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RESEARCH ARTICLE

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Gender-specificity of resilience in major depressive disorder

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Abstract

Introduction: The major stressors associated with the COVID-19 pandemic provide an opportunity to understand the extent to which protective factors against depression may exhibit gender-specificity.

Method: This study examined responses from multiple waves of a 50 states non-probability internet survey conducted between May 2020 and January 2021. Participants completed the PHQ-9 as a measure of depression, as well as items characterizing social supports. We used logistic regression models with population reweighting to examine association between absence of even mild depressive symptoms and sociodemographic features and social supports, with interaction terms and stratification used to investigate sex-specificity.

Results: Among 73,917 survey respondents, 31,199 (42.2%) reported absence of mild or greater depression—11,011/23,682 males (46.5%) and 20,188/50,235 (40.2%) females. In a regression model, features associated with greater likelihood of depression-resistance included at least weekly attendance of religious services (odds ratio [OR]: 1.10, 95% confidence interval [CI]: 1.04–1.16) and greater trust in others (OR: 1.04 for a 2-unit increase, 95% CI: 1.02–1.06), along with level of social support measured as number of social ties available who could provide care (OR: 1.05, 95% CI: 1.02–1.07), talk to them (OR: 1.10, 95% CI: 1.07–1.12), and help with employment (OR: 1.06, 95% CI: 1.04–1.08). The first two features showed significant interaction with gender ($p < .0001$), with markedly greater protective effects among women.

Conclusion: Aspects of social support are associated with diminished risk of major depressive symptoms, with greater effects of religious service attendance and trust in others observed among women than men.

KEYWORDS
depression, major depressive disorder, resilience, resilient, SARS-CoV2, survey

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1 | INTRODUCTION

A substantial proportion of the risk for most mood and anxiety disorders is environmental, with acute stressors among the best-understood risk factors (Gilman et al., 2015; Smoller, 2016). On the contrary, a subset of individuals with such stressors will not develop mood or anxiety symptoms. Understanding the characteristics of these individuals—namely, the features that confer resilience in the face of stress (Schetter & Dolbier, 2011)—may facilitate the development of interventions aimed at enhancing resilience for primary or secondary prevention.

Social supports are well-understood to confer resilience to the effects of stress, using a variety of study designs (Ozbay et al., 2007; Southwick et al., 2016). What is less clearly defined is whether these protective factors exhibit sex-specificity—that is, are there differences in the extent to which women are protected compared to men. Two lines of evidence suggest that sex-specificity is likely. First, major depressive disorder, and multiple other mood and anxiety disorders, exhibit differential prevalence among women (Bebbington et al., 1998). Second, social behavior on average differs by sex, from mouse models through primates as well as in human psychological studies (Dudek et al., 2021; Ma et al., 2019).

The COVID-19 pandemic presents an opportunity to better understand resilience effects, particularly as they may inform efforts to enhance resilience (Kunzler et al., 2020). In addition to chronic stress, the financial consequences of the pandemic as acute stressors have become apparent. In the present study, we utilized data from a multi-wave US survey that included questions about COVID-19 encompassing 50 states and the District of Columbia. As respondents did not know the survey topic before opting in, the design is less susceptible to selection bias than many alternate designs. We sought to understand, first, whether individual characteristics of social interaction and supports were associated with diminished likelihood of depression during the COVID-19 pandemic—that is, enhanced resilience against depression—and second, whether such effects might exhibit gender-specificity.

2 | METHOD

2.1 | Study design

We utilized 10 waves of an online survey between May 2020 and January 2021 across 50 states and the District of Columbia, applying nonprobability sampling using representative quotas to balance age, gender, and race/ethnicity. Survey results were weighted to balance on age, gender, race/ethnicity, education, region, and rural/urban area of residence, based on US Census data. The study was reviewed by the Institutional Review Board of Harvard University and determined to be exempt. Participants signed consent online before survey access. We followed AAPOR reporting guidelines for survey studies, as described at https://www.aapor.org/Standards-Ethics/AAPOR-Code-of-Ethics/Survey-Disclosure-Checklist.aspx; response rates are not calculable as multiple web-based survey panels could opt-in to complete the survey.

