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## Short communication

# Acute relationships between mental health and cognitive function during the COVID-19 pandemic: Longitudinal evidence from middle-aged and older US adults



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## ABSTRACT

**Background:** The acute impacts of COVID-19-related mental health concerns on cognitive function among middle-aged and older adults are unknown. We investigated whether between-person (BP) differences and within-person (WP) changes in loneliness, anxiety, and worry about COVID-19 were related to cognitive function and abilities in a longitudinal cohort of middle-aged and older United States (US) adults over a nine-month period during the COVID-19 pandemic.

**Methods:** Data were from bimonthly questionnaires in the nationwide COVID-19 Coping Study from August/September 2020 through April/May 2021 (N = 2262 adults aged ≥55). Loneliness was assessed with the 3-item UCLA Loneliness Scale, anxiety with the 5-item Beck Anxiety Inventory, and COVID-19 worry on a 5-point Likert-type scale. Cognitive outcomes were assessed with the 6-item Patient Reported Outcomes Measurement Information System (PROMIS®) Cognitive Function and Abilities scales. Marginal structural models incorporating inverse probability of treatment and attrition weights as well as sampling weights estimated the BP and WP relationships between the mental health predictors and PROMIS® cognitive scores over time.

**Results:** In any given month, experiencing a loneliness or anxiety symptom score higher than the sample mean (BP difference) or higher than one's personal mean across the nine-month period (WP change) was negatively associated with cognitive function and abilities in that month. The observed magnitudes of associations were stronger for BP differences than for WP changes and were the strongest for anxiety symptom scale scores.

**Conclusions:** Elevated loneliness and anxiety symptoms, both relative to other adults and to one's usual levels, were acutely associated with worse perceived cognitive function and abilities over a nine-month period during the COVID-19 pandemic in the United States. The long-term impacts of mental health symptoms experienced during the pandemic for population cognitive health should be explored.

## 1. Introduction

The coronavirus disease 2019 (COVID-19) pandemic has had far-reaching impacts on the mental health of populations worldwide (Kola et al., 2021; Xiong et al., 2020; Pfefferbaum and North, 2020; Pierce et al., 2020). Middle-aged and older adults are typically at higher risk of severe COVID-19 morbidity and mortality, making social distancing, vaccination, and other preventive measures important for this population. Middle-aged and older adults may also experience unique worries

and mental health impacts of the pandemic (Armitage and Nellums, 2020; Kotwal et al., 2021; Galea et al., 2020). From March through June 2020, the US National Poll on Healthy Aging identified that 41% of US adults aged 50–80 years felt a lack of companionship, and 56% felt isolated from others (National Poll on Healthy Aging, 2020). In June 2020, a national survey conducted by the US Centers for Disease Control and Prevention (CDC) identified that 20.3% of adults aged 45–64 and 8.1% of adults aged ≥65 had an anxiety or depressive disorder, and 29.5% of those aged 45–64 and 15.1% of those aged ≥65 had at least one mental or

*Abbreviations:* BP, between-persons; WP, within-persons; US, United States; PROMIS®, Patient Reported Outcomes Measurement Information System.

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behavioural health symptom (Czeisler et al., 2020). These prevalence estimates are thought to be higher than those observed in the year prior to the pandemic (Ettman et al., 2020; Daly and Robinson, 2021). Although adverse mental health effects among middle-aged and older adults during the pandemic are postulated to influence the future burden of dementia (Chong et al., 2020; Manca et al., 2020), it remains unclear whether acute changes in middle-aged and older adults' mental health during the pandemic are related to cognitive outcomes.

Among middle-aged and older adults, mental health symptoms are plausibly related to long-term cognitive outcomes, due to their direct effects on neurobiology and indirect effects on behavioural coping mechanisms that are dementia risk factors, such as physical inactivity, alcohol use, and withdrawal from social networks (Santini et al., 2020; Lam et al., 2021; Wolf et al., 2021; Anker, Kushner). Pre-pandemic evidence from meta-analyses of population-based, longitudinal cohort studies consistently indicates that elevated anxiety symptoms are associated with increased risks of subsequent Alzheimer's disease and related dementias (Santabárbara et al., 2019; Santabárbara et al., 2020). Similarly, loneliness and social isolation have consistently been associated with increased risks of Alzheimer's disease and related dementias in population-based, longitudinal cohort studies (Sutin et al., 2020; Sundström et al., 2020; Lara et al., 2019; Penninkilampi et al., 2018). Depression is also a well-established risk factor for dementia (Livingston et al., 2020). However, the short-term relationship between depression and cognition is challenging to disentangle, as cognitive impairment can be a symptom of depression and the awareness of cognitive impairment may cause people to experience depressed mood (Thomas and O'Brien, 2008). This pre-pandemic body of evidence is based on studies with long-term follow-up periods, given the long pre-clinical period of dementia. Whether there are short-term, acute associations between mental health symptomatology (except for depression) and cognitive function is less well understood, both before and during the pandemic.

