Individual Differences in the Affective Response to Pandemic-related Stressors in COVID-19 Healthcare Workers

SUPPLEMENTARY INFORMATION

SUPPLEMENTARY METHODS

Participants. 2,307 healthcare workers in an academic medical center participated in an online survey. Enrollment was open from May 5th, 2020 through January 6th, 2021. All healthcare workers in the institution were eligible to participate, and there were no exclusion criteria. Participants were made aware of the survey through an announcement by institutional leadership in a video update on the COVID-19 pandemic, through announcements on the home page of the institutional website, and through emails to employee email lists. Individuals who participated in the survey in May or June, 2020 (comprising 1,773 of the 2,307 participants) were invited to participate in a follow-up assessment approximately six months after the initial assessment. 334 (18.8%) of these 1,773 subjects agreed to participate in the follow-up assessment. The content of the baseline and six-month follow-up assessments are described below. Participation in both assessments was anonymous and confidential, and individual subject responses in the baseline and follow-up assessments were linked by assigning each participant a unique, anonymous coded ID number. Demographic data and other details of the sample are described below (in the Results section) and in **Supplementary Table S1.** These procedures were reviewed and approved by the Institutional Review Board at Weill Cornell Medicine, and all subjects provided informed consent to their participation. Reporting procedures were designed to adhere to the standards described in the American Association of Public Opinion Research Code of Professional Ethics and Practice (November 2015).

Survey Measures. *Baseline assessment.* The baseline survey assessment was designed to accomplish three goals. First, we sought to quantify the prevalence of clinically significant depression and anxiety symptoms. The primary outcomes measures were the Patient Health Questionnaire (PHQ-9) and Generalized Anxiety Disorder (GAD-7) self-report scales, assessing depression and anxiety, respectively. As per standard criteria, clinically significant depression and anxiety were defined as PHQ-9 and GAD-7 scores >= 10, providing 88–89% sensitivity and 82–88% specificity for presence of moderate or severe major depression and generalized anxiety disorder in large-scale validation studies (1,2).

Second, we sought to identify risk factors for adverse mental health outcomes. Based on early reports from COVID-19 healthcare workers in China (3), we collected data on age, gender, marital status, occupation (attending physician, resident physician, physician assistant, nurse, clinical psychologist, social worker, chaplain, administrative staff, and hospital support staff, e.g. radiology technicians, respiratory therapists, patient transport, housekeeping and maintenance), and redeployment status (whether a participant was redeployed to other perform other hospital duties distinct from their usual work responsibilities). Age was ascertained in categorical bins (18-25, 26-34, 35-44, 45-54, 55-64, 65-74, 75+) to preserve confidentiality for participants who might otherwise be identified by their gender, age, occupation, and work location. Gender was assessed by asking participants to specify their gender identity: male, female, or other / prefer not to say. To assess the impact of factors related to COVID-19 exposure risk at work, we collected data on three factors: work location (e.g. ICU, Emergency Department, General Medicine, Consults, Telemedicine), self-reported direct contact with COVID-19 patients, and whether a participant was working on site or working remotely. To assess the impact of factors related to pandemic-related stressors, we asked participants to “tell us how much you have been affected by the following problems: 1) fear of contracting COVID-19, 2) child care, 3) financial difficulties / loss of income, 4) isolation from friends and family, 5) family / close friend infected with COVID-19, and 6) family / close friend dying or nearly dying from COVID-19.” For these questions, participants were invited to respond, “not at all affected, somewhat affected, very much affected, or extremely affected,” and their responses were coded 0–3.

Third, as noted above, we sought to connect healthcare workers with counseling and mental health treatment resources if needed. At the end of the survey, participants received immediate feedback on their depression and anxiety symptom scores and information on how to interpret them (mild, moderate,

severe, or very severe as per thresholds established in previous validation studies (1,2). Regardless of their scores, all participants received contact information for counseling services accessible by phone or video conference 7 days per week; referrals for individual psychotherapy or psychiatry if indicated, accessible by phone 7 days per week; and links to self-guided online support resources, including guided meditations and yoga classes.