2.2 | Measures

Survey participants completed the PHQ-9, a well-validated screen for major depressive disorder that measures frequency of individual symptoms in the preceding 2 weeks (Kroenke & Spitzer, 2002). Participants were also asked about social support as putative protective factors (represented as number of people who could provide a particular form of support, from 0 to 11 or more). Specifically, they were asked to identify the number of people who could care for them if they became ill, lend them money, serve as someone to talk to if they felt down or depressed, or help them find employment; these validated questions were drawn from a prior examination of social networks (Lubbers et al., 2019). Additional questions asked about frequency of religious service attendance (from never to more than once a week) and degree of trust in others on a Likert scale ranging from 1 (*you can't be too careful*) to 10 (*most people can be trusted*). A further question asked about number of face-to-face meetings with individuals outside of the household over the past 24 h.

2.3 | Analysis

In primary analysis, we defined resilient individuals as those with no evidence of even mild depression, defined as PHQ-9 score less than 5. Survey results were reweighted using interlocking national weights for age, sex, race/ethnicity, education, and region. We used logistic regression in R 4.0 (R Core Team, 2019) with the "survey" package to examine the association between resilience (again, absence of depressive symptoms despite stressors) and individual features of social network, including response to the 10-point trust Likert scale, frequency of religious service attendance of any sort, and extent of social supports. All analyses were also adjusted for age, self-reported gender, self-reported race/ethnicity indicated on a 5-item questionnaire, income, and rural/suburban/urban area of residence. In sensitivity analysis to examine the extent to which current social interaction might modify or confound these effects, we added a term for current social interaction to these models; to examine the extent to which effects could be impacted by COVID-19 illness, we added a term capturing prior clinician diagnosis and/or positive SARS-CoV2 test. For any social network characteristics exhibiting main effects, we then examined gender specificity in two ways: by incorporating a feature-by-gender interaction term, and by estimating effects stratified by gender. Missing data (Table 1) reflecting the fact that only a randomly-selected subset of respondents received all questions were addressed using case-wise deletion; multiple imputation did not yield meaningfully different results.

TABLE 1 Social features among male and female survey respondents

	Male (*N* = 23,682)	Female (*N* = 50,235)	Total (*N* = 73,917)	*p* value
No depressive symptoms	11,011 (46.5%)	20,188 (40.2%)	31,199 (42.2%)	<.001
Trust score (1–10)				<.001
(missing)	4857	11,100	15,957	
Mean (SD)	5.493 (2.515)	4.870 (2.363)	5.072 (2.431)	<.001
Service attendance				
(missing)	4180	8928	13,108	<.001
Weekly or more frequent	5848 (30.0%)	8802 (21.3%)	14,650 (24.1%)	
Someone to care for				
Mean (SD)	2.84 (2.62)	3.02 (2.62)	2.96 (2.62)	
Someone to lend money				<.001
(missing)	213	465	678	
Mean (SD)	2.35 (2.36)	2.28 (2.21)	2.30 (2.26)	
Someone to talk to				<.001
(missing)	295	583	878	
Mean (SD)	3.37 (3.10)	3.72 (3.10)	3.61 (3.10)	
Someone to find a job				<.001
(missing)	403	953	1356	
Mean (SD)	2.72 (3.08)	2.64 (2.95)	2.66 (3.00)	
Face-to-face meetings				<.001
(missing)	89	187	276	
Mean (SD)	5.48 (12.70)	6.10 (14.34)	5.90 (13.84)	

3 | RESULTS

The full cohort included 73,917 survey respondents with PHQ-9 results, of whom 31,199 (42.2%) reported absence of mild or greater depression—11,011/23,682 males (46.5%) and 20,188/50,235 (40.2%) females. The cohort had a mean age of 40.94 years (SD 16.06), who were 68.0% female, 71.4% white, 10.9% Black, 7.9% Hispanic, and 5.8% Asian. In univariate analyses, those with and without depression differed statistically in all sociodemographic features (Table 2). Social features also differed significantly by gender, as summarized in Table 2.

In a multiple regression model (Figure 1), features associated with greater likelihood of depression-resistance included at least weekly attendance of religious services (odds ratio [OR]: 1.10, 95% confidence interval [CI] 1.04–1.16) and greater trust in others (OR: 1.04 for a 2-unit increase, 95% CI: 1.02–1.06), along with level of social support measured as number of social ties available who could provide care (OR: 1.05 for every two additional supports, 95% CI: 1.02–1.07), talk to them (OR: 1.10, 95% CI: 1.07–1.12), and help with employment (OR: 1.06, 95% CI: 1.04–1.08). Results were not meaningfully changed (i.e., coefficients changed by <10% in all cases) with addition of a term for frequency of face-to-face interactions in the past 24 h. Likewise, in secondary analysis incorporating a term for prior symptomatic COVID-19 diagnosis (4044/73,275 or 5.5%), coefficients changed by <10% with the exception of impact of weekly attendance of religious services (OR: 1.15, 95% CI: 1.09–1.22).

