly consultation and supervision with RLA and/or consultants.

In BA, therapists attempt to help clients re-engage with potentially rewarding/reinforcing behaviors, particularly those consistent with the client's values. The present study utilized a ten-session, structured BA manual developed by study investigators, with content informed by existing BA treatment guides [57]. Due to the population, the wording of the manual included targeting of general negative affect (anxiety and depression) rather than depression only (as BA was originally developed).

In EXP, therapists attempt to help clients confront stimuli or situations that participants avoid due to fear of potential negative outcomes. These exposures are designed to challenge negative expectancies using principles of modern learning theory, recognize the non-occurrence of

**Table 1**

Baseline characteristics across treatment-arms.

|                                           | BA         | EXP         |
|-------------------------------------------|------------|-------------|
| <i>n</i>                                  | 38         | 31          |
| Age [mean (SD)]                           | 35 (11)    | 33 (10)     |
| Sex = Male (%)                            | 7 (13.9)   | 0 (0.0)     |
| Income (%)                                |            |             |
| Not provided                              | 0 (0.0)    | 2 (6.5)     |
| Less than \$50,000                        | 20 (55.6)  | 10 (32.3)   |
| \$50,000 to \$100,000                     | 10 (26.3)  | 13 (41.9)   |
| \$100,000 to \$150,000                    | 6 (15.8)   | 5 (16.1)    |
| Over \$150,000                            | 2 (5.6)    | 1 (3.2)     |
| Race (%)                                  |            |             |
| American Indian                           | 4 (10.8)   | 0 (0.0)     |
| Asian                                     | 0 (0.0)    | 1 (3.4)     |
| Black                                     | 2 (5.4)    | 1 (3.4)     |
| Hispanic                                  | 2 (5.4)    | 1 (3.4)     |
| Multiracial                               | 8 (21.6)   | 5 (17.2)    |
| White                                     | 21 (56.8)  | 21 (72.4)   |
| Education (%)                             |            |             |
| Less than high school                     | 1 (2.6)    | 1 (3.2)     |
| High school or GED                        | 2 (5.3)    | 2 (6.5)     |
| Some college, no degree                   | 10 (26.3)  | 5 (16.5)    |
| Associate's degree                        | 3 (7.9)    | 3 (9.7)     |
| Bachelor's degree                         | 14 (36.8)  | 9 (29.0)    |
| Master's degree                           | 8 (21.1)   | 10 (32.3)   |
| Professional/doctoral degree              | 0 (0.0)    | 1 (3.2)     |
| Isolation/Loneliness [mean (SD)]          | 3.2 (2.0)  | 2.5 (3.1)   |
| PROMIS Social Isolation                   | 56.8 (5.7) | 54.5 (9.1)  |
| NIH Toolbox Loneliness                    | 64.3 (7.6) | 62.5 (11.6) |
| NIH Toolbox Friendship                    | 39.0 (9.6) | 41.9 (12.2) |
| Social Support [mean (SD)]                | -0.1 (2.4) | 0.1 (2.3)   |
| PROMIS Emotional Support                  | 46.7 (8.8) | 48.0 (8.3)  |
| PROMIS Informational Support              | 49.7 (9.5) | 50.6 (8.4)  |
| PROMIS Instrumental Support               | 53.0 (8.8) | 52.7 (8.8)  |
| GAD-7 [Mean (SD)]                         | 11.4 (3.5) | 12.7 (5.2)  |
| PROMIS Depression [Mean (SD)]             | 58.1 (7.1) | 55.8 (7.6)  |
| Working Alliance Inventory – Self-Report* | 44.3 (8.8) | 43.9 (7.2)  |
| MDD Current Episode (%)                   | 20 (52.63) | 10 (32.36)  |
| MDD Lifetime (%)                          | 29 (76.32) | 18 (58.06)  |
| Social Anxiety Disorder (%)               | 12 (31.58) | 11 (35.48)  |
| Agoraphobia                               | 0          | 3 (9.68)    |
| Panic Disorder                            | 1 (2.63)   | 2 (6.45)    |
| PTSD (%)                                  | 0          | 0           |
| Binge Eating Disorder (%)                 | 1 (2.63)   | 1 (3.23)    |

Note. Baseline characteristics assessed at pre-treatment unless noted otherwise. BA: behavioral activation; EXP: exposure; GAD-7: Generalized Anxiety Disorder Scale – 7-item; PROMIS: Patient-Reported Outcomes Measurement Information System.

\*Baseline working alliance assessed at week 3

feared outcomes, and consolidate new learning. A ten-session structured, EXP treatment manual based on an inhibitory learning approach (adapted by study investigators from a previous group-based anxiety treatment manual developed by MGC) [58] was used.

