# **ORIGINAL RESEARCH**

# Psychological Distress in Adults With Congenital Heart Disease Over the COVID-19 Pandemic

Mikyla L. Janzen , MSc; Karen LeComte, MSN, RN, CNCCP(C); Gnalini Sathananthan, MBBS; Jia Wang, MSc; Marla Kiess, MD; Santabhanu Chakrabarti, MD; Jasmine Grewal , MD

**BACKGROUND:** This study sought to better understand the experiences of adults with congenital heart disease throughout the pandemic. Objectives were to determine (1) psychological distress before and throughout the pandemic; (2) changes in day-to-day functioning; and (3) the percentage of adults with congenital heart disease who experienced COVID-19 related symptoms, underwent testing, and tested positive.

**METHODS AND RESULTS:** This was a cross-sectional study paired with retrospective chart review. A web-based survey was distributed to patients between December 2020 and January 2021. Patients reported on psychological distress across 5 categories (Screening Tool for Psychological Distress; depression, anxiety, stress, anger, and lack of social support), whether they experienced symptoms of COVID-19 and/or sought testing, and changes to their work and social behavior. Five hundred seventy-nine survey responses were received, of which 555 were linked to clinical data. Patients were aged 45±15 years. The proportion of patients reporting above-threshold values for all Screening Tool for Psychological Distress items significantly increased during the early pandemic compared with before the pandemic. Stress returned to baseline in December 2020/ January 2021, whereas all others remained elevated. Psychological distress decreased with age, and women reported persistently elevated stress and anxiety compared with men during the pandemic. A consistent trend was not observed with regard to American College of Cardiology/American Heart Association anatomic and physiologic classification. Fifty (9%) patients lost employment because of a COVID-19–related reason. COVID-19 symptoms were reported by 145 (25%) patients, 182 (31%) sought testing, and 10 (2%) tested positive.

**CONCLUSIONS:** A substantial proportion of adults with congenital heart disease reported clinically significant psychological distress during the pandemic.

Key Words: congenital heart disease COVID-19 psychological distress

ongenital heart disease affects ≈1% of the general population, and affected individuals span a wide range of clinical severity.<sup>1</sup> Adults with congenital heart disease (ACHD) are a complex and diverse group. Many adults with less severe congenital heart disease, such as small ventricular septal defects, live relatively asymptomatic normal lives. Others with more severe anatomical defects, such as single ventricle

physiology, have only begun to survive to adulthood because of medical and surgical advances of the past 40 years. Moreover, grouping by anatomical anomalies alone cannot accurately predict clinical status, disease burden, and prognosis in ACHD.<sup>2</sup> To combat this broad range of outcomes and lived experiences, the 2018 American College of Cardiology/American Heart Association Anatomic and Physiological (AP)

© 2022 The Authors. Published on behalf of the American Heart Association, Inc., by Wiley. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

JAHA is available at: www.ahajournals.org/journal/jaha

Correspondence to: Jasmine Grewal, MD, St. Paul's Hospital, 478-1081 Burrard St., Vancouver, BC, Canada V6Z 1Y6. Email: jagrewal@providencehealth.bc.ca Supplemental Material is available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.121.023516

For Sources of Funding and Disclosures, see page 11.

The abstract of this work was presented at the International Symposium on ACHD, October 13 to 15, 2021.

# **CLINICAL PERSPECTIVE**

### What Is New?

- Psychological distress increased during the COVID-19 pandemic compared with before the pandemic in a diverse cohort of adults with congenital heart disease.
- Younger patients and women were more likely to experience significant psychological distress, but a consistent trend of anatomical complexity of congenital heart disease or physiological status was not observed.
- Adults with congenital heart disease contracted COVID-19 at a similar rate as the general population and conservatively followed public health guidelines.

### What Are the Clinical Implications?

- The COVID-19 pandemic has had a profound impact on psychological distress in adults with congenital heart disease, highlighting the need for mental health support in this population.
- A comprehensive multifactorial measure of psychological distress, such as the Screening Tool for Psychological Distress survey, should be used, because different aspects (depression, anxiety, stress, anger, and lack of social support) behaved differently throughout the pandemic.

## Nonstandard Abbreviations and Acronyms

AP Classification	Anatomic and Physiological Classification
ACHD	adults with congenital heart disease
STOP-D	Screening Tool for Psychological Distress

Classification was developed to better stratify patients who were ACHD.<sup>3</sup> In this system, patients are assigned an anatomic classification of mild to great complexity based on underlying lesion(s), and a physiologic stage of A to D based on clinical status. The American College of Cardiology/American Heart Association AP Classification has been used to stratify patients across a large range of ACHD studies; for example, complex anatomical status and worsening physiologic status have been suggested predictors of psychological distress.<sup>4</sup>

The COVID-19 pandemic has caused unprecedented challenges to the health care system and stress for individuals. People with preexisting cardiac conditions, such as ACHD, are at a higher risk of experiencing serious health consequences if they contract the SARS-CoV-2 virus, both because of systemic effects and direct cardiac manifestations of COVID-19.5-8 Interestingly, worsening American College of Cardiology/American Heart Association physiological stage has stronger prognostic implications for ACHD that contract COVID-19, rather than more complex anatomical classification.<sup>9</sup> Furthermore, the pandemic has brought unforeseen economic strain and life adjustments for many individuals, worsening the mental health of many people.<sup>10</sup> When combined with the health risk, the psychological distress of individuals with chronic disease has become an area of concern for many clinicians. An increased prevalence of psychological distress, depression, and anxiety have all been well documented in ACHD and associated with poorer clinical outcomes, although a limited number seek specific psychological care.<sup>11–13</sup> However, objectively assessing mental health status and psychological distress can be difficult in complex clinical populations. The Screening Tool for Psychological Distress (STOP-D) survey is a validated screening tool to quantify psychological distress, which was developed specifically for patients with heart disease and is routinely used clinically to identify patients who may benefit from directed psychological support.<sup>14</sup> To date, published analysis of psychological distress and/or mental health in the ACHD population during the COVID-19 pandemic has been limited to the first month of widespread restrictions (March 2020/April 2020).<sup>15</sup>

The objectives of this study were to determine (1) the psychological distress in ACHD well into the COVID-19 pandemic compared with early and prepandemic psychological distress; (2) the impact of COVID-19 on the day-to-day functioning of ACHD; and (3) the percentage of adult patients with congenital heart disease who experienced COVID-19–related symptoms, underwent testing, and tested positive compared with the general population of British Columbia.