If there are short-term, acute relationships between mental health and cognitive function in the aging population during the COVID-19 pandemic, there may be longer term implications of the pandemic period for the future population burden of Alzheimer's disease and related dementias. We thus aimed to investigate whether between-person differences and within-person changes in loneliness, anxiety, and worry about COVID-19 were related to self-reported cognitive function and abilities on a month-to-month basis in a longitudinal cohort of middle-aged and older United States (US) adults. We hypothesized that experiencing higher than average loneliness, anxiety, and worry about COVID-19, both on between-persons and within-person levels, would be associated with worse self-reported cognitive function and abilities.

## 2. Materials and methods

### 2.1. Study design

Data were from the COVID-19 Coping Study, a national longitudinal cohort study of adults aged  $\geq 55$  years residing in all 50 US states, the District of Columbia, and Puerto Rico (Kobayashi et al., 2021). Details of the study design, recruitment, and methodology are available elsewhere (Kobayashi et al., 2021). In brief, participants were recruited through multi-frame non-probability sampling from 2 April through 31 May, 2020 and completed monthly online questionnaires through the end of May 2021 (13 months of follow-up). The present analysis used longitudinal data on mental health exposures and cognitive outcomes assessed at the four-month (August/September 2020; analytic baseline), six-month (October/November 2020), eight-month (December 2020/January 2021), ten-month (February/March 2021), and twelve-month follow-ups (April/May 2021), as the cognitive outcome variables were measured at these time points. Contextual details on key events during the COVID-19 pandemic in the United States over this period are available in Supplemental Table 1, in the Supplemental Material.

Participants were excluded from this analysis if they were missing any baseline covariate data ( $N = 252/4,401$ , 6%), if they had more than two missing follow-up questionnaires ( $N = 1861/4,149$ , 45%), if they had more than two missing observations for any of the mental health exposure variables over the follow-up ( $N = 62$ , 3% for loneliness;  $N = 9$ , <1% for anxiety;  $N = 1$ , <1% for worry about COVID-19), or if they were missing inverse probability of treatment weights ( $N = 22$ , 1% for loneliness;  $N = 26$ , 1% for anxiety;  $N = 27$ , 2% for worry about COVID-19). The final analytical sample sizes were  $N = 2204$  for the loneliness model,  $N = 2253$  for the anxiety model, and  $N = 2260$  for the worry about COVID-19 model, with a total of 2262 unique individuals contributing data to at least one model.

### 2.2. Exposures: loneliness, anxiety, and worry about COVID-19

Loneliness in the past week was assessed with the 3-item UCLA Loneliness Scale (Russell, 1996), which included the items: "How often did you feel you lacked companionship?", "How often did you feel left out?", and "How often did you feel isolated from others?", with response options of "hardly ever" (1 point), "some of the time" (2 points), and "often" (3 points). The scale had a range of 3–9, with higher scores indicating higher loneliness.

Anxiety symptoms in the past week were assessed with the 5-item Beck Anxiety Inventory, adapted from the US Health and Retirement Study (Smith et al., 2017), which included the items: "I had fear of the worst happening", "I was nervous", "I felt my hands trembling", "I had a fear of dying", and "I felt faint", with response options of "never" (1 point), "hardly ever" (2 points), "some of the time" (3 points), and "most of the time" (4 points). Scores on the scale were summed across all items and averaged, to give a range of 1–4, with higher scores indicating greater anxiety symptomatology.

Current worry about the COVID-19 pandemic was assessed on a 5-point Likert-type scale, consistent with existing measures of worry about health conditions including cancer (Deimling et al., 2006), Zika virus infection (Blakey and Abramowitz, 2017), dementia (Kessler et al., 2012), and general health (Blakey and Abramowitz, 2017). This scale was newly developed for the current study, given the novelty of the COVID-19 pandemic in 2020. The scale is intended to capture the construct of worry, which is a functional psychological response to a perceived threat (e.g., COVID-19) that can keep the body in a prolonged state of physiological arousal, especially when reduction or avoidance of the threat is not possible (Dijkstra and Brosschot, 2003). The scale was developed with survey methodologists and pilot-tested for comprehension and appropriateness with a group of adults aged  $\geq 55$  years who did not become part of the study sample, as described in detail elsewhere (Kobayashi et al., 2021). Response options were "not at all worried" (0 points), "slightly worried" (1 point), "somewhat worried" (2 points), "moderately worried" (3 points), and "extremely worried" (4 points), for a range of 0–4 with higher scores indicating greater worry (Kobayashi et al., 2021).