Follow-up assessment. 334 of the 1,773 subjects who enrolled in the study in May or June also participated in a follow-up assessment approximately six months after their baseline assessment. The content of the follow-up assessment was identical to the baseline assessment, except that we also asked participants to report whether they had accessed any of the support resources identified at the end of the baseline survey. As described in more detail below**,** 58.7% of participants in the follow-up assessment reported using at least one support resource listed on the referral page.

Statistical Analyses. All analyses were conducted in Matlab.

Descriptive statistics. For the analyses in Figures 1 and 2, we generated histograms and boxplots of PHQ-9 and GAD-7 scores by age, gender, and occupation, and calculated the median and interquartile range to describe the distribution of both outcome measures in the baseline assessment sample. Wilcoxon rank sum tests and Kruskal Wallis ANOVA were used to test for effects of age, gender, and occupation on PHQ-9 and GAD-7 scores

Identification of Risk Factors for Depression and Anxiety. For the analyses in Supplementary Figure S1 and Figure 3, we first assessed the impact of three factors that may be related to COVID-19 exposure at work: working on site vs. working remotely, work location (e.g. ICU, Emergency Department, General Medicine, Consults, Telemedicine), and self-reported direct contact with COVID-19 patients. We also assessed the impact of six pandemic-related stressors described above. For both analyses, we used Wilcoxon rank sum tests (working on site, COVID patient contact) or Kruskal Wallis ANOVA (all other factors) to test whether PHQ-9 and GAD-7 scores varied with each factor. We used the Benjamini Hochberg method to control for multiple testing and ensure a false discovery rate (FDR) < 0.05.

Next, to assess how each of the factors above influenced risk for clinically significant depression or anxiety, PHQ-9 and GAD-7 scores were converted to a binary outcome (indicating the presence or absence of moderate or severe depression or anxiety) based on a standard threshold (PHQ-9 or GAD-7 >= 10). We then used a logistic regression model to evaluate the impact of each factor on depression or anxiety risk (two separate models), while controlling for the confounding influence of other correlated risk factors. Adjusted odds ratios and 95% confidence intervals were calculated from the logistic regression model for risk factors found to be statistically significant after FDR correction ($q < 0.05$). In addition to the statistically significant risk factors reported in Figure 3, each logistic regression model also included variables representing gender, marital status, occupation, work location, whether a subject was working on site or remotely, whether a subject reported direct contact with COVID patients at work, and whether a subject reported close friends and family who were infected with COVID-19 or had died from COVID-19. Age-associated risk factors were calculated with respect to the 18-24 year-old age group as a reference. All other variables were binary (e.g. working on site vs. not) or were converted to binary variables (e.g. more than “somewhat affected” by social isolation stress vs. not). As above, we used the Benjamini Hochberg method to control for multiple testing (FDR < 0.05).

Analyses of Changes in Symptoms over Time. To evaluate how PHQ-9 and GAD-7 scores changed over time in Figure 4, we first conducted a cross-sectional analysis testing how the PHQ-9 and GAD-7 scores varied as a function of the day of a participant’s enrollment in the study. We calculated the median PHQ-9 or GAD-7 score for all respondents on each day from May 5th, 2020 to January 6th, 2021. We then used a sliding window of +/– 10 days to calculate a rolling average by day, to enable us to detect trends on the order of 1–2 weeks while reducing noise due to variability in the number of