## **METHODS**

This is a cross-sectional study of adult patients (≥18 years) with congenital heart disease actively followed at the Yasmin and Amir Virani Provincial Adult Congenital Heart Program at St. Paul's Hospital, University of British Columbia. A web-based survey hosted on Qualtrics was emailed to all active patients of the Adult Congenital Heart Program who had previously provided consent to contact for research.<sup>16</sup> Responses were collected from December 18, 2020 to January 16, 2021. The first page of the survey was a consent form; all patients provided consent to participate before proceeding to the survey questions.

Retrospective clinical data for consented patients were also collected by chart review. This study was approved by the University of British Columbia Research Ethics Board, and procedures followed were in accordance with institutional guidelines. The data that support the findings of this study are available from the corresponding author upon reasonable request.

The survey (and second pandemic time point) occurred at the height of British Columbia's second wave, reporting the highest daily cases and deaths up until that point. Provincial public health orders were similar between the 2 pandemic time points, with restricted inperson gatherings (indoors or outdoors) and encouraged only essential visits out of the house. Notably, this was also before the roll-out of the COVID-19 vaccination program for clinically vulnerable patients and the general public.

#### **Survey Questions**

The survey included questions related to 3 components: psychological distress, lifestyle changes, and experience with COVID-19. Survey questions are outlined in Table 1. The first part of the survey assessed psychological distress. These questions were adapted from the STOP-D survey, which was developed specifically for patients with heart disease and uses a 9-point Likert scale to assess 5 aspects of psychological distress (Table 1): depression, anxiety, stress, anger, and lack of social support.<sup>14</sup> In development of the STOP-D survey, depression was correlated to the Beck Depression Inventory II, anxiety and stress to the Beck Anxiety Index, anger to the State-Trait Anger Expression Inventory 2, and lack of social support to the Medical Outcomes Study Social Support Survey.

The STOP-D data are reported by item as the proportion of patients above cutoff scores for each item. Cutoff scores used were previously validated by receiver operating characteristic curve analysis, which identified clinically relevant distress for each factor.<sup>14</sup> A cutoff score of 4 out of 9 on the Likert scale was used for the depression and anxiety items, and 5 for stress, anger, and lack of social support. Participants were asked to report on their mental health in March 2020 to April 2020 (the first pandemic time point) and in the

Question	Response format
Quality of life	
<ul> <li>How did COVID-19 impact how you were feeling between March 2020 and April 2020? (STOP-D, Time 1)</li> <li>Feeling sad, down, or uninterested in life (depression)</li> <li>Feeling anxious or nervous</li> <li>Feeling stressed</li> <li>Feeling angry</li> <li>Not having the social support you need</li> </ul>	Likert scale 0–9 for each factor
Over the past 2 weeks, have you been feeling better since March 2020/April 2020?	Yes/no
<ul> <li>How did COVID-19 impact how you were feeling between December 2020 and January 2021? (STOP-D, Time 2)</li> <li>1. Feeling sad, down, or uninterested in life (depression)</li> <li>2. Feeling anxious or nervous</li> <li>3. Feeling stressed</li> <li>4. Feeling angry</li> <li>5. Not having the social support you need</li> </ul>	Likert scale 0–9 for each factor
Lifestyle changes	
Are you currently working? 1. If yes, what is your current work environment? 2. If no, select the option that best reflects your situation since March 2020	Yes/no Work from home/going into workplace/mix of both Laid off/quit because of COVID-19/quit because of other reasons/no change/other
Are you currently/planning to attend school? 1. If yes, what mode of delivery is your class/program?	Yes/no Online only/in-person only/both
What is your current level of social activity?	Strictly staying home/essential visits only/essential visits and/or exercise/social bubble <6 people/or social bubble >6 people
COVID-19 experience	
Have you experienced any symptoms of COVID-19 since March 2020? (Select all that apply.)	None, fever (temperature >38 °C/100.4 °F), new cough, worsening shortness of breath or difficulty breathing, loss of smell/taste, muscle aches/ unexplained fatigue, nausea, vomiting, abdominal pain or diarrhea
Have you been tested for COVID-19? 1. If yes, what was the result?	Yes/no Positive/negative

#### Table 1. Survey Questions

2 weeks before completing the survey (December 2020 or January 2021, the second pandemic time point).

The second part of the survey included questions surrounding lifestyle changes compared with before the pandemic with respect to work and social behavior. These questions were developed in conjunction with the clinical staff to better understand how major parts of patients' lives (work, school, social life) had changed in response to the pandemic.

The third part of the survey asked about patients' experiences with COVID-19. Patients were asked to report if they had experienced any symptoms of COVID-19 at any time, and whether or not they sought testing for SARS-CoV-2. A small minority of tests completed in British Columbia were done through private avenues; as such, they would not have been recorded in the public health records, so including this question in the survey was important to capture these tests, if any.

Providing identifiable information (name and date of birth) on the survey was optional. Participants who could not be identified were included in the survey responses but not in the clinical assessment. Responses in which no questions were answered were removed. If a patient completed the survey multiple times, the most complete response was taken or, in the case of multiple complete responses, the first response was taken. Incomplete responses were included because these data were still relevant. As such, questions with the submaximal number of responses are noted.

#### **Clinical Assessment**

Survey responses were linked with retrospective clinical data to assess the underlying anatomy and current physiological state of each participant by review of electronic medical records. Race and ethnicity data were not collected. The ACHD AP Classification, developed as part of the 2018 American College of Cardiology/American Heart Association guidelines, was used to categorize patients based on underlying anatomy and current physiology status.<sup>3</sup> This system classifies anatomical lesions by complexity (simple, moderate, complex) and physiologic status on an escalating scale of A to D. AP Classifications were assigned to all patients who provided identifiable data on their survey response so that the electronic medical records could be reviewed.

Testing for SARS-CoV-2 was reported by each participant on the survey and validated by search of electronic medical records. Only reverse transcriptase– polymerase chain reaction nasopharyngeal swab or saliva tests were included; antigen and antibody testing were not included, because neither was used in British Columbia at the time of study. In the case of a discrepancy between reported tests and electronic medical records tests, the higher number of tests was recorded.

The STOP-D survey is included in standard clinical care at the Adult Congenital Heart Program, with every patient completing the questionnaire at each visit. STOP-D survey responses completed at the time of 2 clinic visits before March 1, 2020 were recorded. These responses were completed before the pandemic and as such were not based on recall.