These treatments are similar, but distinct. Across both BA and EXP, therapists (a) assist clients in identifying maladaptive patterns of behavior, (b) assign weekly behavioral homework, and (c) collaborate with clients to plan for long-term behavior change. However, the focus of the behavioral exercises differ, with BA emphasizing engaging in positively reinforcing activities and processing whether these activities improved one's mood while EXP emphasizes the testing of negative expectancies to anxiety-provoking situations and processing whether or not the expected negative outcomes occurred.

## 2.4. Sample size and power analysis

The larger study for which these data were collected sought to evaluate neuroimaging predictors of treatment response and planned to recruit no less than 100 participants. This number was selected to allow for appropriately powered longitudinal data analyses after accounting for a 20 % attrition rate (approximately  $n = 40$  completers per treatment

arm). The secondary data analysis conducted for this study included  $N = 69$  individuals who completed treatment (operationalized as attending 7 or more sessions).

## 2.5. Statistical analyses

Relevant treatment manuals (<https://osf.io/8cfwk/>), as well as analysis scripts and data (<https://data.mendeley.com/datasets/38s6g3p3t3/1>), are publicly available. All statistical analyses were run using R statistical software (R version 4.2.1). Differences between treatment-arms in demographic and clinical characteristics at baseline were assessed using Welch's  $t$ -tests for continuous variables and chi-squared analyses for categorical variables (if any cell contained  $< 5$  observations, Fisher's exact test was used). To decrease the risk of family-wise type I error, and to address the significant conceptual overlap discussed previously, factor extraction was performed on data derived from six measures of loneliness, social isolation, and social support. For this purpose, correlation matrices and regularized factor analyses were conducted for social well-being measures at pre- and post-test. Based on these results, composite variables for pre- and post-test were formed by summing the  $z$ -scores for the instruments associated with each composite identified. Changes over time in working alliance (WAI) and each social well-being composite (isolation/loneliness and social support) were assessed separately using two-way mixed ANOVA. Regression analyses were used to examine whether baseline social well-being composite scores moderated symptom severity across 10 weekly sessions and at post-treatment (as measured by GAD-7 or PROMIS Depression), with baseline symptom severity included as a covariate and participant ID entered as a random effect. We report whether findings that meet  $p < .05$ , focusing on the three-way interactions (e.g., social composite\*treatment\*timepoint) for each of the two symptom outcomes (GAD-7, PROMIS Depression) and report effect sizes for all analyses. Sensitivity analyses were also conducted re-estimating the regression models while covarying for group therapy cohort and format differences introduced by the COVID-19 protocol modification; results were unchanged (see supplement for additional details, including Table S1). Regularized common factor analysis was conducted using the 'fareg' function from the 'fungible' package [59], linear mixed-effects regressions (LMEs) were conducted via the 'lmer' function from the 'lme4' package [60], and Johnson-Neyman analyses were conducted via the 'sim\_slopes' and 'johnson\_neyman' functions from the 'interactions' package [61].

## 3. Results

### 3.1. Demographic and clinical characteristics

All 69 (31 EXP, 38 BA) participants who completed treatment (i.e., attended at least 7 sessions) were included in analyses (see Table 1 for demographic and baseline clinical characteristics). Participants who started but did not complete treatment included (a) fewer participants with education equal to or greater than a Bachelor's degree, and (b) higher depression at baseline. Observed differences between participants who did not start treatment ( $n = 25$ ), participants who started but did not complete ( $n = 25$ ), and participants who completed treatment ( $n = 69$ ) are described in supplemental materials. No significant differences were observed between treatment groups in rates of treatment completion and follow-up completion (Table S2).

### 3.2. Composite social well-being variables

Correlation matrices (Table S3) calculated separately at pre-test and post-test provided initial support for two latent variables: (a) isolation/loneliness (PROMIS Social Isolation; NIH Toolbox Friendship, and Loneliness), and perceived social support (PROMIS Emotional Support, Instrumental Support, and Informational Support). These latent

variables were further supported through regularized factor analysis (Table S4). Given both the data and previous literature [21,22,62–64] supported a two-factor solution for data reduction, composite variables were formed by summing the  $z$ -scores for the three instruments associated with each composite.

### 3.3. Treatment effects on symptom outcomes

As has been reported in our prior publication [49], statistically significant linear improvements were found in both treatments-arms (BA and EXP) across primary (GAD-7) and secondary clinical outcomes (PROMIS Depression and Anxiety, SDS). Although no significant time-point by treatment interaction was observed for GAD-7, BA was associated with steeper linear declines in PROMIS Depression, PROMIS Anxiety and SDS. A statistical summary of observed main effects and interactions are included in Table S5.

