



# Article COVID-Related Distress Is Associated with Increased Menstrual Pain and Symptoms in Adult Women

Laura A. Payne <sup>1,2,\*</sup>, Laura C. Seidman <sup>1</sup>, Boyu Ren <sup>1,2</sup> and Shelly F. Greenfield <sup>1,2</sup>

- <sup>1</sup> McLean Hospital, Belmont, MA 02478, USA
- <sup>2</sup> Harvard Medical School, Boston, MA 02115, USA

Correspondence: lpayne@mclean.harvard.edu

Abstract: The COVID-19 pandemic resulted in heightened stress for many individuals, with women reporting more stress than men. Although a large body of evidence has demonstrated that stress, in general, can impact the menstrual cycle, it is not yet clear if COVID-specific stress would impact women's menstrual health. The current study explored the relationship between COVID-related stress and distress and menstrual variables (menstrual pain, number and severity of menstrual symptoms, and menstrual pain interference) in a sample of reproductive-age adult women. Seven-hundred fifteen women completed the initial survey and were re-contacted to complete the same survey three months later. Of those recontacted, 223 completed the follow-up survey. Results indicated that COVID-related stress and distress was associated with higher levels of menstrual pain, more frequent and more severe menstrual symptoms, and greater menstrual pain interference, even after accounting for age, hormonal use, bodily pain, and pain catastrophizing. Our findings suggest that women experience unique vulnerabilities that directly impact their health and functioning, and both research and clinical care should address these symptoms through careful assessment and treatment of menstrual pain and symptoms, particularly during and after periods of high stress and distress.

Keywords: dysmenorrhea; COVID; stress; menstrual symptoms



Citation: Payne, L.A.; Seidman, L.C.; Ren, B.; Greenfield, S.F. COVID-Related Distress Is Associated with Increased Menstrual Pain and Symptoms in Adult Women. *Int. J. Environ. Res. Public Health* **2023**, 20, 774. https://doi.org/10.3390/ ijerph20010774

Academic Editors: Mike Armour and Carolyn Ee

Received: 3 November 2022 Revised: 23 December 2022 Accepted: 25 December 2022 Published: 31 December 2022



**Copyright:** © 2022 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). 1. Introduction

The Coronavirus Infection Disease (COVID) pandemic dramatically changed the lives of most individuals in the world, beginning in February 2020. In an effort to curb the transmission and infection rates of the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), most communities in the United States and around the world implemented a series of "stay at home" orders, where public and private facilities, including schools and places of employment, and community gatherings were discouraged and/or prohibited. Anxiety about the virus itself, as well as the impact of the efforts to reduce the incidence of the virus, resulted in psychological stress for many individuals [1]. Women, in particular, were vulnerable to these stressors [2], in part due to their role as caregivers [3] and as essential workers [4]. These and other COVID-related stressors unique to women had a direct impact on their health and well-being [5].

A key indicator of women's health is the functioning and cyclicity of the menstrual cycle [6,7], and there is a well-established link between psychological stress and menstrual cycle disruption via activation of the hypothalamic–pituitary–adrenal (HPA) and hypothalamic–pituitary–ovarian (HPO) axes [8]. Emerging reports have indicated disturbances in women's menstrual cycles during the COVID pandemic, including changes in length of the menstrual cycle, duration of menses, and Premenstrual Syndrome (PMS) symptoms [9,10]. Specifically, those who reported higher levels of overall stress during the pandemic also reported greater menstrual symptoms, such as heavier bleeding during menstruation, longer menstrual cycles, and more severe symptoms of PMS. However, other studies have found different patterns, with the COVID pandemic associated with decreased duration of menstruation [11] or no changes in menstrual cycle length at all [12]. The lack of consistency in these findings may point to differences in assessment of stress, methodology (e.g., time frame that the study measures were administered in relation to the timing of the pandemic), or individual differences among women with regard to how stress impacts the menstrual cycle.

Menstrual pain (i.e., dysmenorrhea) is one common and disabling menstrual symptom for many reproductive-age women that may also be susceptible to stress experienced during the pandemic [13]. One study of Jordanian medical students reported significant increases in rates of severe dysmenorrhea and related activity disruption following the pandemic, although these changes were not linked to measures of stress, specifically [14]. A more recent cross-sectional study of 1335 women found that increased anxiety during the pandemic was associated with a change from non-painful to painful periods [15]. Additional data on the impact of COVID-related stress on non-menstrual pain populations supports the notion that increased stress during and due to the pandemic can worsen the pain symptom trajectory [16–18]. For example, adults with fibromyalgia reported higher levels of COVID-related fear and anxiety, compared to adults without fibromyalgia [19]. Worry and stress, as well as a pre-existing sensitivity to somatic symptoms, have been associated with self-report of greater somatic symptoms during the pandemic [20]. In a study of 150 patients with chronic pain, women were at greater risk of increased pain severity and pain interference, even after accounting for other demographic variables [21]. These findings all point to the importance of accounting for menstrual symptoms, menstrual pain, and overall body pain in a single study to better understand reproductive-age women's responses to the COVID pandemic.