### **Statistical Analysis**

Patient characteristics were summarized as mean and SD for continuous variables and frequency and percentage for categorical variables. The primary outcome of interest was psychological distress in each of 5 STOP-D items (depression, anxiety, stress, anger, and lack of social support). For each STOP-D item, psychological distress was treated as a binary outcome (above versus below threshold) and fitted to a generalized linear mixed model, where patients were treated as random effects with an unstructured covariance matrix to account for the underlying correlation among measures across 3 time points within individual patients. In the model, age, sex, time point of measure, anatomical class, and physiological stage were included as fixed effects and reported as odds ratio (OR) with corresponding 95% Cl. The model-based adjusted proportions of above-threshold psychological distress for each time point and the difference between pre- and postpandemic time points were also calculated. The linearity assumption of age in the model was assessed by restricted cubic spline method. No obvious violation was observed. To explore the effect of sex on psychological distress at different time points, we fitted a separate generalized linear mixed model by including an interaction term of sex and time point.

All statistical analyses were conducted with the use of SAS 9.4 software (SAS Institute, Cary, NC), and figures were created using R software version 4.1.2 (R Foundation for Statistical Computing, Vienna, Austria).<sup>17,18</sup> A P<0.05 was considered statistically significant in all analyses with no adjustment of multiple testing.

To include the maximum number of responses, survey responses were still included in analysis if not all questions were answered. As such, Tables S1 and S2 include the unadjusted proportions of patients reporting psychological distress, including the number of responses received for each item.

### RESULTS

The survey was sent to 1688 patients followed by the Adult Congenital Heart Program and who had provided consent to contact for research. Twenty-nine

emails were not successfully delivered (undeliverable or bounced). Five hundred seventy-nine (35%) complete or partially complete responses were received, of which 555 (96%) were successfully matched to clinical data to be included in the clinical analyses. The mean age was 45±15 years, and 314 (57%) were women (Table 2). The majority of patients were of moderate anatomic complexity (68%), with bicuspid aortic valve and aortic coarctation being the most common diagnoses in this moderate complexity group.<sup>3</sup> Sixteen percent were of severe complexity, with transposition of the great arteries being the most common diagnosis (Table 2). Most patients were classified as physiological class B (149, 27%) or C (234, 42%). In group B, mild hemodynamic sequelae were the most common reason for classification, whereas significant valvular or ventricular dysfunction was most common in group C.

# Table 2. Demographics and Most Common Anatomic and Physiological Classification of Identifiable Patients

	N, total=555
Age, y	45±15
Sex	240 (43%) men
	314 (57%) women
	1 (0.2%) nonbinary
Anatomic class	
1	87 (16%)
Connective tissue disease (Marfan or Ehlers-Danlos)	25 (29%)
Repaired secundum ASD or sinus venosus	16 (18%)
2	378 (68%)
Bicuspid aortic valve	112 (30%)
Aortic coarctation	70 (19%)
3	90 (16%)
TGA	43 (48%)
Fontan surgery	23 (26%)
Physiological stage	
A	89 (16%)
В	181 (33%)
Mild hemodynamic sequelae	107 (59%)
Mild valvular disease	77 (43%)
Arrhythmia not requiring treatment	21 (12%)
С	264 (48%)
Significant (moderate or greater) valvular disease or ventricular dysfunction	165 (63%)
Arrhythmia controlled with treatment	119 (45%)
D	21 (4%)
Arrhythmia refractory to treatment	11 (52%)
End organ failure	4 (19%)

ASD indicates atrial septal defect; and TGA, transposition of the great arteries.

Table 3 reports the odds ratios for above-threshold psychological distress for each of the 5 STOP-D items. Psychological distress decreased with age, with similar ORs reported for each STOP-D item (ORs ranged from 0.75-0.83). Men were significantly less likely to report above-threshold anxiety (OR, 0.45 [95% CI, 0.36-0.57]; P<0.001) and stress (OR, 0.66 [95% Cl, 0.53-0.84]; P<0.001) compared with women. Compared with prepandemic psychological distress, patients were more likely to report above-threshold distress across all STOP-D items at the first pandemic time point (March 2020/April 2020). Similarly, patients were more likely to report above-threshold distress at the second pandemic time point (December 2020/January 2021) across all STOP-D items except for stress (OR, 1.33 [95% CI, 0.98–1.81]; P=0.07). Patients with the highest anatomical class (C3) were less likely to report abovethreshold anxiety compared with those with the lowest anatomical class (C1) (OR, 0.62 [95% Cl, 0.40-0.96]; P=0.03). Patients with physiologic stage B were less likely to report above-threshold depression (OR, 0.63 [95% CI, 0.44–0.92]; P=0.02) and stress (OR, 0.66 [95% CI, 0.46–0.94]; P=0.02), whereas patients with physiologic state D were more likely to report above-threshold anxiety (OR, 2.27 [95% Cl, 1.08-4.77]; P=0.03) compared with those of physiologic state A. No other significant trends were seen on AP Classification.

Before the pandemic, at most 36% of patients reported above-threshold psychological distress, with the highest proportions of patients reporting anxiety (36% [95% CI, 29%-43%]) and stress (32% [95% CI, 26%-40%]; Figure 1, Table S1). At the first pandemic time point, this significantly increased to over half of patients reporting anxiety (59% [95% Cl. 52%-65%]; P<0.001) and stress (51% [95% Cl, 45%-58%]; P<0.001). Anxiety remained elevated at the second pandemic time point (52% [95% CI, 45%-58%]; P < 0.001), whereas stress returned to prepandemic levels (39% [95% CI, 33%-45%]; P=0.07). At the second pandemic time point, around a quarter of patients reported anger (23% [95% CI, 18%-30%]) and lack of social support (25% [95% CI, 19%-32%]). Depression showed an increasing trend across all 3 time points, from 20% (95% CI, 15%-26%) before the pandemic, to 31% (95% CI, 25%-37%) at the first pandemic time point, and to 39% (95% CI, 33%-45%) at the second pandemic time point. On the survey, 55% of patients reported feeling better in December 2020/January 2021 compared with March 2020/April 2020.