### 3.4. Changes in social well-being and working alliance

Two-way mixed ANOVA were used to assess changes in isolation/loneliness, social support, and working alliance over time (see Table S6). Significant main effects of time included a significant decrease in isolation/loneliness (pre to post;  $p < .001$ ,  $\eta^2 = 0.333$ ), and significant increases in both social support (pre to post;  $p < .001$ ,  $\eta^2 = 0.19$ ) and working alliance (week three to week nine;  $p < .001$ ,  $\eta^2 = 0.359$ ). While there were no significant time by treatment interaction effects, post-hoc within-subjects ANOVAs revealed trends towards larger effects sizes for BA than EXP (see Table S6), including isolation/loneliness (BA:  $p < .001$ ,  $\eta^2 = 0.41$ ; EXP:  $p = .004$ ,  $\eta^2 = 0.249$ ), social support (BA:  $p = .001$ ,  $\eta^2 = 0.267$ ; EXP:  $p = .068$ ,  $\eta^2 = 0.107$ ), and working alliance (BA:  $p < .001$ ,  $\eta^2 = 0.377$ ; EXP:  $p = .011$ ,  $\eta^2 = 0.202$ ). Pre- to post-treatment change across individual measures of each composite variable are provided in Table S7.

### 3.5. Social well-being and trajectory of treatment outcome

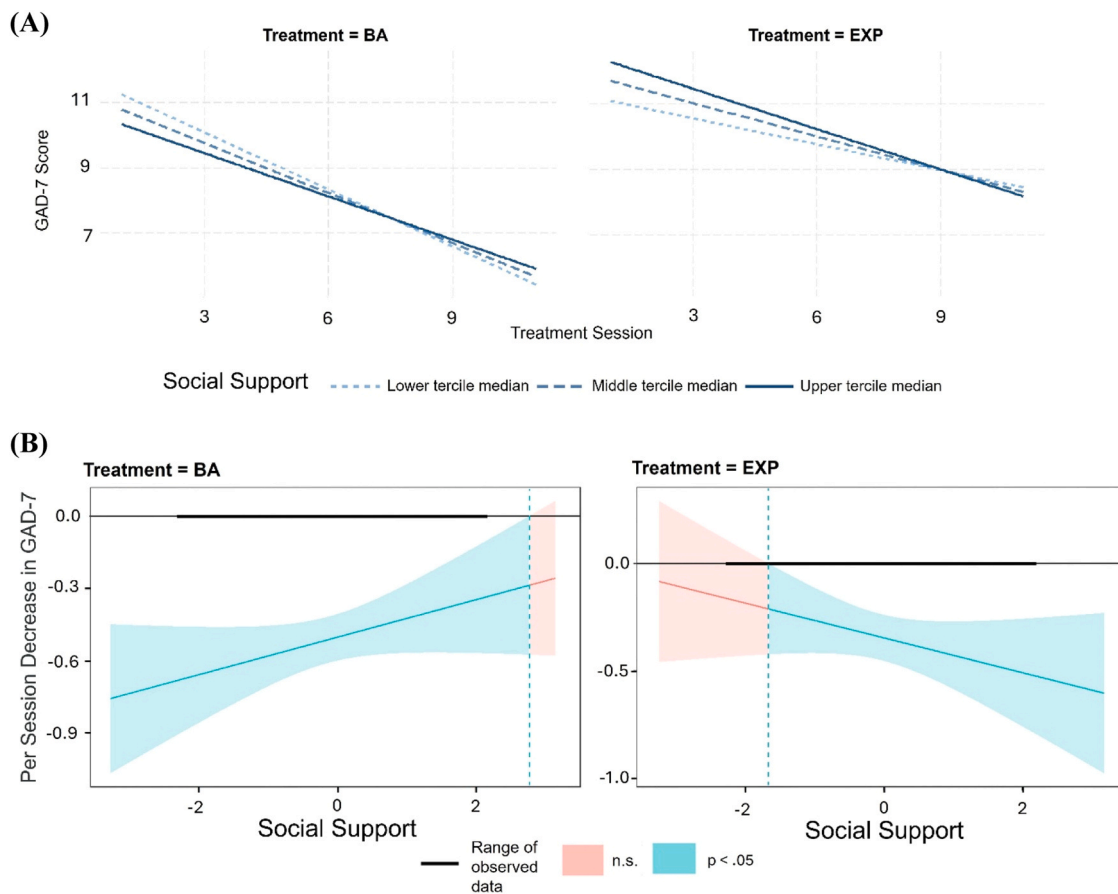
#### 3.5.1. Social well-being and anxiety