All three variables were analysed continuously, to capture symptom burden while avoiding loss of information through categorisation. To differentiate between between-person (BP) and within-person (WP) relationships, we derived two variables for each mental health exposure for each person. To create the BP exposure variables, we first calculated the sample grand means for the loneliness, anxiety, and worry scales across all time points. Then, for each scale, we centred each person's score at each time point to the sample grand mean. To create the WP exposure variables, we first calculated the person-specific grand means for the loneliness, anxiety, and worry scales across all time points. Then, for each scale, we centred each person's score at each time point to their personal grand mean.

### 2.3. Outcomes: cognitive function and abilities

Cognitive outcomes were assessed with the 6-item Patient Reported Outcomes Measurement Information System (PROMIS®) Cognitive Function and Abilities scales (HealthMeasures, 2019). The Cognitive

Function scale captures negative sentiments about cognition, while the Cognitive Abilities scale captures positive sentiments about cognition, both as applied to scenarios of daily life (HealthMeasures, 2019; Terwee et al., 2021). Both scales give a series of statements about cognitive function or abilities in the past 7 days, with statements such as “My thinking has been slow” and “I have had trouble concentrating” (Cognitive Function scale), and “My mind has been as sharp as usual” and “My memory has been as good as usual” (Cognitive Abilities scale). Response options were “Never”, “Rarely (once)”, “Sometimes (two or three times)”, “Often (about once a day)”, “Very often (several times a day)” for the Cognitive Function scale and “Not at all”, “A little bit”, “Somewhat”, “Quite a bit”, and “Very much” for the Cognitive Abilities scale. The Cognitive Function scale was reverse-coded, so that higher scores indicate better cognitive outcomes.

Scores on the PROMIS® scales have been validated against clinical diagnoses, they are considered relevant to assessing daily quality of life as affected by perceived cognitive function and abilities, and they have been recommended for use in COVID-19 research to harmonize measures and data across studies of older adults (HealthMeasures, 2019). The PROMIS® Cognitive Function and Abilities raw scores were converted to T-scores using the HealthMeasures Scoring Service, which is the most accurate method for scoring a PROMIS® instrument (HealthMeasures, 2019). The T-score is a standardized score calibrated to the US general population with a mean of 50 and standard deviation of 10 (HealthMeasures, 2019). A higher T-score represents greater cognitive function or abilities. Within-person changes in PROMIS® T-scores of 2–6 points are thought to represent the minimal degree of change that patients perceive as important or meaningful (HealthMeasures, 2021). More information about the HealthMeasures calibration and interpretation of the T-scores can be found elsewhere (HealthMeasures, 2019).

#### 2.4. Covariates

Potential confounders of the relationships between the mental health exposures and cognitive outcomes were: age (continuous, in years), sex (male; female), race/ethnicity (non-Hispanic white; other racial/ethnic group), highest educational attainment (high school or less; some college or two-year associate's degree; four-year college or university degree; postgraduate or professional degree), pre-COVID-19 employment status (employed; unemployed; retired), relationship status (single, never married; single, divorced/separated; single, widowed; married or in a relationship), previous physician diagnosis of hypertension, diabetes, heart disease, asthma, chronic obstructive pulmonary disease, cancer, other physical or mental health condition (all yes; no), use of a mobility aid (yes; no), pre-COVID-19 social isolation (score out of five on the English Longitudinal Study of Ageing social isolation index, with one point assigned for each of: less than monthly contact with each of children, other family, or friends; living alone; and not belonging to any social organizations or clubs) (Kobayashi and Steptoe, 2018), and number of depressive symptoms according to the 8-item Center for Epidemiologic Studies Depression (CES-D) scale (Radloff, 1977). The covariates were measured at the initial cohort baseline (April/May 2020), except for depressive symptoms, which was assessed one month prior to each analytical time point and treated as a time-varying confounder.

#### 2.5. Statistical analysis

As we aimed to estimate the time-varying BP and WP relationships between anxiety, loneliness, and worry about COVID-19 with perceived cognitive function and abilities, we considered depressive symptoms to be a potential time-varying confounder and mediator of the relationships under study. In this scenario, antecedent depressive symptoms would predict both the current mental health exposure and cognitive outcome under study (i.e., the confounding effect), while current depressive symptoms could mediate any effects of the prior mental health exposures on the cognitive outcomes (i.e., the mediating effect).