Given the impact of stressors and related distress on the menstrual cycle and pain conditions, the present study aimed to examine the relationship between COVID-related stress and distress and menstrual pain, menstrual symptoms, and menstrual pain interference in a large sample of reproductive-age women assessed during the pandemic and three months later. We hypothesized that COVID-related stress and distress would be associated with menstrual pain, menstrual symptom severity, number of menstrual symptoms, and menstrual pain interference, and these relationships would remain stable over the course of three months. Additionally, we hypothesized that these relationships would exist independent of other factors that may contribute to menstrual pain and symptoms, such as report of overall bodily pain, hormonal treatments used, and pain catastrophizing.

# 2. Materials and Methods

# 2.1. Participants

Participants for the current study were recruited from a convenience sample of individuals who had agreed to answer survey questions for a survey-based company (Market Cube, Inc., Schlesinger Group; see description below). Invitations were stratified by age to represent the age spread across the United States. We aimed to enroll participants to obtain a range of menstrual pain ratings, with 25% of participants reporting menstrual pain ratings of 0–2 on the 0–10 Numeric Rating Scale (NRS; see description under Measures), 60% reporting ratings of 3–7, and 15% reporting ratings of 8–10. Survey completion was monitored in real time and the REDCap screening page logic was modified periodically to temporarily close "bins" to ensure that approximately such a distribution was achieved. Inclusion criteria included: (1) female, aged 18–55 years; (2) at least one menstrual cycle during the previous 3 months; and (3) self-reported regular menstrual cycles during the previous 12 months. Participants could be either naturally menstruating or using 1 or more exogenous hormones. Exclusion criteria included: (1) not able to read and understand English; and (2) currently pregnant.

Three thousand and thirty individuals completed the initial screening/eligibility questions in September 2020. Six participants were identified as duplicates of an existing record and removed. For three of these duplicates, the screening questions were identical both times and only one of the surveys was completed beyond the screening page. In these

instances, the full survey was retained in the database, and the duplicate was removed. For one duplicate case, answers to the screening questions differed between the two cases, so both were removed. One additional case was removed because both the survey and the ineligibility page were completed, indicating that the participant paged back in the browser and changed her answers to the eligibility questions.

One thousand three hundred and ninety-six individuals were excluded as ineligible due to pregnancy (n = 131), not having a period during the prior three months (n = 61), not having regular periods over the prior 12 months (n = 405), or neither having a period during the prior three months nor having regular periods over the prior 12 months (n = 799). An additional 336 individuals were excluded from completing the survey based on menstrual pain NRS bin being full. Of the 1292 who were eligible, 60 choose to not participate (i.e., they were directed to the survey but did not answer any questions). One thousand two hundred and thirty-two women at least partially completed the baseline survey and were then recontacted three months after the baseline survey (December 2020) for completion of the identical set of measures. For the current study, 715 participants had complete data from baseline and were included in the baseline analyses. Of these 715, 223 also completed the survey follow-up and were included in the baseline + follow-up group. See Figure 1 for a flow chart of study enrollment.

#### 2.2. Procedures

Survey invitations were sent to women in the target age range who were registered as research panelists in UniVox (managed by Market Cube, Inc. (Mt Pleasant, SC, USA), Schlesinger Group (Iselin, NJ, USA)). Interested participants clicked the included link and were directed to four screening/eligibility questions assessing pregnancy, having a period over the prior three months, having regular periods over the prior 12 months, and average menstrual pain. Ineligible participants were redirected to a Market Cube webpage; eligible participants were directed to the information sheet and proceeded to the survey if they agreed to participate. Study data were collected and managed using REDCap (Research Electronic Data Capture [22,23]) electronic data capture tools hosted at McLean Hospital. REDCap is a secure, web-based software platform designed to support data capture for research studies, providing (1) an intuitive interface for validated data capture; (2) audit trails for tracking data manipulation and export procedures; (3) automated export procedures for seamless data downloads to common statistical packages; and (4) procedures for data integration and interoperability with external sources. For completing the survey, participants were compensated 200 points (equivalent to \$2) within their UniVox account; points are redeemable for gift cards, etc. This study was reviewed by the Partners Healthcare IRB (protocol #2020P002578) and was determined to meet the criteria for exemption. Due to the anonymous nature of this survey study, informed consent was not required.