The LME predicting trajectory of GAD-7 using baseline social support revealed a three-way interaction ( $p = 0.030$ ,  $d = 0.17$ ; social support\*treatment\*timepoint), with no significant main effect or two-way interactions (see Table S8 for full statistical results). Simple slopes analysis (see Fig. 1) demonstrated the treatment effect of BA increased for those with lower social support ( $-1$  SD: standardized  $\beta = -0.58$ ,  $SE = 0.07$ ,  $t = -8.91$ ,  $p < .001$ ;  $0$  SD:  $\beta = -0.51$ ,  $SE = 0.05$ ,  $t = -10.47$ ,  $p < 0.001$ ;  $+1$  SD:  $\beta = -0.44$ ,  $SE = 0.07$ ,  $t = -6.84$ ,  $p < .001$ ), while the treatment effect of EXP decreased with lower social support ( $-1$  SD:  $\beta = -0.26$ ,  $SE = 0.08$ ,  $t = -3.46$ ,  $p = .001$ ;  $0$  SD:  $\beta = -0.34$ ,  $SE = 0.05$ ,  $t = -6.38$ ,  $p < 0.001$ ;  $+1$  SD:  $\beta = -0.41$ ,  $SE = 0.07$ ,  $t = -5.89$ ,  $p < .001$ ). Johnson Neyman (JN) analyses indicated the significance region for the treatment effect of BA included all participants in the present sample; however, for EXP, the slope of the treatment effect was not significant for those with baseline social support  $\leq -1.60$  SD (observed range =  $-2.19$  –  $-2.26$ ). The LME predicting trajectory of GAD-7 using baseline isolation/loneliness revealed no significant main effect, two-way interactions, or three-way interactions.

#### 3.5.2. Social well-being and depression

The LME predicting trajectory of PROMIS depression using baseline isolation/loneliness revealed a trend level three-way interaction ( $p = 0.025$ ,  $d = 0.17$ ; isolation/loneliness\*treatment\*timepoint), with no significant main effect or two-way interactions (see Table S9 for full statistical results). Simple slopes analysis (see Fig. 2) demonstrated that greater isolation/loneliness related to a better treatment response for BA ( $-1$  SD:  $\beta = -0.60$ ,  $SE = 0.12$ ,  $t = -4.98$ ,  $p < .001$ ;  $0$  SD:  $\beta = -0.69$ ,  $SE = 0.07$ ,  $t = -10.22$ ,  $p < 0.001$ ;  $+1$  SD:  $\beta = -0.75$ ,  $SE = 0.10$ ,  $t = -7.54$ ,  $p < .001$ ) and worse treatment response for EXP (negative;  $-1$  SD:  $\beta =$





**Fig. 1. Moderating influence of social support on trajectory of anxiety treatment response.** Fig. 1. Johnson-Neyman (JN) and Interaction plots reflecting the differential influence of baseline social support on the trajectory of anxiety symptoms (GAD7) throughout the course of Behavioral Activation (BA) and Exposure Therapy (EXP). **A**) Interaction plot for linear relationship between timepoint, GAD7 score, and treatment depicting degree of social support by tertile for BA (left) and EXP (right); lower tertile (light blue dotted line), middle tertile (blue dashed line), and upper tertile (dark blue solid line). Lower scores reflect lower levels of anxiety. **B**) JN plot representing slope of relationship between treatment session and GAD7 scores in BA (left) and EXP (right) as a function of baseline social support. The vertical axis represents the mean change in GAD-7 scores each session. Blue shaded region represents social support values where BA was effective (i.e., had a significant impact on symptoms over time), while the bold horizontal line represents range of observed social support within sample (z-scores).

$-0.37$ ,  $SE = 0.09$ ,  $t = -4.03$ ,  $p < .001$ ;  $0\ SD$ :  $\beta = -0.18$ ,  $SE = 0.08$ ,  $t = -2.27$ ,  $p = 0.024$ ;  $+1\ SD$ :  $\beta = -0.04$ ,  $SE = 0.10$ ,  $t = -0.39$ ,  $p = .70$ ). JN analyses indicated the treatment effect of BA was not significant for those with baseline isolation/loneliness  $\leq -2.52\ SD$ , while the treatment effect of EXP was not significant for those with baseline isolation/loneliness  $\geq 0.23\ SD$ . The LME predicting trajectory of PROMIS Depression using baseline social support revealed no significant main effect, two-way interactions, or three-way interactions.