As shown in Figure 2 and Table S2, before the pandemic there were no differences in the proportion of men and women reporting above-threshold psychological distress on any of the STOP-D items (*P* values ranged from 0.12–0.91). However, at the first pandemic

	Depression		Anxiety		Stress		Anger		Lack of social sup	port
	OR (95% CI)	P value	OR (95% CI)	<i>P</i> value	OR (95% CI)	P value	OR (95% CI)	<i>P</i> value	OR (95% CI)	P value
Age, per 10-y increment	0.80 (0.73-0.87)	<0.001	0.75 (0.69–0.81)	<0.001	0.76 (0.70–0.83)	<0.001	0.83 (0.74–0.93)	<0.001	0.78 (0.69–0.88)	<0.001
Sex, men	0.87 (0.68–1.12)	0.28	0.45 (0.36–0.57)	<0.001	0.66 (0.53-0.84)	<0.001	0.96 (0.71–1.29)	0.77	1.01 (0.73–1.39)	0.95
Time point, ref: prepandemic										
March2020/April 2020	1.76 (1.27–2.44)	<0.001	2.54 (1.90–3.41)	<0.001	2.19 (1.61–2.96)	<0.001	1.61 (1.11–2.35)	0.013	3.73 (2.38–5.85)	<0.001
December 2020/January 2021	2.51 (1.81–3.47)	<0.001	1.92 (1.43–2.57)	<0.001	1.33 (0.98–1.81)	0.07	1.86 (1.28–2.71)	0.001	3.62 (2.30–5.70)	<0.001
Anatomical class, ref: C1										
C2	1.06 (0.74–1.51)	0.76	0.86 (0.61–1.20)	0.36	0.90 (0.64–1.25)	0.52	1.53 (0.95–2.44)	0.08	1.55 (0.95–2.52)	0.08
C3	0.80 (0.51–1.28)	0.35	0.62 (0.40–0.96)	0.032	0.88 (0.57–1.36)	0.56	1.23 (0.68–2.21)	0.49	1.28 (0.69–2.36)	0.44
Physiological stage, ref: A										
В	0.63 (0.44–0.92)	0.017	0.90 (0.63–1.29)	0.57	0.66 (0.46-0.94)	0.021	0.65 (0.41–1.04)	0.07	1.01 (0.63–1.64)	0.96
O	0.94 (0.66–1.34)	0.73	1.12 (0.79–1.59)	0.53	0.86 (0.60–1.22)	0.39	0.99 (0.64–1.54)	0.97	0.77 (0.48–1.24)	0.28
D	1.04 (0.50–2.17)	0.92	2.27 (1.08–4.77)	0.031	0.56 (0.26–1.19)	0.13	1.03 (0.40–2.67)	0.95	0.86 (0.29–2.58)	0.79
The second of the second of the second	00000									

Generalized linear mixed model was implemented to account for the underlying correlation of multiple measures within the same patient. and rei, reterence. allo; Dads 1 5

Multivariable Analysis of Psychological Distress Above Threshold\*

Fable 3.

time point, a significantly higher proportion of women reported anxiety (72% [95% Cl, 65%–78%] versus 43% [95% Cl, 35%–51%]; *P*<0.001, *P*<sub>interaction</sub>=0.01) and stress (60% [95% Cl, 52%–66%] versus 42% [95% Cl, 34%–50%]; *P*<0.001, *P*<sub>interaction</sub>=0.02). This difference was maintained at the second pandemic time point, although the magnitude of the difference of adjusted proportions appeared to decrease. Otherwise, depression, anger, and lack of social support were similar between sexes at all time points.

# Impact of COVID-19 on Day-to-Day Functioning

At the second pandemic time point, 223 (38%) patients were not working, of whom 138 (62%) reported that this did not reflect a pandemic-related change because they were either not working, retired, or on long-term disability before March 2020. Eighty-three patients (14% of the total cohort) reported a loss of employment since March 2020, of which 50 (9% of the total cohort) lost work because of COVID-19; 29 reported being laid off, and 21 quit or went on leave because of COVID-19. Of the 356 participants who were currently working, 102 (29%) were exclusively working from home, 182 (51%) were going to an office/ workplace each day, and 71 (20%) reported a mix of both.

Fifty-nine (10%) patients were currently attending school, of which 41 (69%) reported an online-only method of delivery, 6 (10%) in-person only, and 12 (20%) a mix of both. All patients were aged over 19 years, and as such, were likely all attending postsecondary studies. On current social interaction, 233 (40%) were going out for only essential visits and 149 (26%) were socializing with a bubble of <6 others.

### **COVID-19 Symptoms and Testing**

At least 1 symptom of COVID-19 was reported by 136 (24%) patients, with 74 (51%) reporting muscle aches or unexplained fatigue and 57 (39%) reporting a new cough (Table 4). Five hundred sixty-two patients responded to the survey question about SARS-CoV-2 testing, of which 187 (33%) were tested. Ten patients tested positive, representing 1.7% of the cohort between March 2020 and January 2021. This is similar to the incidence in the general population of British Columbia throughout the pandemic (1.3%).<sup>19,20</sup> No patients were hospitalized or died directly because of COVID-19. One patient tested positive while in the hospital for an unrelated cause and did not show symptoms of COVID-19. A total of 262 tests were completed, and most patients were tested once (interguartile range, 1-2). The total test-positivity rate in the ACHD cohort was 3.8%, again similar to the provincial positive rate of 5.5%. Of those who reported symptoms, 91 (62%) were also tested for SARS-CoV-2, and 8



# **Figure 1.** Adjusted proportions of patients above threshold psychological distress for each Screening Tool for Psychological Distress (STOP-D) item at the 3 time points.

The proportion of patients reporting above-threshold psychological distress increased across all STOP-D items in March 2020/April 2020. This remained elevated at the second pandemic time point (December 2020/January 2021), except for stress. \*P<0.05. \*\*P<0.01. \*\*\*P<0.001. Error bars represent 95% confidence intervals. ns indicates not significant.

tested positive. Hence, 2 patients who tested positive did not report symptoms.

#### DISCUSSION

In this study, we sought to better understand the experience of adults with congenital heart disease during the COVID-19 pandemic. This is the first study to directly compare psychological distress before and during the pandemic in the ACHD population. Although the studied population was in British Columbia, Canada, the local environment at the second pandemic time point (December 2020/January 2021) reflected the worldwide peak of winter cases of COVID-19 and limited vaccination, and the AP Classification distribution reflected that of other centers.<sup>9</sup> As such, the findings are generalizable to the broader ACHD population, which is growing; therefore, understanding the experience of adult patients with congenital heart disease in Canada is incredibly important.<sup>21</sup>

#### **Psychological Distress**

Overall, psychological distress increased during the pandemic compared with prepandemic, perhaps as a reaction to the prolonged restrictive measures and absence of a normal routine and life. The current literature corroborates the evidence that the COVID-19 pandemic has resulted in elevated and long-lasting emotional distress; however, it is unclear whether people with chronic disease or ACHD have experienced greater distress compared with the general population.<sup>15,22,23</sup> Interestingly, although the daily case rates in British Columbia increased over the 2 studied pandemic time points, participants reported less stress compared with the beginning of the pandemic, at similar levels to baseline before the pandemic. Patients also reported feeling better in December 2020/ January 2021 compared with their recalled mental state in March 2020/April 2020. This is likely because of a reduction of unknowns because both society and scientists learned more about the virus and hope of imminent vaccine approval grew. Nevertheless, when comparing the overall results of psychological distress within the ACHD population, we found the rates during the pandemic to be higher compared with before the pandemic and generally similar between both pandemic time points.