To address this potential time-varying confounding structure in our longitudinal data, we fit marginal structural models using inverse probability of treatment weights (IPTWs) (Hernán and Robins, 2020). The IPTWs were constructed with the goal of making the time-varying mental health exposure variables independent of the prior values of the time-varying depressive symptom variable, by balancing the previous depressive symptoms variable across levels of each mental health exposure at each time point (Hernán and Robins, 2020). First, at each analytical time point, we fit logistic regression models to estimate the predicted probabilities of each dichotomized mental health exposure variable. For these models, loneliness was dichotomized at  $<6$  vs.  $\geq 6$  (80th percentile of the baseline distribution), anxiety was dichotomized at  $<2$  vs.  $\geq 2$  (80th percentile of the baseline distribution), and COVID-19 worry was dichotomized at  $<3$  vs.  $\geq 3$  (3 points corresponds to “moderately worried”). The numerator of each IPTW was the predicted probability of the dichotomized mental health exposure variable, conditional on baseline confounders, at the analytical time point,  $T$ . The denominator of each IPTW was the predicted probability of the dichotomized mental health exposure variable at the analytical time point,  $T$ , conditional on baseline confounders, the number of depressive symptoms at the previous month ( $T-1$ ), and the mental health exposure measured at  $T-1$  (Pool et al., 2018; Heeringa et al., 2017). We constructed stabilized weights at each analytic time point using the formulas shown below (Pool et al., 2018; Heeringa et al., 2017).

$$IPTW = \left( \frac{\text{numerator}}{\text{denominator}} \right) \text{if dichotomized mental health exposure} = 1$$

$$IPTW = \left( \frac{1 - \text{numerator}}{1 - \text{denominator}} \right) \text{if dichotomized mental health exposure} = 0$$

The weights were multiplied cumulatively across all time points to construct the final IPTW. We constructed separate sets of IPTWs for each of loneliness, anxiety, and worry about COVID-19. An additional set of IPTWs was constructed for each mental health exposure variable, for which the denominator was additionally conditioned on the values of the other two mental health exposure variables at  $T-1$ . All weights were trimmed at their 99th percentiles.

We specified marginal structural models for repeated outcome measures with random person-specific intercepts and slopes to predict the PROMIS® Cognitive Function and Abilities T-scores as the two study outcomes. The BP model coefficients describe the mean change in cognitive T-score in any month associated with having a loneliness, anxiety, or worry score one-unit greater than the sample grand mean in that same month. The WP model coefficients describe the mean change in cognitive T-score in any month associated with having a loneliness, anxiety, or worry score one-unit greater than an individual's personal grand mean in that same month. For the BP and WP models for each of loneliness, anxiety, and worry about COVID-19 in relation to each cognitive outcome, we applied both sets of IPTWs: those that were and were not conditional on the prior values of the other two mental health exposures. The purpose of this approach was to qualitatively assess the presence of confounding across the mental health exposures under study by comparing estimates from models with each set of IPTWs.

All models adjusted for baseline age, sex, race/ethnicity, highest level of education, relationship status, pre-COVID-19 employment status, use of any mobility aid, pre-COVID-19 social isolation score, and presence of physician-diagnosed hypertension, diabetes, heart disease, asthma, chronic obstructive pulmonary disease, cancer, or other limiting long-standing health condition, and were additionally weighted to represent the US general population aged  $\geq 55$  based on age, sex, race, ethnicity, education, marital status, and census region of residence according to the 2018 American Community Survey (Kobayashi et al., 2021). To reduce any potential bias due to study attrition after the cohort baseline (April/May 2020), we also applied attrition weights that were calculated as the inverse probability of retention through the 12-month follow-up. Please see the Supplementary Methods for more details on the

construction of the attrition weights. The IPTWs were applied at level 1 (observation-level) of the models, and the population and attrition weights at level 2 (person-level) of the models (Heeringa et al., 2017).

We conducted a sensitivity analysis to further assess whether study attrition between the cohort baseline (April/May 2020) and analytic baseline (August/September 2020) could have affected our results, which would happen if attrition was differential according to loneliness, anxiety, and COVID-19 worry as well as cognitive status. We compared loneliness, anxiety, COVID-19 worry, and self-rated memory scores at the cohort baseline according to attrition status between the cohort baseline and analytical baseline. Self-rated memory scores were examined in this sensitivity analysis, as the PROMIS® Cognitive Function and Abilities scales were not included at the cohort baseline. All analyses were conducted using Stata 17.0SE (College Station, TX).

### 2.6. Ethical approval

The University of Michigan Health Sciences and Behavioural Sciences Institutional Review Board approved the COVID-19 Coping Study protocol (HUM00179632) and all participants provided informed consent.

### 3. Results

Table 1 shows the population and attrition-weighted characteristics of the sample. Mean age of the sample was 68.2 years (95% CI: 67.5, 68.8).