### 3.5.3. Social well-being and working alliance

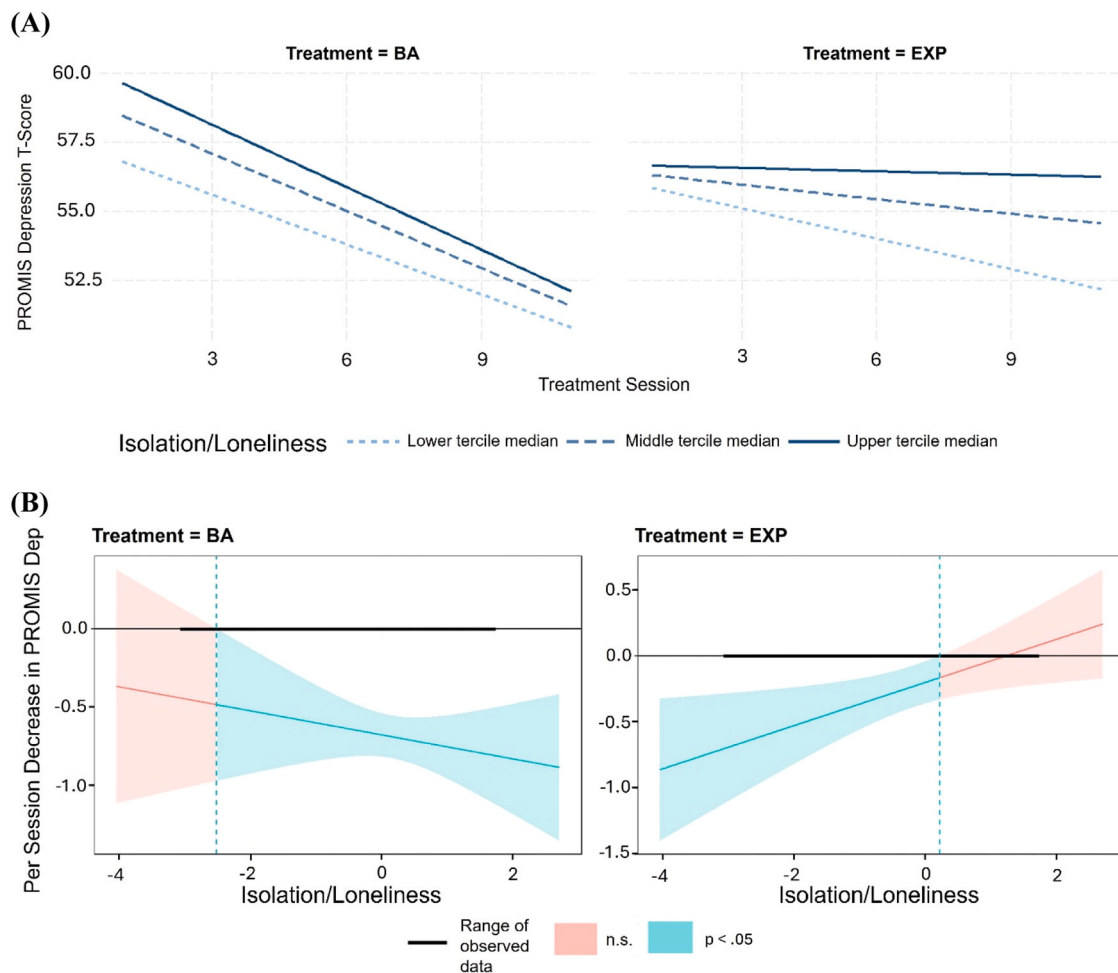
The LME predicting trajectory of client self-reported working alliance using baseline isolation/loneliness revealed a significant three-way interaction ( $p = 0.015$ ,  $d = 0.44$ ; isolation/loneliness  $\times$  treatment  $\times$  timepoint), with no significant main effect or two-way interactions (see Table S10 for full statistical results). Simple slopes analysis (see Fig. 3) demonstrated that greater isolation/loneliness related to less of an increase in working alliance over time for BA (negative;  $-1\ SD$ :  $\beta = 0.15$ ,  $SE = 0.04$ ,  $t = 3.41$ ,  $p = .001$ ;  $0\ SD$ :  $\beta = 0.10$ ,  $SE = 0.02$ ,  $t = 4.05$ ,  $p < 0.001$ ;  $+1\ SD$ :  $\beta = 0.05$ ,  $SE = 0.04$ ,  $t = 1.52$ ,  $p = .13$ ) and a greater increase in working alliance over time for EXP (positive;  $-1\ SD$ :  $\beta = 0.05$ ,  $SE = 0.03$ ,  $t = 1.75$ ,  $p = .08$ ;  $0\ SD$ :  $\beta = 0.11$ ,  $SE = 0.03$ ,  $t = 4.11$ ,  $p < .001$ ;  $+1\ SD$ :  $\beta = 0.15$ ,  $SE = 0.04$ ,  $t = 4.07$ ,  $p < .001$ ). JN analyses indicated the effect of time on working alliance for BA was not significant for those with baseline emotional isolation  $\geq 1.71\ SD$ , while the effect of time on working alliance for EXP was not

significant for those with baseline isolation/loneliness  $\leq -0.80\ SD$ . The LME predicting trajectory of working alliance using baseline social support revealed no significant main effect, two-way interactions, or three-way interactions.