#### 2.3. Measures

#### 2.3.1. Demographics

Demographic variables were obtained, including age, race, and education level.

#### 2.3.2. Menstrual History and Pain

For the purposes of this study, a self-report measure was included assessing menarche age, number of hormonal treatments currently using, whether the participant was menstruating in the last seven days (yes/no), average menstrual pain (without the use of pain medication) rated on a 0 (none) to 10 (worst pain imaginable) NRS [24,25]. An additional variable of interference in daily living due to menstrual pain (0; no interference to 10; complete interference NRS) was also included.



Figure 1. Enrollment flow diagram.

# 2.3.3. Menstrual Symptoms

Endorsement and severity of menstrual symptoms beyond menstrual pain (e.g., low back pain, headache/migraine, nausea, diarrhea, etc.) was assessed with a well-established measure that was developed to evaluate and test symptom-based phenotypes of women with dysmenorrhea [26–28]. This measure asks participants to indicate the severity of each symptom on a 0 (not present) to 10 (extremely severe) scale over the past 6 months (when menstruating). For the purposes of this study, the total of the severity ratings for each of the symptoms endorsed (Menstrual Symptom Severity), and the number of menstrual symptoms endorsed (i.e., any symptom rated at a severity of at least "1"; Menstrual Symptom Count), were each used as outcome variables.

# 2.3.4. Bodily Pain

Bodily pain was assessed using the Collaborative Health Outcomes Information Registry (CHOIR) Body Map [29], which is fully integrated into REDCap and allows each participant to select the body location where she has experienced pain the last month *while not menstruating*. The Body Map is a well-established measure of widespread pain [30] that can be used with chronic pain (e.g., [31]) and non-chronic pain populations [32–34]. For the

current study, the total number of body map locations endorsed as being painful over the past month (range 0–74) was used. Additionally, participants rated body pain severity in the past month using a 0 (none) to 10 (worst pain imaginable) NRS.

#### 2.3.5. COVID Stress Scales (CSS)

The CSS [35] is a 36-item measure assessing stress and anxiety in response to the COVID-19 pandemic. The CSS is comprised of 5 sub-scales: danger and contamination fears (e.g., "I am worried that people around me will infect me with the virus"), fears about economic consequences (e.g., "I am worried about grocery stores running out of food"), xenophobia (e.g., "If I met a person from a foreign country, I'd be worried that they might have the virus"), compulsive checking and reassurance seeking (e.g., "Checked social media posts concerning COVID-19"), and traumatic stress symptoms (e.g., "I had trouble sleeping because I worried about the virus") about COVID-19.

2.3.6. COVID-19 Exposure and Family Impact Survey—Adolescent and Young Adult Version (CEFIS-AYA)

The CEFIS-AYA [36,37] is a self-report measure that assesses participants' experiences during the COVID-19 pandemic and the impact of the pandemic on psychological and social functioning. The Exposure subscale inquires whether the participant has been exposed to COVID and related events (e.g., "I had a stay at home order," "I/we had difficulty getting food") and consists of two parts (i.e., self and family member). Responses for this subscale were merged such that a yes responses in either subpart was scored as a yes response for the item. The Impact subscale consists of 15 items assessing the impact of the pandemic on the participant's physical, emotional, and social life (e.g., relationships with friends, ability to be independent, substance use, etc.). Items are scored from 1 ("made it a lot better") to 4 ("made it a lot worse"). An answer choice of "not applicable" was also available for each item. Impact subscale scores are calculated as the mean of all items as long as at least twelve of the subscale's fifteen items were answered (i.e., not missing or answered as not applicable). Means < 2.5 indicate positive valence while means > 2.5 indicate negative valence. The Distress subscale is a single item numeric rating scale on which participants report the level of distress caused by the pandemic from 1 (no distress) to 10 (extreme distress). The AYA version of the measure was used as it includes additional questions that are relevant for the current study and is applicable to a broader range of participants than the original (i.e., caregiver only) version.

#### 2.3.7. Pain Catastrophizing Scale (PCS)

The PCS is a 13-item scale that asks participants to indicate the degree to which they have different thoughts when experiencing pain [38]. This measure assesses fears related to pain experiences. Although it includes three subscales (rumination, magnification, and helplessness), the total score on this measure was used for the analyses.