Among those social features demonstrating significant main effects, religious service attendance and trust showed significant interaction with gender ($p < .0001$), with positive associations with resilience among women (Figure 2)—for trust, OR: 1.11 (95% CI: 1.08–1.14), and for weekly religious service attendance, OR: 1.42 (95% CI: 1.33–1.52). Conversely, weekly or more frequent religious service among males was associated with greater risk (OR: 0.89, 95% CI: 0.82–0.97), while no association with trust was observed (OR: 0.99, 95% CI: 0.96–1.02). The number of identified supports were not associated with statistically significant differential effects—interaction-by-gender for caregiving, $t = -1.90$, $p = .06$; for someone to talk to, $t = 0.81$, $p = .42$; and for help with employment, $t = 1.59$, $p = .11$).

TABLE 2 Characteristics of survey respondents who reported minimal depressive symptoms, compared to mild or greater depressive symptoms

	Mild or greater symptoms (*N* = 42,718)	No depression (*N* = 31,199)	Total (*N* = 73,917)	*p* value
Age				<.001
Mean (SD)	37.07 (14.42)	46.24 (16.67)	40.94 (16.06)	
Female gender (%)	30,047 (70.3%)	20,188 (64.7%)	50,235 (68.0%)	<.001
Household income				<.001
(missing)	3122	1722	4844	
Mean ($1000) (SD)	61.46 (71.34)	71.13 (73.72)	65.59 (72.52)	
Race/ethnicity				<.001
White	30,144 (70.6%)	22,635 (72.6%)	52,779 (71.4%)	
Hispanic	3710 (8.7%)	2111 (6.8%)	5821 (7.9%)	
Black	4506 (10.5%)	3578 (11.5%)	8084 (10.9%)	
Asian	2551 (6.0%)	1741 (5.6%)	4292 (5.8%)	
Other	1807 (4.2%)	1134 (3.6%)	2941 (4.0%)	
Location				<.001
Rural	7400 (17.3%)	5207 (16.7%)	12,607 (17.1%)	
Suburban	24,535 (57.4%)	18,443 (59.1%)	42,978 (58.1%)	
Urban	10,783 (25.2%)	7549 (24.2%)	18,332 (24.8%)	
Trust score				<.001
(missing)	7916	8041	15,957	
Mean (SD)	4.92 (2.44)	5.30 (2.41)	5.07 (2.43)	
Service attendance				<.001
(missing)	5954	7154	13,108	
Weekly or more frequent	8038 (21.9%)	6612 (27.5%)	14,650 (24.1%)	
Someone to care for				<.001
Mean (SD)	2.80 (2.53)	3.18 (2.74)	2.962 (2.62)	
Someone to lend money				<.001
(missing)	406	272	678	
Mean (SD)	2.20 (2.15)	2.44 (2.40)	2.30 (2.26)	
Someone to talk to				<.001
(missing)	522	356	878	
Mean (SD)	3.31 (2.98)	4.01 (3.22)	3.61 (3.10)	
Someone to find a job				<.001
(missing)	798	558	1356	
Mean (SD)	2.51 (2.83)	2.87 (3.20)	2.66 (3.00)	
Face-to-face meetings interactions/24 h				.001
(missing)	166	110	276	
Mean (SD)	6.04 (14.28)	5.70 (13.21)	5.90 (13.84)	