## 4. Discussion

Results from the current study offer preliminary support for the hypothesis that specific facets of social well-being (namely isolation, loneliness, and social support) may moderate treatment outcomes for depression and anxiety [22], consistent with prior studies linking these constructs to poorer treatment outcomes [22,65,66]. Our findings, demonstrating that social support and isolation/loneliness may differ in the types of symptom response (generalized anxiety versus depression) they moderate, are also consistent with studies suggesting these are two distinct but related facets of the same construct [62–64]; with social support being perceived low availability and acceptability of social relationships, and isolation/loneliness relating to perceived low adequacy and negative emotional impact of social relationships. If replicable, these results have the potential to clarify differences in predictive utility between social support and isolation/loneliness, enhancing treatment response through personalized patient-treatment matching.

The hypothesis that facets of social well-being (i.e., lower isolation and loneliness; greater social support assessed at baseline) would relate to better outcomes for BA and worse outcomes for EXP was largely



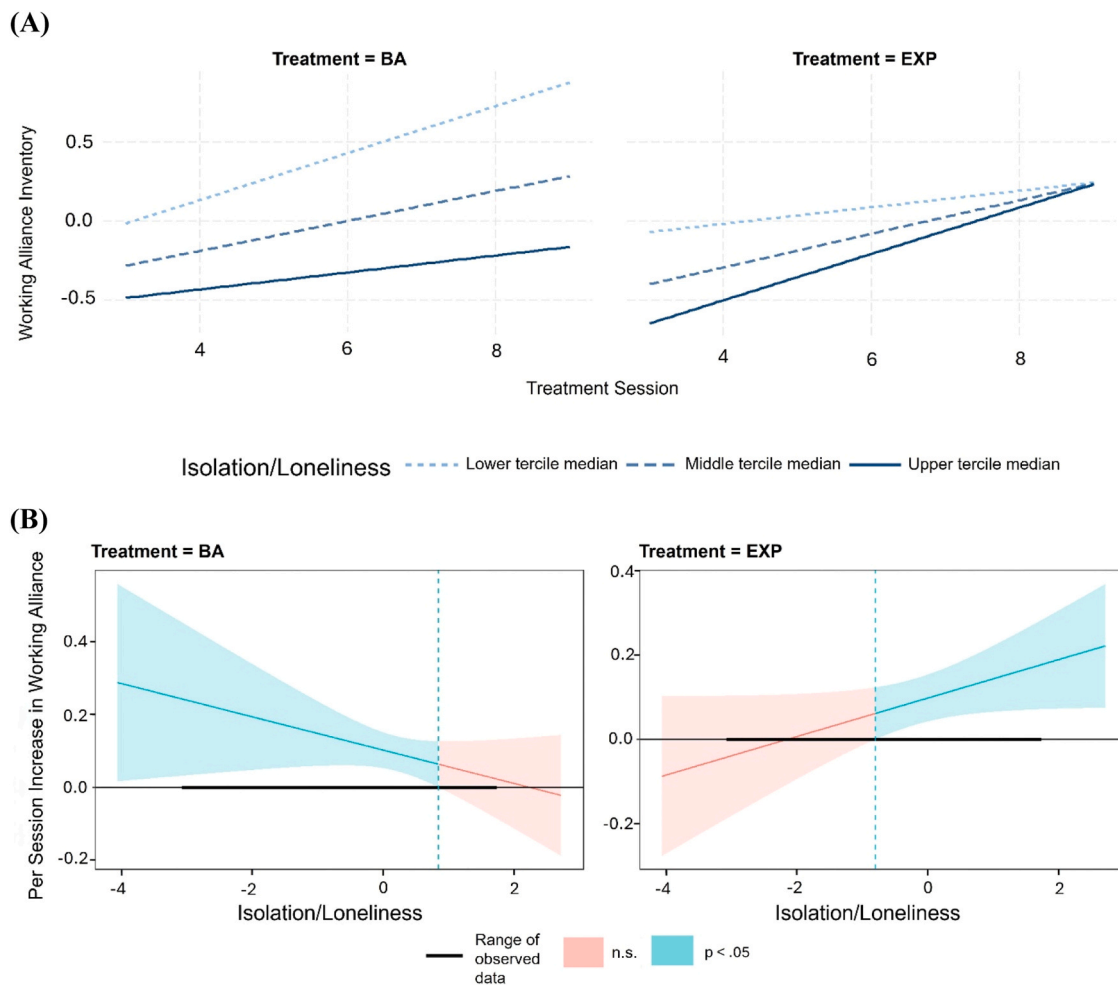
**Fig. 2. Moderating influence of isolation/loneliness on trajectory of depression treatment response.** Fig. 2. Johnson-Neyman (JN) and Interaction plots reflecting the differential influence of baseline isolation/loneliness on the trajectory of depression symptoms (PROMIS-D) throughout course of Behavioral Activation (BA) and Exposure Therapy (EXP). **A**) Interaction plot for linear relationship between timepoint, PROMIS-D score, and treatment depicting degree of isolation/loneliness by tercile for BA (left) and EXP (right); lower tercile (light blue dotted line), middle tercile (blue dashed line), and upper tercile (dark blue solid line). Lower scores reflect lower levels of depression. **B**) JN plot representing slope of relationship between treatment session and PROMIS-D scores in BA (left) and EXP (right) as a function of baseline isolation/loneliness. The vertical axis represents the mean change in PROMIS Depression scores each session. Blue shaded region represents isolation/loneliness values where BA was effective (i.e., had a significant impact on symptoms over time), while the bold horizontal line represents range of observed isolation/loneliness within sample (z-scores).