#### 2.4. Data Analysis

#### 2.4.1. Baseline Analysis

This analysis focuses on subjects with complete records of the relevant variables at either baseline only or at both baseline and follow-up. If a subject has complete records at both time points, she was included in the sensitivity analysis described below. Seven hundred and fifteen subjects were included in the final analysis. Linear regression was used to examine the association between the menstrual health variables (outcome measures) and variables derived from the COVID-related measures after adjusting for six covariates related to demographic and menstrual/health histories. The four menstrual health variables were used as the outcome variables in the regression models and analyzed separately. The reference level for race was "White," and education was regarded as a continuous variable. T-test was used to assess the statistical significance of the regression coefficients. Since this

6 of 15

study is conducted mainly for an exploratory purpose, no multiple testing correction was applied to the *p*-values.

#### 2.4.2. Sensitivity Analysis Using Baseline and Follow-Up Data

There were 223 subjects in the dataset with both baseline and follow-up measurements of the relevant variables. A sensitivity analysis was conducted on these subjects to test the robustness of the results from the baseline analysis. Since each subject now has two measurements for the time-varying variables, the generalized estimating equations (GEE) approach [39,40] was used to recover the population-level associations between the set of variables considered in the baseline analysis while accounting for the correlations between the repeated measures from the same subject. A compound symmetric correlation structure was assumed when fitting the GEE, and the *p*-value for a regression coefficient was obtained by using normal approximation on its robust *z*-score.

#### 3. Results

Demographic characteristics for those in the baseline only and baseline + follow-up groups are shown in Table 1. There were no differences between those who completed the baseline only and those who completed the baseline + follow-up.

	Baseline Only ( <i>n</i> = 715)	Baseline + Follow-Up ( <i>n</i> = 223)
Age		
Mean (SD)	34.5 (9.19)	37.4 (8.42)
Education		
Some high school	25 (3.5%)	3 (1.3%)
High school diploma or GED	149 (20.8%)	43 (19.3%)
Some college or 2-year degree	202 (28.3%)	48 (21.5%)
4-year college graduate	211 (29.5%)	86 (38.6%)
Some school beyond college	14 (2.0%)	3 (1.3%)
Graduate or professional degree	114 (15.9%)	40 (17.9%)
Race		
White	546 (76.4%)	172 (77.1%)
Black or African American	66 (9.2%)	18 (8.1%)
Asian	74 (10.3%)	27 (12.1%)
American Indian/Native Hawaiian/Multi-Racial	29 (4.1%)	6 (2.7%)
Number of Hormones using		
Mean (SD)	0.425 (0.691)	0.455 (0.734)
Age at menarche		
Mean (SD)	12.3 (1.76)	12.6 (1.78)
Had period in the past 7 days (y/n)		
Percent indicating "yes"	46.7%	45.2%

**Table 1.** Descriptive statistics of demographic and clinical variables at baseline for the two groups of subjects (Baseline only vs. Baseline + follow-up).

As shown in Table 2, for those who completed the baseline assessment, results indicated that CEFIS distress scores and body pain severity in the past month were positively related to average menstrual pain, while age, number of exogenous hormones currently using, and CEFIS impact scores were negatively related to average menstrual pain. Asian race tended to have lower level of pain compared to White when controlling for all other variables. A similar pattern was observed for those who completed both the baseline and follow-up assessments, with CSS danger and contamination, CEFIS distress, and body pain severity in the past month positively predicting average menstrual pain. Number of hormones currently using, and CEFIS impact scores negatively predicted average menstrual pain. Other races tended to have higher reported level of pain compared to White while Asian race still tended to have lower reported level of pain.