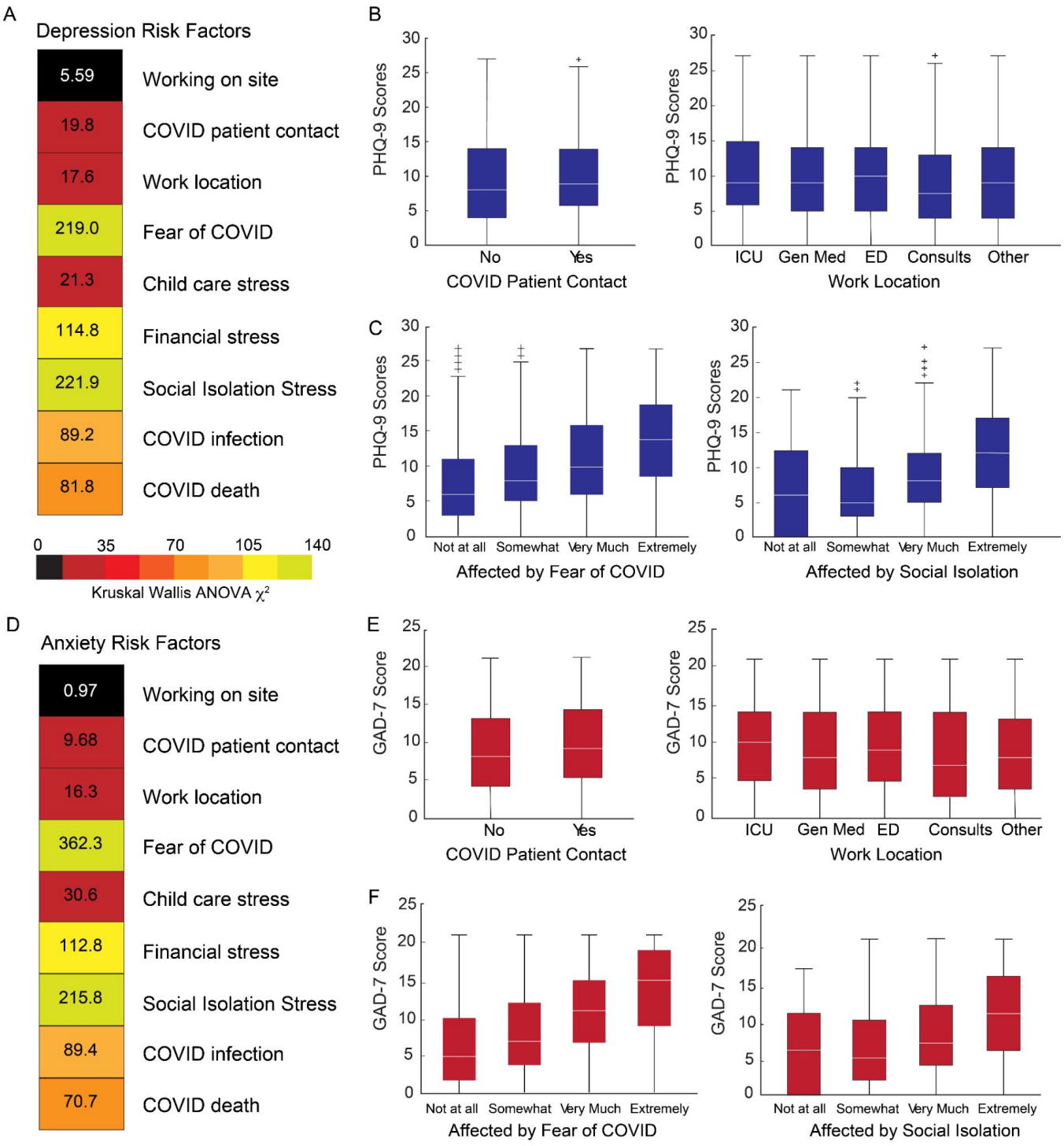
subjects enrolling on a given day. In this way, each daily data point averaged over approximately responses from 900–1000 subjects in May; 260–300 subjects in June; 90–120 subjects in July; 45–60 subjects in August, September, October, and November; and 60–80 subjects in December and January. To test whether changes in PHQ-9 and GAD-7 scores were related to changes in local and national COVID-19 transmission rates, we obtained data on daily new cases from the Centers for Disease Control and Prevention (https://covid.cdc.gov/covid-data-tracker), and computed Pearson correlations between daily new cases and daily mean PHQ-9 and GAD-7 scores.

Next, we conducted a longitudinal analysis of N=334 subjects who enrolled in May or June, 2020 and participated in a follow-up assessment approximately six months later. For this analysis (presented in Figure 5 and Supplementary Figure S2), we generated histograms of PHQ-9 and GAD-7 scores and change in PHQ-9 and GAD-7 scores (follow-up score – baseline score), and we calculated the median and interquartile range to describe the distribution of both outcome measures. We used a Wilcoxon signed rank test to determine whether changes in PHQ-9 and GAD-7 scores were statistically significant in the six-month follow-up assessment. To evaluate the stability of clinically significant depression or anxiety, PHQ-9 and GAD-7 scores were converted to a binary outcome (depressed or not, anxious or not) based on a standard threshold (PHQ-9 or GAD-7 >= 10) as in Figure 3, repeating this process for both the baseline assessment and the six-month follow-up assessment in the N=334-subject follow-up sample.