supported. Consistent with predictions, social support (but not isolation/loneliness) moderated anxiety symptom outcomes in the expected direction, such that lower perceived social support predicted poorer improvement in EXP and greater improvement in BA. Conversely, isolation/loneliness (but not social support) moderated depression symptom outcomes in the expected direction, with higher baseline isolation/loneliness predicting greater symptom improvement in BA. Together, these results suggest that distinct facets of social well-being differentially predicted response to BA and EXP, with social support more strongly linked to anxiety outcomes and isolation/loneliness more strongly linked to depression outcomes.

These findings align with and extend prior research on social well-being and treatment response. Although few studies have examined the relationship between social support and anxiety treatment response, available evidence similarly links lower social well-being at baseline with higher post-treatment anxiety severity [67,68]. Prior studies have also found the predictive relationship between isolation/loneliness and post-treatment anxiety symptoms becomes nonsignificant when controlling for relevant covariates (including baseline symptom severity [69]). In the present study, greater isolation/loneliness corresponded to improved depression treatment response for BA and poorer depression

response for EXP, consistent with recent research suggesting isolation and loneliness are more strongly associated with depression than with anxiety [65,66]. Notably, among participants who received EXP, those experiencing higher levels of isolation/loneliness ( $\geq 0.22$  standard deviations above the sample mean) demonstrated no significant session-to-session improvement in depression symptoms. This pattern may reflect BA's emphasis on engagement in meaningful or rewarding activities, which could be more effective at counteracting emotional loneliness. Additionally, individuals with high levels of isolation/loneliness may have difficulty engaging in or benefiting from EXP activities.

The significant moderation of anxiety and depression by separate facets of social well-being was somewhat unexpected. One possible explanation is that, while overlapping and interrelated [21], perceived social support and self-reported isolation/loneliness may differentially moderate symptom outcomes as a function of their non-overlapping measurement. For example, the perceived availability of social support may relate more to the social avoidance behaviors that often accompany anxiety disorders (e.g., due to social anxiety and/or other fears associated with GAD, such as fears of conflict or evaluation) whereas the perceived adequacy or emotional impact of social



**Fig. 3. Moderating influence of isolation/loneliness on trajectory of working alliance.** Fig. 3. Johnson-Neyman (JN) and Interaction plots reflecting the differential influence of baseline isolation/loneliness on the trajectory of client-reported working alliance (WAI) throughout course of Behavioral Activation (BA) and Exposure Therapy (EXP). **A)** Interaction plot for linear relationship between timepoint, WAI score, and treatment depicting degree of isolation/loneliness by tertile for BA (left) and EXP (right); lower tertile (light blue dotted line), middle tertile (blue dashed line), and upper tertile (dark blue solid line). Lower scores reflect lower levels of working alliance. **B)** JN plot representing slope of relationship between time and WAI scores in BA (left) and EXP (right) as a function of baseline isolation/loneliness. The vertical axis represents the mean change in working alliance scores each session. Blue shaded region represents values of isolation/loneliness where working alliance changed significantly over time, while bold horizontal line represents range of observed working alliance within sample (z-scores).

relationships may relate more directly to depressive symptomatology such as negative cognitive biases or anhedonia. Alternatively, discrepancies between the current and prior findings could reflect differences in sample characteristics (e.g., a focus on GAD in the current sample versus primarily depression in other samples) or in the specific treatment modalities examined.

We also explored the degree to which loneliness predicted participant perception of working alliance with their therapist. For both treatments, baseline isolation/loneliness moderated the relationship between time and working alliance. While working alliance increased over time (on average) for both BA and EXP, greater isolation/loneliness at baseline was associated with weaker improvements in working alliance over time for BA; conversely, decreased baseline isolation/loneliness was associated with weaker increases in working alliance for EXP. Although few studies have investigated the influence of social well-being on working alliance [70], these results are consistent with available evidence showing patient perceptions of social support significantly predicts patient-therapist alliance [41,47]. While speculative, it is possible clients endorsing high levels of isolation/loneliness in BA may experience smaller increases in the therapeutic relationship over time due to the treatment's emphasis on re-engaging with activities consistent with their goals and values outside of therapy, resulting in

re-engagement with valued social relationships and less reliance on the relationship with the therapist. Isolated/lonely clients in EXP may experience larger improvements over time in their relationship with the therapist due to the absence of an explicit component targeting re-engagement with rewarding social contexts, resulting in more reliance on and emotional attachment to the therapeutic relationship itself; alternatively, isolated/lonely clients may rely on increased trust and connection with the therapist to support and motivate participation in anxiety-provoking exposure exercises.