	Baseline Only (n = 715)			Baseline + Follow-Up (n = 223)			
Predictors	Estimates	CI	р	Estimates	CI	р	
(intercept)	5.39	3.90-6.88	<0.001	3.80	0.67–6.93	0.017	
Age	-0.02	-0.04 - 0.0	0.021	-0.01	-0.05-0.03	0.526	
Black or African American race *	-0.05	-0.60-0.50	0.854	-0.98	-2.41- $0.44$	0.176	
Asian race *	-0.68	-1.21 - 0.15	0.011	-1.13	-2.18 - 0.08	0.036	
American Indian/Native Hawaiian/Multi-Racial *	0.45	-0.35-1.24	0.270	2.65	0.65-4.64	0.009	
Education level	-0.12	-0.24 - 0.0	0.06	0.09	-0.16-0.34	0.481	
Number of Hormones using	-0.34	-0.600.09	0.008	-0.51	-1.010.02	0.043	
Age at menarche	-0.03	-0.12 $-0.06$	0.511	-0.03	-0.20 - 0.15	0.760	
Period in last 7 days	-0.12	-0.42 $-0.17$	0.417	-0.08	-0.60-0.44	0.755	
CSS_dc	0.01	-0.00-0.03	0.130	0.06	0.02–0.10	0.001	
CSS_s	-0.01	-0.04 $-0.02$	0.620	-0.01	-0.07 $-0.06$	0.842	
CSS_x	0.00	-0.03 $-0.05$	0.899	-0.02	-0.08-0.05	0.613	
CSS_t	0.01	-0.03 $-0.05$	0.677	-0.01	-0.08-0.06	0.829	
CSS_ch	-0.02	-0.05 - 0.02	0.443	0.02	-0.06-0.10	0.579	
CEFIS (part 1; exposure)	0.01	-0.03 $-0.05$	0.645	-0.01	-0.07 $-0.06$	0.806	
CEFIS (part 2; impact)	-0.24	-0.43 - 0.05	0.014	-0.26	-0.51 - 0.01	0.045	
CEFIS (part 2; distress)	0.20	0.12-0.28	<0.001	0.20	0.06-0.35	0.006	
Body pain in the past month	0.28	0.22-0.34	<0.001	0.20	0.10–0.31	<0.001	
Body map # of locations	0.00	-0.02-0.03	0.701	-0.00	-0.05 - 0.04	0.865	
PCS	0.01	-0.01 $-0.02$	0.340	-0.01	-0.04 $-0.02$	0.524	

**Table 2.** Predictors of Average Menstrual Pain in participants who completed the baseline assessment only and those who completed both baseline and follow-up assessment.

*Note.* \* racial group is in comparison to White (reference group). **Bold** indicates statistical significance of p < 0.05. CSS = COVID Stress Scales; dc = danger and contamination; s = socio-economic; x = xenophobia; t = traumatic stress; ch = compulsive checking; CEFIS = COVID-19 Exposure and Family Impact Scale; PCS = Pain Catastrophizing Scale.

CSS compulsive checking, CEFIS exposure, CEFIS distress, body pain severity in the past month, and PCS scores positively predicted menstrual symptom severity, while Asian race had lower menstrual symptom severity compared to White in those completing the baseline assessment (Table 3). For those with both baseline and follow-up assessments, CSS compulsive checking, CEFIS exposure, CEFIS distress, and body pain severity in the past month positively predicted menstrual symptom severity.

		Baseline Only (n = 715)			Baseline + Follow-Up (n = 223)		
Predictors	Estimates	CI	р	Estimates	CI	р	
(intercept)	26.78	10.91-42.65	<0.001	16.35	-17.51 - 50.20	0.344	
Age	-0.12	-0.31-0.07	0.222	-0.37	-0.80-0.07	0.101	
Black or African American race *	3.88	-1.97-9.73	0.194	8.39	-7.02-23.80	0.286	
Asian race *	-7.81	-13.44 - 2.17	0.007	-5.84	-17.24 - 5.56	0.315	
American Indian/Native Hawaiian/Multi-Racial *	-0.31	-8.80-8.18	0.943	15.99	-5.66-37.65	0.148	
Education level	-0.29	-1.57-0.99	0.659	2.03	-0.66 - 4.72	0.138	
Number of Hormones using	1.16	-1.54-3.87	0.399	2.23	-3.14-7.59	0.416	
Age at menarche	-0.36	-1.32-0.59	0.457	-0.96	-2.84-0.93	0.321	
Period in last 7 days	1.10	-2.07-4.26	0.497	2.02	-3.47-7.52	0.471	
CSS_dc	-0.12	-0.31-0.08	0.250	0.22	-0.16-0.60	0.258	
CSS_s	0.12	-0.23 $-0.48$	0.497	0.15	-0.55-0.84	0.678	
CSS_x	0.18	-0.16-0.53	0.289	0.09	-0.58-0.75	0.801	
CSS_t	0.30	-0.11 $-0.70$	0.148	-0.17	-0.95 $-0.60$	0.664	
CSS_ch	0.47	0.06–0.89	0.024	1.04	0.20–1.88	0.015	
CEFIS (part 1; exposure)	0.41	0.01–0.81	0.042	0.94	0.24–1.64	0.009	
CEFIS (part 2; impact)	-1.72	-3.73-0.28	0.092	0.66	-2.01 - 3.32	0.630	
CEFIS (part 2; distress)	1.23	0.37–2.09	0.005	1.66	0.11–3.22	0.036	
Body pain in the past month	4.20	3.57-4.82	<0.001	3.73	2.61-4.85	<0.001	
Body map # of locations	0.15	-0.10 - 0.41	0.230	0.07	-0.39-0.53	0.767	
PCS	0.21	0.05-0.37	0.011	-0.10	-0.43-0.23	0.539	

**Table 3.** Predictors of Menstrual Symptom Severity in participants who completed the baselineassessment only and those who completed both baseline and follow-up assessment.