Principal Components Analysis. In Figure 6 and Supplementary Figure S3, to better understand individual differences in the affective response to pandemic-related stressors and their correlation structure, we used principal components analysis (PCA) to identify a low-dimensional orthogonalized representation of depression and anxiety symptoms and how they co-vary. We focused our analyses on the first seven components, which together explained >80% of the variance in our sample as depicted in the Scree plot in Supplementary Figure S3D. To test whether symptom scores in each PC domain were associated with distinct risk factors, we used Kruskal Wallis ANOVA to test for effects of age, gender, and each of the nine factors examined in Supplementary Figure S1 on component scores across individuals. As above, we used the Benjamini Hochberg method to control for multiple testing (FDR < 0.05).

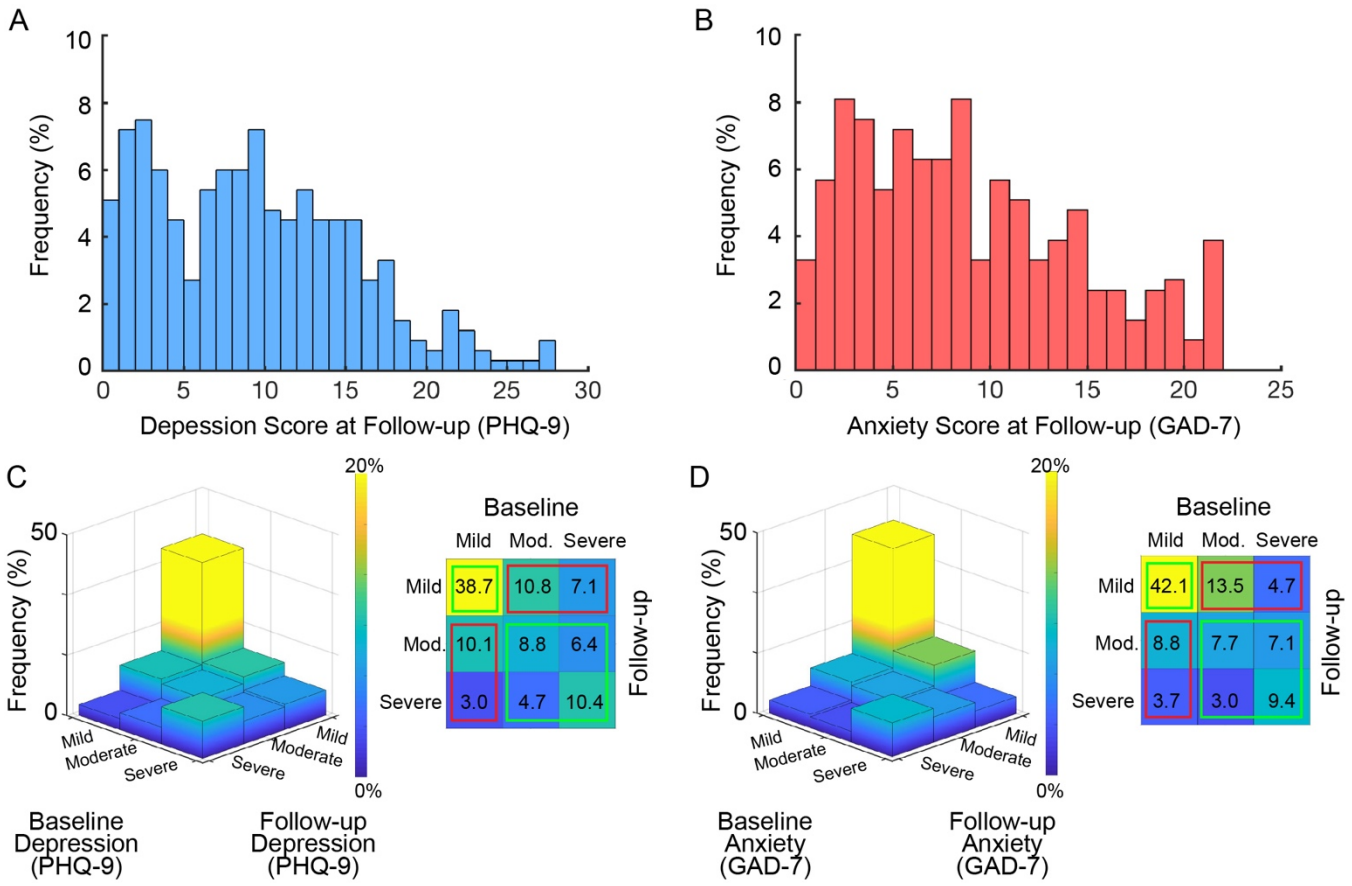
Supplementary Table S1. Demographic Data. Total sample size and demographic data (gender, age, occupation) for the baseline assessment and the 6-month follow-up assessment samples. The PHQ-9 and GAD-7 columns report the median and interquartile range for the total sample and each demographic subset. Note that only individuals who participated in the survey in May or June, 2020 (comprising 1,773 of the 2,307 participants) were eligible to participate in the 6-month follow-up assessment such that the 334-subject follow-up sample represented 18.9% of those eligible.