Despite the observed differential moderation of symptom outcomes and working alliance, both BA and EXP improved social well-being over time to a similar degree (see supplement for further details, including Tables S5 and S6). These improvements were modest, however, with effect sizes ranging from small to moderate; consistent with effect sizes observed in other studies analyzing the effect of psychotherapy on social well-being [71,72]. Given the harmful impact of social disconnection and loneliness on physical and mental health [23–25], these findings support recent arguments that future research on behavioral therapies (and psychotherapy in general) would benefit from increased focus on identifying ways to improve secondary outcomes such as social connectedness, loneliness, and positive emotions [73,74].

#### 4.1. Limitations and future directions

This exploratory secondary analysis, drawn from a larger trial investigating neural predictors of treatment outcomes, should be interpreted with caution. The study was under-powered to detect small differences in predictive relationships and requires replication in larger samples. Focusing on behavioral activation (BA) and exposure-based therapy (EXP) allowed direct comparison of two evidence-based behavioral therapies, but the lack of an attentional control or non-behavioral comparator (e.g., cognitive, interpersonal, etc.) limits inferences regarding alternative therapeutic approaches. Additionally, as most participants received small-group therapy, generalizability to individual treatment formats remains uncertain.

##### 4.1.1. Sample characteristics

Participants were predominately female (90 %) and white (61 %), which may limit the generalizability of these findings to more diverse populations. Further, individuals with severe depression and/or suicidal plan or intent were excluded from recruitment in the larger study, so findings may not extend to these clinical presentations.

##### 4.1.2. Blinding considerations

Participant and therapist blinding were not feasible for the present study, due to both behavioral activation and exposure-based therapy including explicit instruction, rationale, and between-session practice as necessary treatment components. This limitation, however, is inherent to psychotherapy research. Expectancy and allegiance effects were mitigated through manualized protocols, matched session structure, weekly supervision, and independent fidelity ratings.

##### 4.1.3. Self-rated outcomes

This analysis focused on self-report outcomes (GAD-7, PROMIS Depression). Exclusive reliance on self-report may miss discrepancies with clinician-rated assessments. Future research should examine whether these moderation effects replicate using clinician-rated measures and converge across assessment methods.

#### 5. Conclusion

Current findings point towards distinct facets of social well-being, including isolation/loneliness and perceived social support, as potential moderators of treatment response to behavioral therapy for GAD. Of particular importance from a personalized medicine perspective, these moderators were assessed using measures which are psychometrically sound, brief, publicly available, and free (i.e., no associated fees or royalties). The effects of BA and EXP differed according to participants' pretreatment composite scores for two separate components of social well-being (isolation/loneliness, and social support). Specifically, individuals reporting greater isolation/loneliness showed improved outcomes for depression symptoms with BA (but benefitted less from EXP), whereas those reporting greater social support showed improved anxiety outcomes with EXP (but benefitted less from BA). This pattern was most pronounced for depression, with individuals reporting levels of isolation/loneliness  $\geq 0.22$  standard deviations above the sample mean showing no significant reduction in depression symptoms with EXP. Collectively, these findings suggest that baseline assessments of social well-being (i.e., loneliness, isolation, social support) may offer clinically relevant guidance for personalized behavioral treatment planning.

It should be noted that, given this study did not test personalized assignment to BA versus EXP based on social well-being or pre-treatment social well-being interventions, implications for how targeting of social well-being may impact behavioral therapy for GAD remain hypothesis-generating. Clients who report higher isolation and loneliness appeared more likely to benefit from BA for depression outcomes, whereas clients with relatively stronger perceived social support showed better anxiety outcomes with EXP. For clients presenting with high loneliness and

isolation or low social support, incorporating a brief focus on social well-being before or during the early stages of exposure-based work may help optimize response. Future studies examining the moderating effects of multiple components of social well-being on treatment outcomes should include diverse measures and more than one symptom domain, as distinct facets may moderate different clinical outcomes. Prospective research assigning individuals to BA versus EXP is needed to determine the relevance of these findings for personalized intervention approaches.

#### Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Martin Paulus reports a relationship with Wolters Kluwer UpToDate that includes: consulting or advisory. Declaration of Competing Interest. The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Christopher Martell reports receiving royalties for four books on the topic of behavioral activation; Martin Paulus has received royalties for an article, published in UpToDate, on the subject of methamphetamine; all other authors have no conflicts of interest to declare. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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#### Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.xjmad.2025.100160](https://doi.org/10.1016/j.xjmad.2025.100160).

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