*Note.* \* racial group is in comparison to White (reference group). **Bold** indicates statistical significance of p < 0.05. CSS = COVID Stress Scales; dc = danger and contamination; s = socio-economic; x = xenophobia; t = traumatic stress; ch = compulsive checking; CEFIS = COVID-19 Exposure and Family Impact Scale; PCS = Pain Catastrophizing Scale.

CSS traumatic stress and menstrual pain in the past month were positively related to menstrual symptom count, and age and CSS danger and contamination were negatively related to menstrual symptom count in those who completed the baseline assessment only (Table 4). In participants with baseline and follow-up data, education level, CSS compulsive checking, and body pain severity in the past month were positively related to menstrual symptom count, and age was negatively related to menstrual symptom count.

	Baseline Only $(n = 715)$			Baseline + Follow-Up (n = 223)			
Predictors	Estimates	CI	р	Estimates	CI	р	
(intercept)	8.93	6.84–11.02	<0.001	9.17	4.85-13.48	<0.001	
Age	-0.03	-0.060.01	0.008	-0.07	-0.130.02	0.010	
Black or African American race *	0.10	-0.68-0.87	0.808	1.26	-0.071-3.22	0.210	
Asian race *	-0.49	-1.24-0.26	0.199	-0.44	-1.90-1.02	0.553	
American Indian/Native Hawaiian/Multi-Racial *	0.19	-0.93-1.32	0.734	1.36	-1.41-4.13	0.337	
Education level	0.10	-0.07 $-0.27$	0.232	0.44	0.10-0.79	0.011	
Number of Hormones using	0.23	-0.13-0.59	0.210	0.02	-0.66-0.70	0.953	
Age at menarche	-0.03	-0.16-0.09	0.617	-0.12	-0.36-0.12	0.327	
Period in last 7 days	0.12	-0.29-0.53	0.552	0.33	-0.35 - 1.02	0.340	
CSS_dc	-0.03	-0.05 - 0.00	0.047	0.00	-0.05 - 0.05	0.960	
CSS_s	0.03	-0.02- $0.07$	0.274	0.00	-0.08-0.09	0.947	
CSS_x	0.03	-0.02- $0.07$	0.265	0.04	-0.04 $-0.13$	0.327	
CSS_t	0.07	0.02–0.12	0.007	0.06	-0.03-0.16	0.199	
CSS_ch	0.05	-0.00-0.11	0.051	0.11	0.00-0.21	0.044	
CEFIS (part 1; exposure)	-0.00	-0.05 - 0.05	0.977	0.05	-0.04 $-0.13$	0.311	
CEFIS (part 2; impact)	-0.18	-0.44- $0.07$	0.157	-0.06	-0.38-0.27	0.736	
CEFIS (part 2; distress)	-0.01	-0.13-0.10	0.798	-0.07	-0.26-0.13	0.507	
Body pain in the past month	0.33	0.25–0.41	<0.001	0.24	0.10-0.38	0.001	
Body map # of locations	0.02	-0.02-0.05	0.287	0.03	-0.03-0.08	0.368	
PCS	0.01	-0.01- $0.03$	0.225	-0.02	-0.06-0.03	0.453	

**Table 4.** Predictors of Menstrual Symptom Count in participants who completed the baseline assessment only and those who completed both baseline and follow-up assessment.

*Note.* \* racial group is in comparison to White (reference group). **Bold** indicates statistical significance of p < 0.05. CSS = Covid Stress Scales; dc = danger and contamination; s = socio-economic; x = xenophobia; t = traumatic stress; ch = compulsive checking; CEFIS = COVID-19 Exposure and Family Impact Scale; PCS = Pain Catastrophizing Scale.

When examining predictors of menstrual pain interference, CEFIS exposure, CEFIS distress, and body pain severity in the past month were positive predictors, and age and CEFIS impact were significant negative predictors in the baseline sample (Table 5). In the baseline and follow-up sample, CSS danger and contamination, CSS compulsive checking, CEFIS distress, and body pain severity in the past month emerged as positive predictors of menstrual pain interference, while CEFIS impact negatively predicted menstrual pain interference. Other races were associated with a lower level of pain interference compared to White.

