Data Supplement for Garland et al., Mindfulness-Oriented Recovery Enhancement for Veterans and Military Personnel on Long-Term Opioid Therapy for Chronic Pain: A Randomized Clinical Trial, Amer J Psychiatry (doi: 10.1176/appi.ajp.20230272).

Supplemental Materials.

Additional Details of Analytic Models.

For further clarification of our constrained longitudinal data analysis (cLDA) models, baseline measurements were taken prior to randomization to supportive psychotherapy (Support) or MORE conditions, so treatment group means are assumed equal at baseline, but free to vary at times 2-5. Covid-19 restrictions, which were instituted mid-study, necessitated a change in format. Therapy sessions were initially conducted face-to-face (FACE), but were subsequently implemented remotely via ZOOM to comply with requirements. Since this format change could not be randomized, we treat online status as an observational stratification variable. All patients experienced either one format or the other; there was no cross-over. Conceptually, separate randomized analyses of treatment impact were conducted within each format, and the principal estimand of overall treatment impact was taken to be the unweighted mean of the two administrative formats.

The full analysis model for each outcome measure *m* incorporates the complication of the unforeseen administrative format change by positing that each individual i is nested within one of four mutually exclusive groups *g* (1=Support+FACE, 2=Support+ZOOM; 3=MORE+FACE; 4=MORE+ZOOM):

$$(1)\quad y_{igt}^{(m)} = \mu_{gt}^{(m)} + b_{ig}^{(m)} + \varepsilon_{igt}^{(m)},\ b_{ig}^{(m)} \sim N(0,\psi_i^{(m)}),\ \varepsilon_{igt}^{(m)} \sim N(0,\theta^{(m)}),$$
$$where\ \mu_{11}^{(m)} = \mu_{31}^{(m)}\ and\ \mu_{21}^{(m)} = \mu_{41}^{(m)},$$

and all other means vary freely. The two constraints fix MORE and Support population means equal at pre-randomization baseline within, but not between, the FACE and ZOOM formats. Serial dependence is modeled by normally distributed random intercepts, along with normally distributed random error. Under maximum likelihood, and with no additional covariates, mixed effects and structural equation formulations of the model are equivalent and produce identical results.

Equation (1) defines the full, unrestricted model given within-setting baseline equality of MORE and Support. For each outcome m, the overall treatment impact within each setting is given by

$$\delta_{FACE}^{m} = \sum_{t>1}(\mu_{1t}^{(m)} - \mu_{3t}^{(m)})/4\ \ and$$
$$\delta_{ZOOM}^{m} = \sum_{t>1}(\mu_{2t}^{(m)} - \mu_{4t}^{(m)})/4 \quad .$$

The each outcome is defined as in:

$$\delta_{TX}^{m} = (\delta_{FACE}^{m} + \delta_{ZOOM}^{m})/2\ ,$$

which represents the expected overall (mean) benefit of treatment over four timepoints in a population where the presentation modalities (in-person versus remote) are equally likely. As a mixed effects model, each outcome is estimated and evaluated as a custom contrast on the parameters of model (1). As a structural equation model, the unrestricted and restricted models are compared, yielding the same estimates and hypothesis test.

The SEM reference model (1) is unrestricted apart from the two mean baseline equality specifications. The constrained model is obtained by further imposition of direct equality restrictions on the within-format MORE and supportive psychotherapy adjusted post-baseline means. Other standard assumptions of the mixed effects context (eg, equality of covariance structures across the four groups) are imposed on the unrestricted model and maintained in the restricted model, resulting in an overall single degree-of-freedom test that

$H_0 : \delta^m_{TX} = (\delta^m_{FACE} + \delta^m_{ZOOM}) / 2 = 0$.

Conditional on significance of the omnibus multivariate test, we examined the univariate treatment impact on each outcome using the cLDA approach under a mixed effects model likelihood framework. For each outcome, the null hypothesis posited equal baseline-adjusted mean treatment arm differences over the four post-baseline timepoints, assuming equal treatment arm means at pre-randomization baseline, with compound symmetry covariance structure. The single degree-of-freedom estimates and tests were implemented using SAS "Estimate" coefficients, and evaluated against the null at alpha=.05, two-sided, with conservative Kenward-Roger degrees of freedom. Time was treated as a categorical factor with four post-baseline levels. The unforeseen administration format change (face-to-face versus Zoom) was modeled as an observational stratification variable under the assumption that Support and MORE population baseline means were equal within, but not across, each stratum. The overall estimate of impact was obtained for each outcome as the unweighted mean of the within-stratum MORE minus Support benefits. No additional covariates were considered for these primary analyses.