Table 1	Baseline Sample			Longitudinal Sample Time 1			Longitudinal Sample Time 2		
	N	PHQ-9	GAD-7	N	PHQ-9	GAD-7	N	PHQ-9	GAD-7
Total	2307	9 (5-14)	8 (5-14)	334	9 (5-14)	8 (4-12)	334	8 (3-13)	8 (4-12)
Gender									
Women	1821	9 (5-14)	8 (5-14)	250	9 (6-14)	8.5 (5-14)	250	8.5 (3-13)	8 (4-12)
Men	457	8 (3-14)	7 (3-13)	84	9 (4-16)	7.5 (4-14)	84	9 (3-15)	7 (3-13)
Other / prefer not to say	29	9 (4.75-16)	9 (4.75-12)	0	N/A	N/A	0	N/A	N/A
Age									
18-24	204	11 (7-15)	10 (5-14)	35	15 (8-16)	10 (6-15)	35	11 (7-15)	11 (6-14)
25-34	783	10 (6-15)	10 (5-15)	109	10 (6-13)	11 (5-14)	109	8 (4-14)	7 (4-12)
35-44	600	8 (5-13)	8 (4-14)	84	8 (5-12)	7 (4-14)	84	8 (3-13)	8 (4-11)
45-54	370	8 (4-14)	7 (4-13)	50	10 (5-16)	8 (5-13)	50	9 (6-13)	8 (5-14)
55-64	280	6 (3-10.5)	5 (2-9.5)	44	8.5 (4.5-12)	4.5 (3.5-12)	44	6.5 (1-12)	6 (2.5-9.5)
65+	70	5 (3-10)	4 (2-9)	12	4 (4-17)	4 (4-5)	12	3 (2-9)	3 (2-6)
Occupation									
Attending Physician	192	6 (3-10)	5 (2-10)	44	5 (3-10.5)	7 (4-13)	44	4 (2-12)	3 (2-13)
Resident or Physician Assistant	124	8 (5-12)	7 (4-11)	15	12 (8-12)	5 (1-7)	15	3 (2-10)	3 (3-7)
Nurse	768	9 (6-14)	9 (5-14)	85	9 (7-13)	8 (4-12)	85	9 (6-12)	8 (5-12)
Support Staff	124	12 (7.5-16)	11 (6-16)	20	16 (12-16)	13 (11-15)	20	14 (9-16)	10 (7-14)
Clinical Psychologist, Social Worker, or Chaplain	380	7 (4-13)	7 (4-12)	73	9 (4-13)	8 (4-14)	73	7 (3-12)	7 (3-12)
Administrative Staff / Other	719	9 (5-15)	9 (5-14)	97	9 (5-15)	8 (5-15)	97	10 (3-14)	8 (5-13)