		Baseline Only (n = 715)			Baseline + Follow-Up (n = 223)			
Predictors	Estimates	CI	р	Estimates	CI	р		
(intercept)	3.75	2.13–5.38	<0.001	2.67	-0.58 - 5.92	0.107		
Age	-0.03	-0.05 - 0.01	0.004	-0.02	-0.060.02	0.372		
Black or African American race *	0.49	-0.11-1.09	0.107	0.20	-1.27-1.68	0.788		
Asian race *	-0.30	-0.88-0.28	0.308	-0.69	-1.78-0.39	0.209		
American Indian/Native Hawaiian/Multi-Racial *	0.40	-0.47 - 1.27	0.364	2.22	0.16-4.27	0.034		
Education level	0.01	-0.13 $-0.14$	0.939	0.20	-0.06-0.46	0.130		
Number of Hormones using	-0.12	-0.40-0.15	0.381	-0.20	-0.71-0.32	0.456		
Age at menarche	-0.03	-0.13 $-0.07$	0.552	-0.10	-0.28-0.08	0.289		
Period in last 7 days	-0.13	-0.45 $-0.20$	0.450	0.08	-0.47 $-0.64$	0.771		
CSS_dc	0.01	-0.01 $-0.03$	0.249	0.08	0.04–0.11	<0.001		
CSS_s	0.01	-0.03 $-0.04$	0.671	-0.01	-0.08-0.05	0.688		
CSS_x	-0.02	-0.06-0.01	0.258	-0.06	-0.12 - 0.01	0.077		
CSS_t	0.02	-0.02 $-0.06$	0.262	-0.03	-0.11 $-0.05$	0.425		
CSS_ch	0.02	-0.02 $-0.06$	0.357	0.10	0.01–0.18	0.027		
CEFIS (part 1; exposure)	0.05	0.00-0.09	0.030	0.03	-0.04 $-0.10$	0.362		
CEFIS (part 2; impact)	-0.30	-0.51 - 0.09	0.005	-0.29	-0.56 - 0.01	0.041		
CEFIS (part 2; distress)	0.19	0.10-0.27	<0.001	0.20	0.04–0.35	0.013		
Body pain in the past month	0.30	0.24–0.36	<0.001	0.25	0.14–0.36	<0.001		
Body map # of locations	0.00	-0.02-0.03	0.716	-0.00	-0.05 - 0.04	0.897		
PCS	0.01	-0.00-0.03	0.153	-0.00	-0.03-0.03	0.979		

**Table 5.** Predictors of Menstrual Pain Interference in participants who completed the baseline assessment only and those who completed both baseline and follow-up assessment.

*Note.* \* racial group is in comparison to White (reference group). **Bold** indicates statistical significance of p < 0.05. CSS = COVID Stress Scales; dc = danger and contamination; s = socio-economic; x = xenophobia; t = traumatic stress; ch = compulsive checking; CEFIS = COVID-19 Exposure and Family Impact Scale; PCS = Pain Catastrophizing Scale.

# 4. Discussion

The current study aimed to clarify the relationship of COVID-related stress and distress, menstrual pain and related symptoms, and menstrual pain interference, after accounting for demographic and menstrual variables, self-reported (non-menstrual) bodily pain, and pain catastrophizing in a large sample of reproductive-age women. Given the well-established link between stress and menstrual cycle changes, as well as more recent evidence linking COVID-specific stress to menstrual changes and, separately, to increased pain and somatic symptoms, we hypothesized that COVID-related stress and distress would both be associated with increased menstrual pain, number and severity of menstrual symptoms, and menstrual pain interference.

Data analyses provided support for this hypothesis, with many measures positively predicting the four outcome variables, which suggests that higher levels of COVID stress and distress were associated with higher levels of menstrual pain and symptoms. In particular, CEFIS distress (a single item asking participants how much distress they experienced as a result of the pandemic) was positively related to all outcome measures, with the exception of menstrual symptom count, in both the baseline only and baseline + follow-up samples. On the other hand, CEFIS exposure (a subscale that quantifies the number of COVID-related exposures to stressful situations) was not a significant predictor of the menstrual outcome variables (with the exception of Menstrual Symptom Severity). These data suggest that the experience of distress, regardless of the actual number of stressful events, may have the greatest impact on menstrual pain and related symptoms.

Additionally, body pain severity showed a strong, positive relationship with all four menstrual-related outcome variables. This is consistent with previous data in clinical populations suggesting that many women who experience chronic pain also experience menstrual pain [41–43]. Although our data did not identify those with chronic pain, the results still suggest a strong link between overall body pain severity and menstrual pain, symptoms, and interference. However, COVID-related stress and distress variables were still significantly related to the menstrual outcome variables over and above the relationship with body pain.