**Table 1**  
Population and attrition-weighted characteristics of the sample, COVID-19 Coping Study, United States, April/May 2020 to April/May 2021, N = 2262.

Characteristic	%	95% CI
Age, mean (95% CI)	68.2	(67.5, 68.8)
Female sex	58.2	(54.8, 61.6)
Race/ethnicity		
Racial/ethnic minority	15.7	(12.8, 19.1)
Non-Hispanic white	84.3	(80.9, 87.3)
Highest level of education		
High school diploma/equivalency or less	11.8	(8.8, 15.6)
Some college or 2-year associate degree	26.3	(23.0, 29.8)
Four-year college or university degree	29.4	(26.7, 32.2)
Postgraduate or professional degree	32.5	(30.0, 35.2)
Relationship status		
Single, never married	8.2	(6.4, 10.5)
Single, divorced/separated	14.5	(12.3, 17.0)
Single, widowed	10.5	(8.5, 13.0)
Married or in a relationship	66.8	(63.4, 70.0)
Pre-COVID-19 employment status		
Employed	36.9	(33.7, 40.2)
Unemployed or homemaker/family caregiver	8.7	(6.7, 11.3)
Retired or in school	54.4	(51.0, 57.8)
Pre-existing physician-diagnosed health conditions		
Hypertension	48.3	(44.9, 51.7)
Diabetes	14.5	(11.9, 17.5)
Heart disease	10.4	(8.5, 12.6)
Asthma	11.5	(9.5, 13.7)
Chronic obstructive pulmonary disease	5.2	(3.8, 7.1)
Cancer	16.3	(14.1, 18.8)
Other mental or physical health condition	20.2	(17.5, 23.2)
Use of a mobility aid	7.4	(5.7, 9.6)
Pre-COVID-19 social isolation score, mean (95% CI)	1.0	(1.0, 1.1)
Depressive symptoms, mean (95% CI)	1.8	(1.7, 2.0)
Loneliness score, mean (95% CI)	4.7	(4.6, 4.8)
Anxiety symptom score, mean (95% CI)	1.5	(1.5, 1.6)
Worry about COVID-19, mean (95% CI)	2.2	(2.2, 2.3)
PROMIS Cognitive Function T-score, mean (95% CI)	49.3	(48.7, 49.9)
PROMIS Cognitive Abilities T-score, mean (95% CI)	52.7	(52.1, 53.3)

Note: All estimates applied population weights based on 2018 American Community Survey data and are weighted for attrition. Data are from the cohort baseline in April/May 2020, except for the mean values for depressive symptoms, anxiety symptoms, loneliness, worry about COVID-19, and PROMIS scores, which were calculated as the grand means over the analytical study period from August/September 2020 to April/May 2021.

68.8), 58.2% were female (95% CI: 54.8%, 61.6%), and 84.3% were non-Hispanic white (95% CI: 80.9%, 87.3%; Table 1). Across all analytical time points, the sample mean loneliness score was 4.7 out of 9 (95% CI: 4.6, 4.8), the sample mean anxiety score was 1.5 out of 4 (95% CI: 1.5, 1.6), and the sample mean COVID-19 worry score was 2.2 out of 4 (95% CI: 2.2, 2.3), corresponding to “somewhat worried” about the COVID-19 pandemic (Table 1). Across all analytical time points, the sample mean PROMIS® cognitive function T-score was 49.3 (95% CI: 48.7, 49.9) and the sample mean PROMIS® cognitive abilities T-score was 52.7 (95% CI: 52.1, 53.3; Table 1). Supplementary Table 3 shows characteristics of the sample according to inclusion at each analytical time point, indicating that response over the follow-up was similar by sociodemographic group, pre-existing health conditions, mental health scores, and cognitive outcome scores.

Table 2 shows the MSM estimates for the BP and WP relationships between the three mental health exposures and cognitive function and abilities. BP differences in all three of the mental health exposure variables were negatively associated with cognitive function and abilities (Table 2). WP changes in loneliness and anxiety were negatively associated with cognitive function and abilities, while WP changes in worry about COVID-19 were not. For all three mental health exposure variables, the BP associations were stronger in magnitude than the WP associations, and the strongest magnitudes of association were observed for anxiety symptoms and cognitive outcomes (Table 2). When models were additionally conditioned on the time-varying histories of all three mental health exposures, the results were similar (Table 3). In this model set, having an anxiety score that was one unit greater than the sample grand mean at any time point was associated with a 5.45 (95% CI: -6.36,

**Table 2**

Results from marginal structural models of the between-persons (BP) and within-person (WP) associations between loneliness, anxiety, worry about COVID-19, and cognitive outcomes, COVID-19 Coping Study, August/September 2020 to April/May 2021, N = 2262.