We did not find a difference between sexes in any of the STOP-D items at the prepandemic time point, in keeping with previous studies before the pandemic,



# Figure 2. Adjusted proportions of psychological distress above threshold by sex across different time points.

There were no differences in psychological distress reported before the pandemic. At both the first (March 2020/April 2020) and second (December 2020/January 2021) pandemic time points, a higher proportion of women reported above-threshold anxiety and stress. \*P<0.05; \*\*\*P<0.001. ns indicates not significant.

#### Table 4. Symptoms Reported (N=145)

Symptom	No. (%)
Fever, temperature above 38 °C/100.4 °F	29 (20%)
New cough	58 (40%)
Worsening shortness of breath or difficulty breathing	42 (29%)
Loss of smell and/or taste	15 (10%)
Muscle aches or unexplained fatigue	74 (51%)
Nausea, vomiting, abdominal pain, or diarrhea	48 (33%)

which have not reached a consensus on sex differences of mental health disorders in the ACHD population.<sup>4,11,24</sup> However, it is difficult to directly compare studies because of varying methods and definitions of psychological distress. We did observe increased anxiety and stress in women at both pandemic time points compared with before the pandemic. Similarly, increased distress in women has also been reported in the general population during the COVID-19 pandemic.<sup>25</sup> Gender roles may be a factor, because women are known to be more likely to both perceive a need for and seek mental health support; however, men are more likely to die by suicide, suggesting psychological distress does not disproportionately impact women.<sup>26</sup> Other possible factors include self-report bias or a greater disruption in everyday life. Interestingly, by the second time point, the gap between anxiety and stress reported by men and women had decreased. The delayed increase (and maintained elevation of stress and anxiety) may be attributable to women considering COVID-19 a more serious entity than men, thus a prolonged pandemic life was required for men to experience psychological distress.<sup>27</sup>

We found that psychological distress decreased with age. This is similar to a large international study, which found a higher prevalence of psychological distress during the COVID-19 pandemic in both the general population and students aged under 40 years.<sup>28</sup> Moreover, 2 separate studies of individuals in Alberta and British Columbia, Canada reported the greatest levels of stress, anxiety, and depression in younger people during the COVID-19 pandemic.<sup>29,30</sup> Given the likelihood of adverse health events because of COVID-19 increases with age, it is perplexing why older people have consistently reported lower levels of psychological distress in the pandemic compared with younger counterparts.<sup>25,29</sup> A common hypothesis is that an important underlying factor of psychological distress within the pandemic is because of the degree of life interruption; however, this has not yet been directly studied. In theory, younger individuals are more likely to have experienced an increased disruption in both social and work activities, combined with a higher likelihood of being in school and impending decisions about one's long-term future. As more research on the topic is completed and the pandemic progresses, it will be important to gain a better understanding into the underlying causes of this consistently reported trend.

Although the pandemic has resulted in increased rates of psychological distress, it appears to have mostly affected the population relatively proportionately, because anatomic/physiologic complexity of the underlying congenital heart lesions sporadically contributed to psychological distress items. Outside of the pandemic, more complex anatomical status and worse physiologic status are likely predictors of psychological distress. In a large study of 6924 adult patients with congenital heart disease, greater lesion complexity correlated to greater prevalence of anxiety, as did a recent history of cardiac procedures.<sup>4</sup> When looking at physiologic status, a higher New York Heart Association class and/or physiologic classification has been consistently associated with greater psychological distress in adult patients with congenital heart disease.31,32 Interestingly, the opposite was reflected in our data, because those with the highest complexity of anatomical lesions (class 3) and most advanced psychological stage (stage D) were the only group to be significantly less likely to report above-threshold anxiety. This may be in part because these patients were following more conservative lifestyle modifications in response to COVID-19, and as such, having a greater sense of control and less anxiety in their everyday lives. However, this trend was not observed across other STOP-D items, supporting the notion that multifactorial measures of psychological distress are important to assess specific aspects of mental health. Interestingly, a study also based in British Columbia did not find increased anxiety or depression in patients with chronic disease compared with those without chronic disease as a result of the COVID-19 pandemic, though they did not include any adult patients with congenital heart disease.<sup>30</sup> Although this study did not compare psychological distress before the pandemic, it does support our overall finding that anatomic and physiologic complexity did not drastically impact the degree of psychological distress experienced during the COVID-19 pandemic.

As reflected by the high level of psychological distress reported in this study, there is clearly a need for psychological care in this vulnerable population, especially in times of crisis. Previous studies report a high prevalence of distress but low prevalence of psychological support and/or treatment, suggesting access to psychological care is not meeting the needs of adult patients with congenital heart disease.<sup>11,13</sup> Given the high prevalence of psychological distress consistently reported in the ACHD population, especially during the COVID-19 pandemic, access to psychological care should be integrated into the clinical care of ACHD in a systematic fashion.<sup>15</sup> At the Yasmin and Amir Virani

Psychological Distress of ACHD During COVID-19

Provincial Adult Congenital Heart Program, a specialized psychologist works with patients who request care or report distress above threshold values on the STOP-D survey. Although not all patients who report above-threshold distress will choose to access support, the option should be provided to ensure optimal care. Based on the results of this study, care may be indicated in over 50% of patients. Furthermore, the prevalence of isolated depression was low, supporting the use of multifactorial assessments of psychological distress such as the STOP-D survey used in the present study.

# Impact of COVID-19 on Day-to-Day Functioning

Nine percent of patients stopped working because of COVID-19-related reasons, either because of layoffs or taking a leave of absence. This resulted in an increase of the percentage of unemployed patients by 5% compared with before the pandemic. Interestingly, this is similar to the change in the unemployment rate in Canada, which rose 4.4% from January 2020 to January 2021.33 As such, it does not appear that a disproportionate number of patients with ACHD left the workforce because of COVID-19 compared with the general population. Similarly, most patients were conservatively following current public health measures, limiting social interactions and nonessential activities. At the second pandemic time point, restrictions were at their most strict, making it difficult to determine whether adult patients with congenital heart disease reduced interactions more than the general population. Given the similarities between ACHD and the general population on other factors, it is likely that adherence to orders remained similar between groups.