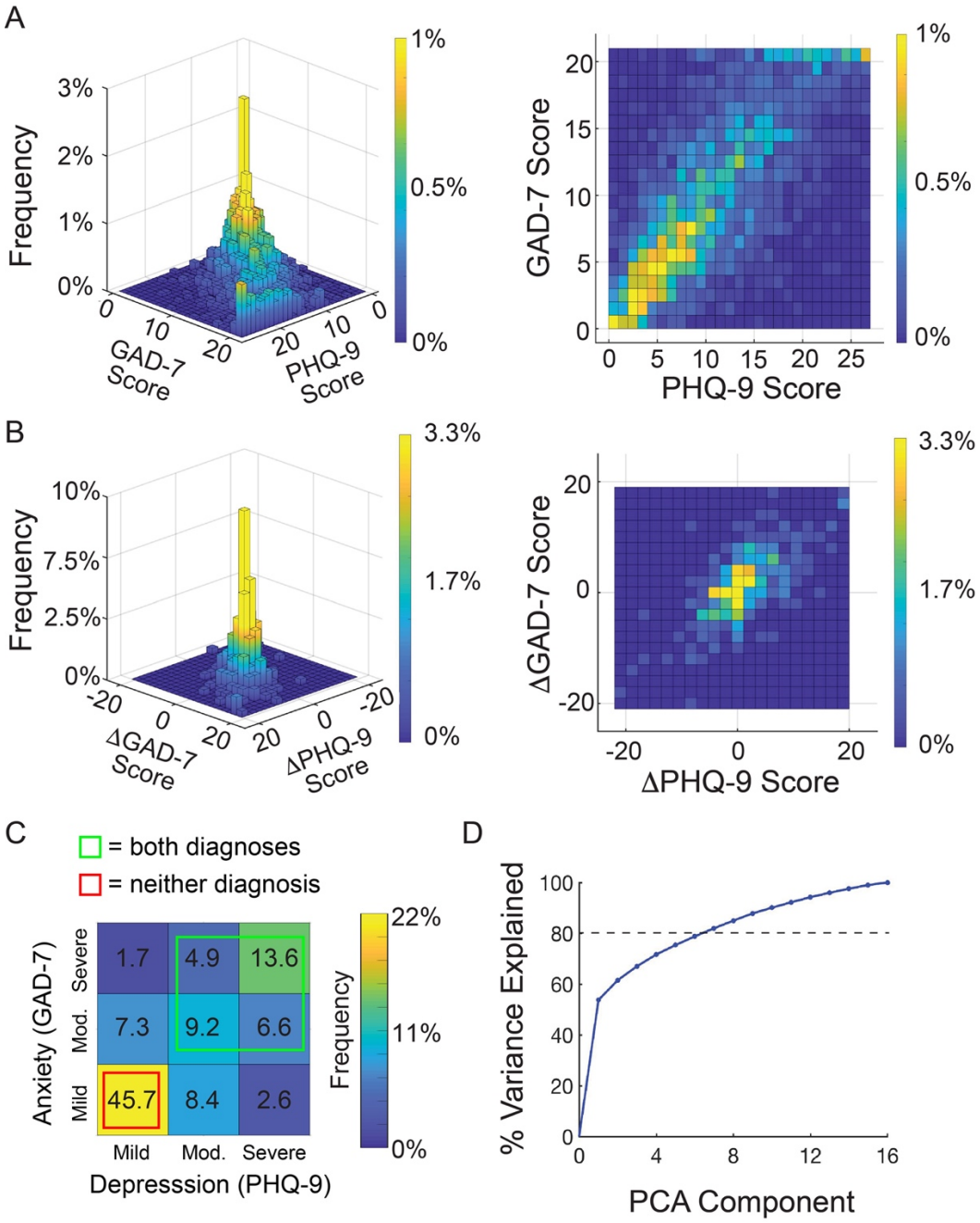


Supplementary Figure S1. Nominal risk factors for clinically significant depression and anxiety. **A.** Heatmap depicting the effect (Kruskal Wallis ANOVA Chi^2) of work-related risk factors and pandemic-related stressors on PHQ-9 depression scores. “COVID infection” and “COVID death” refer to the degree to which a participant reported being affected by a close friend or family member having contracted COVID or having died from COVID. There was no significant effect of working on site. All other effects were significant after FDR correction for multiple testing ($q<0.05$). **B.** Effects of self-reported COVID-19 patient contact (left; Kruskal Wallis ANOVA Chi^2 = 19.8, P = 8.75e-6) and work location (right; Kruskal Wallis ANOVA Chi^2 = 17.6, P = 0.0015) on PHQ-9 depression scores. **C.** Effects