Estimate	Cognitive Function		Cognitive Abilities	
	β	95% CI	β	95% CI
<b>Between-persons (BP)</b>				
<i>Loneliness</i>	N = 2204			
BP estimate	-1.01	(-1.43, -0.59)	-0.95	(-1.19, -0.72)
Time	0.05	(-0.02, 0.13)	-0.04	(-0.12, 0.04)
<i>Anxiety</i>	N = 2253			
BP estimate	-5.48	(-6.38, -4.57)	-5.57	(-6.42, -4.72)
Time	-0.01	(-0.09, 0.07)	-0.13	(-0.21, -0.05)
<i>Worry about COVID-19</i>	N = 2260			
BP estimate	-0.54	(-0.94, -0.14)	-0.49	(-0.80, -0.19)
Time	0.05	(-0.04, 0.13)	-0.03	(-0.11, 0.06)
<b>Within-person (WP)</b>				
<i>Loneliness</i>	N = 2204			
WP estimate	-0.83	(-1.40, -0.26)	-0.74	(-1.10, -0.38)
Time	0.06	(-0.01, 0.14)	-0.03	(-0.11, 0.05)
<i>Anxiety</i>	N = 2253			
WP estimate	-4.22	(-5.29, -3.15)	-4.27	(-5.29, -3.25)
Time	0.02	(-0.05, 0.10)	-0.09	(-0.17, -0.01)
<i>Worry about COVID-19</i>	N = 2260			
WP estimate	-0.21	(-0.68, 0.26)	-0.22	(-0.57, 0.13)
Time	0.07	(-0.02, 0.16)	-0.00	(-0.09, 0.08)

Note: Time-varying inverse probability of treatment weights were applied to each model to account for confounding by time-varying history of depressive symptoms, which were measured monthly and treated as a time-varying confounder. Models additionally adjust for age, sex, race/ethnicity, highest level of education, relationship status, pre-COVID-19 employment status, use of any mobility aid, pre-COVID-19 social isolation score, and presence of physician-diagnosed hypertension, diabetes, heart disease, asthma, chronic obstructive pulmonary disease, cancer, and other limiting long-standing health condition, each of which were measured at the cohort baseline (April/May 2020). BP and WP relationships for each mental health exposure were modelled separately. All estimates applied population weights based on 2018 American Community Survey data and are weighted for attrition.

–4.54) lower cognitive function T-score and a 5.43 (95% CI: –6.30, –4.56) lower cognitive abilities T-score at that same time point (Table 3). Similarly, having an anxiety score that was one unit greater than one's personal grand mean at any time point was associated with a 4.12 (95% CI: –5.21, –3.03) lower cognitive function T-score and a 4.05 (95% CI: –5.06, –3.04) lower cognitive abilities T-score at that same time point (Table 3).

In our sensitivity analysis, we found that loneliness, anxiety, COVID-19 worry, and self-rated memory at the cohort baseline (April/May 2020) were similar among those who remained in the study at the analytical baseline (August/September 2020) compared to those who dropped out, indicating that study attrition between the cohort baseline and analytical baseline does not bias our results (Supplemental Table 4).

#### 4. Discussion

In this longitudinal study of US adults aged  $\geq 55$  over a nine-month period during the COVID-19 pandemic, we found that elevated loneliness and anxiety symptoms, both relative to other adults and to one's usual level, were acutely associated with worse perceived cognitive function and abilities. Elevated worry about COVID-19, relative to other adults but not relative to one's usual level, was also associated with worse perceived cognitive function and abilities. The associations for anxiety symptoms were of magnitudes considered to be of importance to patients in evaluating their own cognitive changes. For example, a one-unit increase on the anxiety scale relative to one's usual level was associated

**Table 3**

Results from marginal structural models of the between-persons (BP) and within-person (WP) associations between loneliness, anxiety, worry about COVID-19, and cognitive outcomes, with adjustment for time-varying confounding across the mental health exposures, COVID-19 Coping Study, August/September 2020 to April/May 2021, N = 2258.