## **COVID-19 Symptoms and Testing**

A substantial proportion of patients reported experiencing COVID-19 symptoms (25%) and seeking testing (31%). Most symptoms of COVID-19 are nonspecific, and in light of the clinical status of adult patients with congenital heart disease, a quarter of patients reporting symptoms is not surprising. At the time of survey distribution, testing was widely available and free to the public of British Columbia, removing 2 major barriers faced in other jurisdictions. This likely facilitated test-seeking behavior, because testing was strongly encouraged for any person experiencing even mild symptoms. Although the testing rates seem high, they were comparable to the general local population as was the incidence of COVID-19 infection. It may be expected that testing rates would be higher in a population with a preexisting condition given heightened concerns around becoming infected. However, the ACHD population is quite heterogeneous, with a range of anatomical and physiological classifications in this cohort. The healthier patients may be more likely to seek testing to maintain work, school, and social obligations. Those with complex disease may be more likely to strictly isolate and not seek testing. This was supported by findings of a study at the beginning of the pandemic that found adult patients with congenital heart disease with heart failure were more likely to be totally self-isolated compared with those without heart failure.<sup>15</sup> Limited details surrounding the clinical course of those who contracted SARS-CoV-2 were available, presumably because no patients experienced severe disease and did not seek medical care. Although the risk of adverse outcomes is likely higher in adult patients with congenital heart disease, the absolute risk appears to remain low.<sup>34</sup>

## Limitations

An unavoidable degree of self-report bias may be present with regard to the STOP-D responses; however, the STOP-D survey was developed to limit the impact of any bias, because it correlates with other psychological assessment tools.<sup>14</sup> Not all patients responded to the complete survey, reducing the number of responses for each question and hence limiting the ability to compare changes in psychological distress over time. Statistical adjustments have been made in these cases, as described in the Methods and Results sections. There was no difference observed between sex and age of responders versus nonresponders; however, other factors were not analyzed. The psychological distress assessment in March 2020/April 2020 may be limited by recall bias for the first pandemic time point, because it was determined several months later. However, given that the onset of the COVID-19 pandemic was such a major life event, recollection of mental status may be less susceptible to recall bias. Furthermore, the results align with the finding that most patients reported feeling better at the second pandemic time point compared with March 2020/April 2020, suggesting consistency at the very least.

## CONCLUSIONS

This is the first study to investigate the psychological distress and changes in day-to-day life of adult patients with congenital heart disease months into the COVID-19 pandemic. A substantial proportion of patients reported significant psychological distress during the COVID-19 pandemic that changed over the course of the pandemic and was increased compared with before the pandemic. Younger patients and women were more likely to report increased psychological distress. Although stress initially increased during the pandemic, levels returned to prepandemic values unlike elevated depression, anxiety, and perceived lack of social support, which persisted well into the pandemic. The rates of COVID-19 and test seeking behavior in adult patients with congenital heart disease was similar to that of the general population. This study highlights the need for increased mental health support for adult patients with congenital heart disease, especially during times of crisis.

#### **ARTICLE INFORMATION**

Received August 6, 2021; accepted January 28, 2022.

#### Affiliations

Yasmin and Amir Virani Provincial Adult Congenital Heart Program, Division of Cardiology, Faculty of Medicine (M.L.J., K.L., G.S., M.K., S.C., J.G.) and Center for Cardiovascular Innovation–Centre d'Innovation Cardiovasculaire (J.W.), University of British Columbia, Vancouver, British Columbia, Canada.

#### Acknowledgments

The authors thank the patients of the Yasmin and Amir Virani Provincial Adult Congenital Heart Program for sharing their experiences.

#### Sources of Funding

None.

#### Disclosures

None.

#### **Supplemental Material**

Tables S1-S2.

#### REFERENCES

- van der Linde D, Konings EE, Slager MA, Witsenburg M, Helbing WA, Takkenberg JJ, Roos-Hesselink JW. Birth prevalence of congenital heart disease worldwide: a systematic review and meta-analysis. *J Am Coll Cardiol*. 2011;58:2241–2247. doi: 10.1016/j.jacc.2011.08.025
- Moons P, Luyckx K, Thomet C, Budts W, Enomoto J, Sluman MA, Lu C-W, Jackson JL, Khairy P, Cook SC, et al. Physical functioning, mental health, and quality of life in different congenital heart defects: comparative analysis in 3538 patients from 15 countries. *Can J Cardiol.* 2021;37:215–223. doi: 10.1016/j.cjca.2020.03.044
- Stout KK, Daniels CJ, Aboulhosn JA, Bozkurt B, Broberg CS, Colman JM, Crumb SR, Dearani JA, Fuller S, Gurvitz M, et al. 2018 AHA/ACC guideline for the management of adults with congenital heart disease: a report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines. *Circulation*. 2019;139:e698–e800. doi: 10.1161/CIR.00000000000000003
- Khanna AD, Duca LM, Kay JD, Shore J, Kelly SL, Crume T. Prevalence of mental illness in adolescents and adults with congenital heart disease from the colorado congenital heart defect surveillance system. *Am J Cardiol.* 2019;124:618–626. doi: 10.1016/j.amjcard.2019.05.023
- Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395:1054–1062. doi: 10.1016/S0140-6736(20)30566-3
- Tan W, Aboulhosn J. The cardiovascular burden of coronavirus disease 2019 (COVID-19) with a focus on congenital heart disease. *Int J Cardiol.* 2020;309:70–77. doi: 10.1016/j.ijcard.2020.03.063
- Alsaied T, Aboulhosn JA, Cotts TB, Daniels CJ, Etheridge SP, Feltes TF, Gurvitz MZ, Lewin MB, Oster ME, Saidi A. Coronavirus disease 2019 (COVID-19) pandemic implications in pediatric and adult congenital heart disease. *J Am Heart Assoc.* 2020;9:e017224. doi: 10.1161/ JAHA.120.017224
- Radke RM, Frenzel T, Baumgartner H, Diller GP. Adult congenital heart disease and the COVID-19 pandemic. *Heart.* 2020;106:1302–1309. doi: 10.1136/heartjnl-2020-317258