of self-rated fear of contracting COVID-19 (left; Kruskal Wallis ANOVA Chi^2 = 219.0, P = 3.33e-47) and social isolation (right; Kruskal Wallis ANOVA Chi^2 = 221.9, P = 7.84e-48) on PHQ-9 depression scores. **D.** Heatmap depicting the effect (Kruskal Wallis ANOVA Chi^2) of work-related risk factors and pandemic-related stressors on GAD-7 anxiety scores. There was no significant effect of working on site. All other effects were significant after FDR correction for multiple testing ($q<0.05$). **E.** Effects of self-reported COVID-19 patient contact (left; Kruskal Wallis ANOVA Chi^2 = 9.68, P = 0.0019) and work location (right; Kruskal Wallis ANOVA Chi^2 = 16.3, P = 0.0026) on GAD-7 anxiety scores. **F.** Effects of self-rated fear of contracting COVID-19 (left; Kruskal Wallis ANOVA Chi^2 = 362.2, P = 3.28e-78) and social isolation (right; Kruskal Wallis ANOVA Chi^2 = 215.8, P = 1.64e-46) on GAD-7 anxiety scores.



Supplementary Figure S2. Sustained depression and anxiety in a 6-month follow-up assessment. A-B. Histograms of PHQ-9 depression scores (A: median [IQR] = 8 [3-13]) and GAD-7 anxiety scores (B: median [IQR] = 8 [4-12]) at the 6-month follow-up assessment. Note that the prevalence of depression and anxiety were lower in the 6-month follow-up sample than in the sample of participants assessed for the first time in December or January and reported in Figure 4, which may relate to the fact that all first-time participants received referral information for counseling and psychiatric treatment. See the Discussion for additional details. **C.** Bivariate histogram (left) and heatmap (right) depicting the distribution of participants in the follow up assessment with stable diagnoses (i.e. depressed or not depressed at both time points [green boxes]) vs. changing diagnoses (depressed at one time point but not the other [red boxes]). **D.** Same as C but depicting stability of anxiety diagnoses over time. 59.9%–62.9% of participants with clinically significant depression or anxiety at baseline also had clinically significant depression or anxiety symptoms at follow-up. N=334 subjects for all plots.



Supplementary Figure S3. Parsing heterogeneity in the affective response to pandemic stressors. A. Bivariate histogram (left) and heatmap (right) depicting co-variance in PHQ-9 depression and GAD-7 anxiety scores in the baseline assessment sample (r = 0.764, P < 1e-50, N=2,307 subjects). **B.** Bivariate histogram (left) and heatmap (right) depicting co-variance in the change (follow-up score – baseline score) in PHQ-9 depression and GAD-7 anxiety scores (r = 0.681, P = 7.88e-42, N=334 subjects). **C.** Heatmap depicting the proportion (%) of participants in the baseline assessment sample (N=2,307) meeting criteria for both depression and anxiety diagnoses (green box, 34.3% of sample), neither diagnosis (red box, 45.7% of sample), or just one diagnosis (19.9% of sample). **D.** PCA identified 7 components explaining 82.0% of the variance in symptoms (dashed line = 80%).

SUPPLEMENTAL REFERENCES

1. Spitzer RL, Kroenke K, Williams JBW, Löwe B (2006): A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med* 166: 1092–1097.

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3. Lai J, Ma S, Wang Y, Cai Z, Hu J, Wei N, *et al.* (2020): Factors Associated With Mental Health Outcomes Among Health Care Workers Exposed to Coronavirus Disease 2019. *JAMA Netw Open* 3: e203976.