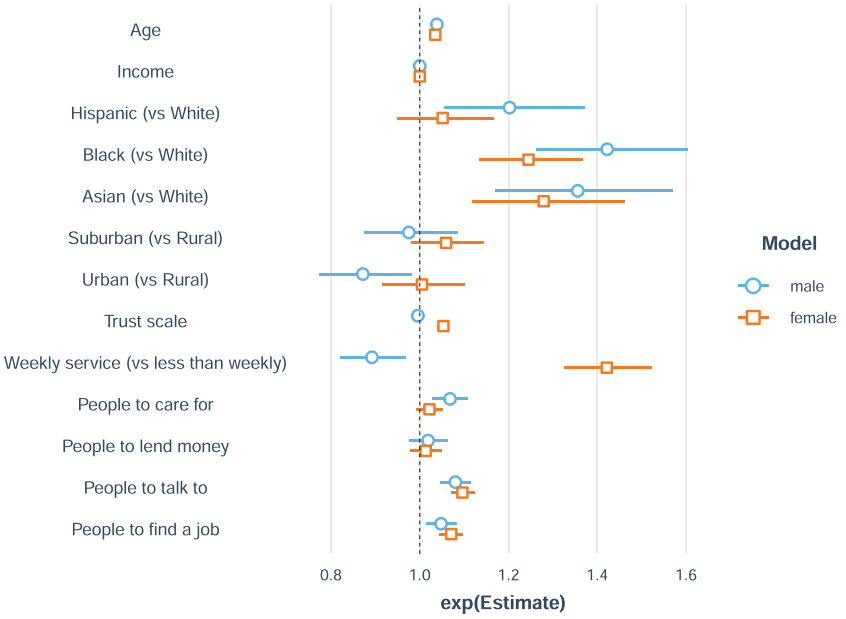

FIGURE 1 Logistic regression model of minimal depressive symptoms, stratified by gender Caption: Trust score effects are reported per unit increase on 1–10 scale; social support effects are reported per two-person increase in supports identified

Variable		N	Odds ratio	p
Age		56482	1.04 (1.04, 1.04)	<0.001
Gender	Male	18349	Reference	
	Female	38133	0.75 (0.71, 0.78)	<0.001
Income		56482	1.00 (1.00, 1.00)	<0.001
Race	White	40004	Reference	
	Hispanic	4689	1.14 (1.05, 1.24)	0.001
	Black	6029	1.36 (1.26, 1.46)	<0.001
	Asian	3396	1.36 (1.23, 1.50)	<0.001
	Other	2364	1.10 (0.98, 1.24)	0.096
Setting	Rural	9643	Reference	
	Suburban	32653	1.02 (0.95, 1.08)	0.647
	Urban	14186	0.92 (0.85, 0.99)	0.031
Trust thermometer		56482	1.04 (1.02, 1.06)	<0.001
Service attendance weekly		56482	1.10 (1.04, 1.16)	<0.001
People who could care for		56482	1.05 (1.02, 1.07)	<0.001
People who could lend money		56482	1.01 (0.98, 1.04)	0.470
People to talk to		56482	1.10 (1.07, 1.12)	<0.001
People to find a job		56482	1.06 (1.04, 1.08)	<0.001

0.8 1 1.21.4

FIGURE 2 Logistic regression model of minimal depressive symptoms. Trust score effects are reported per unit increase on 1–10 scale; social support effects are reported per two-person increase in supports identified

4 | DISCUSSION

In this analysis of national survey data from 73,917 survey respondents, 31,199 (42.2%) reported absence of mild or greater depression, suggesting resilience in the face of chronic stressors. Greater age, male gender, and being non-white were associated with lesser likelihood of reporting depression. In general, greater number of social supports were also associated with lesser likelihood of reporting depressive symptoms; these effects were modest in comparison with other effect sizes and did not exhibit gender-specificity. In contrast, greater trust in others, and more frequent religious service attendance, exhibited significantly larger association with resilience among women.

As a cross-sectional analysis, we cannot infer causation, and must acknowledge the possibility that depressive symptoms impact reporting of social network features, or contribute to reduction in social network size. We do note that incorporating face-to-face interaction in the past 24 h does not meaningfully change associations, as we might expect if depression was simply causing less social activity overall—that is, if the causal arrow were reversed. Longitudinal cohort studies, particularly those that include data preceding onset of widespread COVID-19

infection, will be important to investigate causal effects of social behavior.

The psychiatric consequences of the COVID-19 pandemic, in terms of mood and anxiety symptoms, became apparent early and have been well-documented in a range of studies (Ettman et al., 2020; Rossi et al., 2020). The stressors associated with the pandemic are somewhat different from those of past disasters such as the 9/11 terrorist attack or the Fukushima nuclear power plant disaster, particularly in terms of their chronicity, but also in that they disrupt the very social supports that may represent important factors in resilience. As such, studies to understand what kind of social supports enhance resilience—and, if possible, how they can be maintained and augmented—are needed.

Despite recent enthusiasm for precision medicine in psychiatry, one of the most basic differences between individuals—that is, gender—is honored more in the abstract. A small number of studies suggest that, in general, psychological factors contributing to adverse outcomes may differ by gender or sex (Smaardijk et al., 2020). In this study, we sought to understand whether social effects differ in their capacity to confer resilience by gender. An abundant literature supports differences in depression and anxiety by gender, beginning with prevalence and onset age (Bebbington et al., 1998) and extending through phenomenology and putative neuroanatomy (Yang et al., 2017). Marked differences in stress response have been observed in animal models (Dudek et al., 2021; Ma et al., 2019). Likewise, phenomenology and neurobiology of social functioning also differs by gender (Masi et al., 2021). However, the capacity of social interaction to contribute to resilience by gender is less extensively studied, particularly for chronic stresses.