- Broberg CS, Kovacs AH, Sadeghi S, Rosenbaum MS, Lewis MJ, Carazo MR, Rodriguez FH III, Halpern DG, Feinberg J, Galilea FA, et al. COVID-19 in adults with congenital heart disease. *J Am Coll Cardiol.* 2021;77:1644–1655. doi: 10.1016/j.jacc.2021.02.023
- Vindegaard N, Benros ME. COVID-19 pandemic and mental health consequences: systematic review of the current evidence. *Brain Behav Immun.* 2020;89:531–542. doi: 10.1016/j.bbi.2020.05.048
- Gleason LP, Deng LX, Khan AM, Drajpuch D, Fuller S, Ludmir J, Mascio CE, Partington SL, Tobin L, Kim YY, et al. Psychological distress in adults with congenital heart disease: focus beyond depression. *Cardiol Young*. 2019;29:185–189. doi: 10.1017/S1047951118002068
- Huntley GD, Tecson KM, Sodhi S, Saef J, White KS, Ludbrook PA, Cedars AM, Ko JM. Cardiac denial and expectations associated with depression in adults with congenital heart disease. *Am J Cardiol.* 2019;123:2002–2005. doi: 10.1016/j.amjcard.2019.03.011
- Roseman A, Kovacs AH. Anxiety and depression in adults with congenital heart disease: when to suspect and how to refer. *Curr Cardiol Rep.* 2019;21:145. doi: 10.1007/s11886-019-1237-2
- Young QR, Ignaszewski A, Fofonoff D, Kaan A. Brief screen to identify 5 of the most common forms of psychosocial distress in cardiac patients: validation of the screening tool for psychological distress. *J Cardiovasc Nurs*. 2007;22:525–534. doi: 10.1097/01.JCN.0000297383.29250.14
- Frogoudaki AA, Farmakis D, Tsounis D, Liori S, Stamoulis K, Ikonomidis I, Filippatos G, Parissis J. Telephone based survey in adults with congenital heart disease during COVID-19 pandemic. *Cardiol J.* 2020;27:636– 638. doi: 10.5603/CJ.a2020.0092
- 16. Qualtrics. Qualtrics. 2005. https://www.qualtrics.com
- 17. R Development Core Team. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing. 2021.
- 18. SAS Institute Inc. SAS/ACCESS 9.4 interface to ADABAS. 2013.
- 19. Stats B. 2020 sub-provincial population estimates highlights. 2020.
- 20. Control BCCfD. British columbia COVID-19 dashboard. 2021;2021.
- Beauchesne LM, Therrien J, Alvarez N, Bergin L, Burggraf G, Chetaille P, Gordon E, Kells CM, Kiess M, Mercier L-A, et al. Structure and process measures of quality of care in adult congenital heart disease patients: a pan-Canadian study. *Int J Cardiol.* 2012;157:70–74. doi: 10.1016/j.ijcard.2010.12.024
- Ozamiz-Etxebarria N, Dosil-Santamaria M, Picaza-Gorrochategui M, Idoiaga-Mondragon N. Stress, anxiety, and depression levels in the initial stage of the COVID-19 outbreak in a population sample in the northern spain. *Cad Saude Publica*. 2020;36:e00054020. 10.1590/0102-311X0 0054020
- Choi EPH, Hui BPH, Wan EYF. Depression and anxiety in Hong Kong during COVID-19. Int J Environ Res Public Health. 2020;17:3740. doi: 10.3390/ijerph17103740
- Desai R, Patel K, Dave H, Shah K, DeWitt N, Fong HK, Varma Y, Varma K, Mansuri Z, Sachdeva R, et al. Nationwide frequency, sequential trends, and impact of co-morbid mental health disorders on hospitalizations, outcomes, and healthcare resource utilization in adult congenital heart disease. *Am J Cardiol.* 2020;125:1256–1262. doi: 10.1016/j. amjcard.2020.01.024
- González-Sanguino C, Ausín B, Castellanos M, Saiz J, López-Gómez A, Ugidos C, Muñoz M. Mental health consequences during the initial stage of the 2020 coronavirus pandemic (COVID-19) in Spain. *Brain Behav Immun.* 2020;87:172–176. doi: 10.1016/j.bbi.2020.05.040
- Andrade LH, Alonso J, Mneimneh Z, Wells JE, Al-Hamzawi A, Borges G, Bromet E, Bruffaerts R, de Girolamo G, de Graaf R, et al. Barriers to mental health treatment: results from the WHO World Mental Health surveys. *Psychol Med.* 2014;44:1303–1317. doi: 10.1017/S0033291713001943
- Galasso V, Pons V, Profeta P, Becher M, Brouard S, Foucault M. Gender differences in covid-19 attitudes and behavior: panel evidence from eight countries. *Proc Natl Acad Sci USA*. 2020;117:27285–27291. doi: 10.1073/pnas.2012520117
- Xiong J, Lipsitz O, Nasri F, Lui LMW, Gill H, Phan L, Chen-Li D, lacobucci M, Ho R, Majeed A, et al. Impact of COVID-19 pandemic on mental health in the general population: a systematic review. *J Affect Disord*. 2020;277:55–64. doi: 10.1016/j.jad.2020.08.001
- Nwachukwu I, Nkire N, Shalaby R, Hrabok M, Vuong W, Gusnowski A, Surood S, Urichuk L, Greenshaw AJ, Agyapong VIO. COVID-19 pandemic: age-related differences in measures of stress, anxiety and depression in Canada. *Int J Environ Res Public Health*. 2020;17:6366. doi: 10.3390/ijerph17176366
- Budu MO, Rugel EJ, Nocos R, Teo K, Rangarajan S, Lear SA. Psychological impact of COVID-19 on people with pre-existing chronic

disease. Int J Environ Res Public Health. 2021;18:5972. doi: 10.3390/ ijerph18115972

- Jackson JL, Hassen L, Gerardo GM, Vannatta K, Daniels CJ. Medical factors that predict quality of life for young adults with congenital heart disease: what matters most? *Int J Cardiol.* 2016;202:804–809. doi: 10.1016/j.ijcard.2015.09.116
- Westhoff-Bleck M, Briest J, Fraccarollo D, Hilfiker-Kleiner D, Winter L, Maske U, Busch MA, Bleich S, Bauersachs J, Kahl KG. Mental

disorders in adults with congenital heart disease: unmet needs and impact on quality of life. *J Affect Disord*. 2016;204:180–186. doi: 10.1016/j. jad.2016.06.047

- 33. Statistics Canada. Labour force survey. January 2021. 2021;2021.
- Sabatino J, Ferrero P, Chessa M, Bianco F, Ciliberti P, Secinaro A, Oreto L, Avesani M, Bucciarelli V, Calcaterra G, et al. COVID-19 and congenital heart disease: results from a nationwide survey. *J Clin Med.* 2020;9:1774. doi: 10.3390/jcm9061774