Estimate	Cognitive Function		Cognitive Abilities	
	$\beta$	95% CI	$\beta$	95% CI
<b>Between-persons</b>				
<i>Loneliness</i>	N = 2203			
BP estimate	–0.98	(–1.39, –0.56)	–0.94	(–1.16, –0.71)
Time	0.06	(–0.02, 0.13)	–0.04	(–0.12, 0.04)
<i>Anxiety</i>	N = 2250			
BP estimate	–5.45	(–6.36, –4.54)	–5.43	(–6.30, –4.56)
Time	0.00	(–0.08, 0.08)	–0.11	(–0.19, –0.03)
<i>Worry about COVID-19</i>	N = 2257			
BP estimate	–0.56	(–0.96, –0.16)	–0.46	(–0.76, –0.15)
Time	0.05	(–0.04, 0.14)	–0.02	(–0.11, 0.07)
<b>Within-person</b>				
<i>Loneliness</i>	N = 2203			
WP estimate	–0.79	(–1.35, –0.23)	–0.72	(–1.06, –0.37)
Time	0.07	(–0.01, 0.14)	–0.03	(–0.11, 0.05)
<i>Anxiety</i>	N = 2250			
WP estimate	–4.12	(–5.21, –3.03)	–4.05	(–5.06, –3.04)
Time	0.04	(–0.04, 0.12)	–0.07	(–0.16, 0.01)
<i>Worry about COVID-19</i>	N = 2257			
WP estimate	–0.24	(–0.70, 0.23)	–0.18	(–0.53, 0.16)
Time	0.07	(–0.02, 0.17)	0.01	(–0.08, 0.09)

Note: Time-varying inverse probability of treatment weights were applied to each model to account for confounding by time-varying history of depressive symptoms, loneliness, anxiety symptoms, and worry about COVID-19, each of which were measured monthly and treated as time-varying confounders. Models additionally adjust for age, sex, race/ethnicity, highest level of education, relationship status, pre-COVID-19 employment status, use of any mobility aid, pre-COVID-19 social isolation score, and presence of physician-diagnosed hypertension, diabetes, heart disease, asthma, chronic obstructive pulmonary disease, cancer, and other limiting long-standing health condition, each of which were measured at the cohort baseline (April/May 2020). BP and WP relationships for each mental health exposure were modelled separately. All estimates applied population weights based on 2018 American Community Survey data and are weighted for attrition.

with PROMIS® T-score decrements of 4.12 to 4.05 points, just above one-third of a population standard deviation. Given the prevalence of clinically meaningful anxiety symptoms during the COVID-19 pandemic, both the short-term and long-term impacts of anxiety experienced during the COVID-19 pandemic for population cognitive health should be further investigated.

#### 4.1. Comparison to existing literature

Our results are consistent with pre-pandemic evidence from population-based, longitudinal cohort studies indicating that elevated anxiety symptoms and anxiety disorders are associated with increased risks of Alzheimer's disease and related dementias (Santabárbara et al., 2019; Santabárbara et al., 2020). Anxiety is thought to affect cognitive health directly through neurobiological effects, and indirectly through behavioural coping mechanisms that are dementia risk factors, such as smoking, physical inactivity, and withdrawal from engagement in social relationships (Livingston et al., 2020). We did not identify any studies that have investigated the time-varying, short-term monthly relationships between anxiety symptoms and cognitive outcomes in middle-aged and older adults during or before the COVID-19 pandemic.

Two studies conducted prior to the pandemic found that between-persons differences but not within-person changes in anxiety were associated with measures of cognitive function (Laukka et al., 2018; Marrie et al., 2021). These somewhat conflict with ours, as we observed associations between within-person changes in anxiety and cognitive function and abilities scores. One possible explanation for these inconsistent results is that the anxiety symptoms observed in this study during the COVID-19 pandemic may have been stronger in this sample than in these pre-pandemic samples, such that its relationship with cognitive function was more apparent in the present study. However, comparisons between these previous studies and ours may be difficult, as the previous two studies used different anxiety scales than ours, they had smaller sample sizes and multi-year follow-up times, and one was restricted to multiple sclerosis patients (Laukka et al., 2007; Marrie et al., 2021). A small case-control study identified that older adults with generalized anxiety disorder were more likely to have prevalent cognitive impairment than anxiety-free controls (Mantella et al., 2007), but inference cannot be made about the timing of cognitive impairment onset relative to anxiety onset with that study design. A handful of studies among patients with specific chronic diseases, such as Parkinson's disease, have identified correlations between anxiety symptoms and cognitive function, but these studies are primarily cross-sectional in design (Laukka et al., 2018; Mantella et al., 2007; Burkauskas et al., 2016; Ehgoetz Martens et al., 2018). Additional large, population-based longitudinal studies are needed to further elucidate the short- and long-term relationships between anxiety symptomatology and cognitive aging outcomes.