While multiple surveys of mood in COVID-19 have been reported, few have sought to examine social features contributing to resilience. A recent systematic review of studies among healthcare workers noted the role of social support (both individual, and organizational) but did not characterize gender-specificity (Sirois & Owens, 2020). A survey of healthcare workers suggested that the need for social support was associated with poorer outcomes (Hennein et al., 2021), but also did not investigate gender-specific effects.

Among non-healthcare populations, there are fewer reports of resilience factors related to social networks. Unsurprisingly, a Norwegian survey of ~10,000 individuals identified loneliness during social distancing as associated with greater levels of depression (Hoffart et al., 2020). Our findings regarding religious service attendance also extend prior work. In the largest study to date (Chen et al., 2021), drawing on three prospective cohorts, religious service attendance was associated with diminished risk for depression and greater well-being. Investigations in particular subgroups have yielded similar results, including diminished suicidality among college students (Kim et al., 2021) and reduced hopelessness among middle-aged Black individuals (Mitchell et al., 2020). Notably, however, none of these studies examined sex-specificity of these associations. As with other elements of social functioning, our work highlights the importance of considering sex differences in future work.

A parallel line of evidence (Grossoehme et al., 2020) suggests that religiosity or spirituality itself, with a variety of definitions, may be associated with diminished risk for depressive and anxious symptoms. For example, in a study of 400 Palestinians, coping strategies involving religion were associated with diminished depressive symptoms and lower levels of perceived stress, although the authors did not report gender-specific effects (Mahamid & Bdier, 2021). The relationship between religiosity and religious service attendance is complex, and may change across the lifespan (see, e.g., Dew et al., 2020). The present study cannot distinguish the possibility that the association observed with resilience or risk reflects religiosity rather than religious activity.

We note multiple limitations in our work beyond the cross-sectional nature of the survey. First, we apply a non-probability design with web-based panels, so cannot report a survey response rate, which would aid in understanding generalizability and bias. We emphasize that, because the survey as a whole is not focused solely on COVID-19, and does not recruit by mentioning COVID-19, selection bias should be diminished compared to more focused surveys that might attract individuals with a greater interest in the pandemic. Moreover, large-scale non-probability designs have tended to yield results consistent with the far costlier probability samples (Czeisler, 2020). A further limitation is that our characterization of social functioning is opportunistic—that is, we can characterize only a subset of features of social support and interaction. Here too, prospective cohort studies applying validated instruments will be critical to extend and refine our work. We also emphasize that absence of depression is only one element of resilience; positive affect and well-being reflect more than simply being free from depressive symptoms. Finally, the collection of data during a pandemic represents both a strength and a limitation of this study: the increase in ambient stress levels may make effects on resilience easier to identify, but the extent to which these effects will generalize to other sources of stress, and following the pandemic, will require further investigation as well.

Nonetheless, as a large-scale investigation of gender-specificity of social effects, our study adds to the literature regarding resilience in mood disorders. Consistent with abundant animal modeling work, our results suggest that males and females are quite different in how they respond to chronic stress, particularly in terms of how social characteristics modify the risk of developing depressive symptoms. In light of the profound impact of COVID-19 on mental health, strategies to develop more targeted means of improving resilience (Kunzler et al., 2020) will be needed to diminish risk for depression, anxiety, and related disorders.

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CONFLICT OF INTERESTS

Perlis has received consulting fees from Burrage Capital, Genomind, RID Ventures, and Takeda. He holds equity in Outermost Therapeutics and Psy Therapeutics. The other authors report no disclosures.

AUTHOR CONTRIBUTIONS

Analyzed data, drafted and revised manuscript: Roy H. Perlis, MD, MSc. *Cleaned and analyzed data*: Jon Green, PhD. *Revised manuscript*: Mauricio Santillana, PhD. *Secured funding, oversaw study, revised manuscript*: David Lazer, PhD. *Oversaw data collection, revised manuscript*: Katherine Ognyanova, PhD. *Revised manuscript, oversaw data collection*: Matthew Simonson. *Secured funding, revised manuscript*: Matthew A. Baum, PhD. *Cleaned data, revised manuscript*: Alexi Quintana. *Contributed to data collection, revised manuscript*: Hanyu Chwe. *Revised manuscript*: James Druckman, PhD. *Revised manuscript*: Jennifer Lin.

ENDNOTES

[1]The link will be made available after submission.

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