# SUPPLEMENTAL MATERIAL

Table S1.	Unadjusted	and adjusted	proportions	of psychological	distress above threshold $\dagger$
-----------	------------	--------------	-------------	------------------	------------------------------------

							Differer	nce of adj	usted proportion	
	Ur	nadjusted proport	ion		Adjusted proportion		Mar/Apr 2020 vs. pandemic	pre-	Dec/Jan 2021 vs. j pandemic	pre-
	Pre-pandemic n/N(%)	Mar/Apr 2020 n/N(%)	Dec/Jan 2021 n/N(%)	Pre-pandemic %(95% CI)	Mar/Apr 2020 %(95% CI)	Dec/Jan 2021 %(95% CI)	%(95% CI)	P Value	%(95% CI)	P Value
Depression	76/365 (20.82)	155/493 (31.44)	181/458 (39.52)	20.15 (15.49 ~ 25.79)	30.74 (25.45 ~ 36.59)	38.76 (32.79 ~ 45.08)	10.59 (4.65 ~ 16.54)	< 0.001	18.61 (12.29 ~ 24.92)	< 0.001
Anxiety	125/365 (34.25)	295/518 (56.95)	250/498 (50.20)	35.80 (29.44 ~ 42.70)	58.63 (52.40 ~ 64.58)	51.67 (45.34 ~ 57.94)	22.83 (15.95 ~ 29.71)	< 0.001	15.87 (8.87 ~ 22.87)	< 0.001
Stress	106/309 (34.30)	277/521 (53.17)	205/495 (41.41)	32.48 (26.08 ~ 39.61)	51.26 (44.93 ~ 57.54)	39.03 (33.04 ~ 45.37)	18.78 (11.78 ~ 25.77)	< 0.001	6.55 (-0.41 ~ 13.52)	0.07
Anger	57/365 (15.62)	92/399 (23.06)	94/369 (25.47)	14.07 (10.08 ~ 19.29)	20.88 (15.85 ~ 26.99)	23.35 (17.94 ~ 29.81)	6.81 (1.45 ~ 12.18)	0.013	9.29 (3.62 ~ 14.96)	0.001
Lack of Social Support	31/311 (9.97)	100/361 (27.70)	93/342 (27.19)	8.37 (5.37 ~ 12.80)	25.40 (19.24 ~ 32.73)	24.84 (18.62 ~ 32.30)	17.03 (10.93 ~ 23.13)	< 0.001	16.47 (10.29 ~ 22.65)	< 0.001

† Generalized linear mixed model (GLMM) was implemented to account for the underlying correlation of multiple measures within the same patient

	Unadjuste	d proportion	Adjusted	proportion	Difference of adjusted p	roportion	
	Male n/N(%)	Female n/N(%)	Male %(95% CI)	Female %(95% CI)	%(95% CI)	P Value	P Value for interaction
Depression							0.11
Pre-pandemic	40/172 (23.26)	35/190 (18.42)	22.99 (16.55 ~ 31.00)	17.83 (12.53 ~ 24.74)	5.16 (-3.26 ~ 13.58)	0.23	
Mar/Apr 2020	53/198 (26.77)	97/276 (35.14)	26.25 (19.81 ~ 33.89)	34.49 (27.97 ~ 41.65)	-8.24 (-16.69 ~ 0.20)	0.06	
Dec/Jan 2021	66/179 (36.87)	109/263 (41.44)	36.78 (28.96 ~ 45.37)	40.71 (33.67 ~ 48.17)	-3.93 (-13.37 ~ 5.50)	0.42	
Anxiety							0.014
Pre-pandemic	51/172 (29.65)	72/190 (37.89)	32.48 (24.71 ~ 41.36)	40.84 (32.73 ~ 49.48)	-8.36 (-18.69 ~ 1.98)	0.12	
Mar/Apr 2020	83/207 (40.10)	199/291 (68.38)	43.01 (35.11 ~ 51.28)	71.79 (65.18 ~ 77.57)	-28.8 (-37.51 ~ -20.04)	< 0.001	
Dec/Jan 2021	80/198 (40.40)	160/280 (57.14)	43.47 (35.41 ~ 51.89)	60.42 (53.14 ~ 67.26)	-17.0 (-26.20 ~ -7.70)	< 0.001	
Stress							0.022
Pre-pandemic	52/147 (35.37)	53/160 (33.13)	34.41 (26.05 ~ 43.87)	31.30 (23.62 ~ 40.16)	3.12 (-7.57 ~ 13.8)	0.57	
Mar/Apr 2020	89/210 (42.38)	176/291 (60.48)	41.71 (33.84 ~ 50.02)	59.50 (52.20 ~ 66.41)	-17.8 (-26.78 ~ -8.8)	< 0.001	
Dec/Jan 2021	71/202 (35.15)	125/272 (45.96)	34.14 (26.77 ~ 42.36)	44.01 (36.79 ~ 51.50)	-9.87 (-18.87 ~ -0.88)	0.034	
Anger							0.61
Pre-pandemic	27/172 (15.70)	29/190 (15.26)	14.28 (9.29 ~ 21.32)	13.90 (9.19 ~ 20.48)	0.39 (-6.61 ~ 7.38)	0.91	
Mar/Apr 2020	34/163 (20.86)	55/225 (24.44)	18.68 (12.75 ~ 26.52)	22.61 (16.56 ~ 30.09)	-3.94 (-11.9 ~ 4.03)	0.34	
Dec/Jan 2021	41/154 (26.62)	50/205 (24.39)	24.38 (17.32 ~ 33.16)	22.68 (16.50 ~ 30.33)	1.70 (-7.12 ~ 10.53)	0.70	
Lack of Social Support							0.19
Pre-pandemic	18/147 (12.24)	12/162 (7.41)	10.62 (6.26 ~ 17.44)	6.27 (3.35 ~ 11.44)	4.35 (-1.62 ~ 10.32)	0.15	
Mar/Apr 2020	34/139 (24.46)	63/211 (29.86)	22.25 (15.02 ~ 31.67)	27.28 (20.18 ~ 35.77)	-5.03 (-14.14 ~ 4.08)	0.29	
Dec/Jan 2021	37/135 (27.41)	53/197 (26.90)	25.36 (17.49 ~ 35.26)	24.28 (17.40 ~ 32.80)	1.08 (-8.34 ~ 10.51)	0.82	

Table S2. Unadjusted and adjusted proportions of psychological distress above threshold by sex across different timepoints†

† Generalized linear mixed model (GLMM) was implemented to account for the underlying correlation of multiple measures within the same patient