Previous studies on the relationship between loneliness and cognitive outcomes are primarily either cross-sectional in design or longitudinal studies with long-term follow-ups (Boss et al., 2015). We did not identify any studies investigating the short-term, monthly associations of BP differences or WP fluctuations in loneliness and cognitive function. Notwithstanding, our results are consistent with those from prior longitudinal cohort studies indicating that loneliness is associated with accelerated cognitive decline and increased dementia risk (Sutin et al., 2020; Lara et al., 2019; Sundstrom et al., 2020; Shankar et al., 2013; Ryder et al., 2002). Prolonged loneliness is thought to be a stressor that may affect physiological cardiovascular risk pathways that lead to vascular dementias (Hawkey and Cacioppo, 2010), although evidence for these pathways is mixed (Shankar et al., 2011). Like anxiety, loneliness is thought to adversely influence health and social behaviours that are dementia risk factors (Kobayashi and Steptoe, 2018; Shankar et al., 2013). Future research should further investigate the associations between short-term, within-person fluctuations in loneliness in relation to cognitive aging outcomes, especially in the context of changes to population loneliness during the COVID-19 pandemic.

#### 4.2. Limitations and strengths

The PROMIS® cognitive measures are self-reported. Hence, they may be subject to recall or social desirability bias, and do not objectively capture neuropsychological deficits. However, they are valuable measures that capture the impact of cognition on quality of life, which is highly meaningful to patients. They have been validated against clinical outcomes and are widely used in research studies, thereby improving comparability of our findings to existing literature (HealthMeasures 2019). This study was conducted during a major infectious disease pandemic, and as such does not include those who were too ill to take part, such as those with severe COVID-19. Our data were collected online, and results may not be generalizable to non-Internet users (Kobayashi et al., 2021). However, conducting this study online allowed us to recruit a large sample and rapidly collect relevant data during a period when in-person contact was restricted due to COVID-19 risk (Hlatshwako et al., 2021). Although we applied general population weights developed using American Community Survey data to our models, our results may be subject to residual bias if there are unmeasured drivers of study participation that are correlated with the mental health exposures and cognitive outcomes, but uncorrelated with the sociodemographic variables included in weighting (Hernán et al., 2004). This sample had a higher proportion of non-Hispanic Whites and adults with higher educational attainment than the general US population aged  $\geq 55$  years. Population weighting may thus not fully account for any selection bias of this type that could be introduced by differences in race/ethnicity and education across exposure and outcome groups.

Strengths of this study include the timeliness of data collection during the COVID-19 pandemic, large sample size, national scope, commonly used mental health and cognitive function scales, and rich covariate data. We accounted for potential sampling bias and attrition bias through model weighting, and sensitivity analyses further indicated that attrition does not bias our results. We accounted for time-varying confounding by depressive symptoms. Prior to the COVID-19 pandemic, existing research linking mental health symptoms or disorders to cognitive aging outcomes had been largely based on measures of mental health symptoms or diagnoses assessed once at study baseline, despite their time-varying nature. We were able to investigate how within-person fluctuations in anxiety symptoms, loneliness, and COVID-19 worry were related to perceived cognitive function and abilities. However, despite our approach to account for time-varying confounding by depression and other mental health symptoms and our analysis of within-person changes in mental health, our results may still be subject to confounding by unmeasured factors such as personality. We did not identify any other studies that have examined these time-varying relationships on a short-term scale, highlighting the uniqueness of the present study and the contribution it makes to the literature.

#### 4.3. Conclusions

In this large, nation-wide study of US adults aged  $\geq 55$  years over a nine-month period during the COVID-19 pandemic, we identified that elevated loneliness and anxiety symptoms were associated with worse perceived cognitive function and abilities. These associations were observed both in comparison to other adults of similar age and to one's own usual levels. Elevated worry about the COVID-19 relative to other adults of similar age was also associated with worse perceived cognitive function and abilities. These findings were independent of a range of sociodemographic, social, and health-related covariates, including depressive symptomatology. Adverse mental health effects are a mechanism through which the COVID-19 pandemic is thought to influence the future burden of dementia among the older population (Chong et al., 2020; Manca et al., 2020). However, it remains unclear whether acute changes in population mental health during the pandemic will have long-term implications. Future research in other populations and settings should evaluate how within-person fluctuations in mental health

symptomatology in the wake of the pandemic may affect cognitive outcomes during aging.

#### CRedit authorship statement

**Lindsay C. Kobayashi:** Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Writing – original draft, Writing – review & editing; **Brendan Q. O'Shea:** Conceptualization, Data curation, Formal analysis, Methodology, Writing – review & editing; **Carly Joseph:** Conceptualization, Methodology, Writing – review & editing; **Jessica M. Finlay:** Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Writing – review & editing.

#### Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Lindsay C. Kobayashi reports financial support was provided by National Institute on Aging. Jessica M. Finlay reports financial support was provided by National Institute on Aging. Jessica M. Finlay reports financial support was provided by National Center for Advancing Translational Sciences.

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#### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ssmmh.2022.100097>.

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