Interestingly, Asian race was negatively associated with most outcome variables. Little work has been done on racial/ethnic differences in dysmenorrhea, particularly among Asian women. However, research in Asian populations have reported a general reluctance to seek help for menstrual-related problems [44,45], which may also reflect a tendency to view symptoms of dysmenorrhea as "normal," and perhaps result in lower overall pain scores. Studies examining racial and ethnic differences in the prevalence of self-reported chronic pain have also found lower prevalence in Asian populations [46,47], although other research suggests *heightened* pain sensitivity in response to laboratory pain tasks in Asian individuals [48–50]. The data from the current study supports this notion that the relationship between racial differences and pain is complex, involving many social and cultural factors.

Another interesting finding was that the number of hormones a participant identified as using was *negatively* associated with menstrual pain in both the baseline and baseline + follow-up samples. Hormonal interventions are commonly used for menstrual pain, although in this study we required individuals to still have regular menstrual cycles so they could not be fully suppressing the menstrual cycle. The negative relationship with hormonal use and menstrual pain suggests that reduction of pain is at least somewhat effective, even without menstrual suppression.

Results of this study demonstrated a strong relationship between COVID stress and distress and menstrual pain, initially assessed in the first six months of the pandemic and prospectively three months later. These findings are consistent with the one other study reporting increased rates of dysmenorrhea following the pandemic [14]. Yet, the pathophysiological mechanisms by which pandemic-related stress and distress affect menstrual pain are not entirely clear. Stress is associated with increased synthesis of uterine prostaglandins [51–53], which is a known factor contributing to menstrual pain in many women. However, alterations in pain processing via the central nervous system may also be affected by stress [54] and result in heightened menstrual pain [55,56]. Future research examining the contribution of each of these variables is the important next step to identifying unique risk factors of menstrual pain and symptoms in women.

#### Limitations

The current study has a number of limitations that warrant discussion. First, we did not obtain data on participants' menstrual pain, menstrual symptoms, or menstrual pain interference prior to the onset of the pandemic. Therefore, we cannot conclude that the pandemic or pandemic-related stress and distress *caused* any changes; rather, we are able to determine only that there is a relationship between stress and distress about the pandemic and menstrual pain and symptoms. Additionally, our findings suggest that these relationships were stable, at least over a three-month period. We do not anticipate any bias that would affect completion of the follow-up survey, so these findings appear consistent. Third, we included two measures of COVID-related stress and distress to try to capture various aspects of experiences that people may be having as a result of the pandemic. However, these two measures provided only a limited picture of the many stressors that women may have experienced, so it is important to recognize that we cannot fully understand the total impact of the stress of the pandemic based on these data. Another important consideration is that we did not obtain any vaccine-related data, including vaccination status, timing of the last vaccine, or stress related to the vaccine, specifically. Given emerging evidence of the impact of the COVID vaccine on the menstrual cycle [57–59], it is possible that vaccination status may have impacted our findings. However, given that we saw similar patterns at baseline and 3-month follow-up, vaccination status may have had less of an impact, at least on the menstrual variables we included in this study. Additionally, we asked about *types* of exogenous hormone use (e.g., "pill," IUD, hormonal patch), but we did not obtain any more detailed information about the use of hormones (e.g., for how long or what type of pill).

#### 5. Conclusions

These data show that women who experienced stress related to the COVID pandemic also experienced higher levels of menstrual pain, more frequent and more severe menstrual symptoms, and more menstrual pain interference. These relationships were true, even after accounting for age, the number of exogenous hormones being used, bodily pain, and pain catastrophizing. Additionally, the number of COVID-related stressors experienced was not strongly associated with outcome variables. Our findings suggest that women experience unique vulnerabilities that directly impact their menstrual health and overall functioning, and both research and clinical care should address health through careful assessment and treatment of menstrual pain and symptoms, particularly during and after periods of high stress and distress. Clinical interventions focused on reducing stress may be particularly effective for helping women with menstrual symptoms, even if the stressors they are experiencing cannot be changed.

Author Contributions: Conceptualization, L.A.P. and L.C.S.; methodology, L.A.P. and L.C.S.; software, L.A.P. and B.R.; validation, L.C.S.; formal analysis, B.R.; investigation, L.A.P.; resources, L.A.P. and S.F.G.; data curation, L.A.P. and L.C.S.; writing—original draft preparation, L.A.P.; writing reviewing and editing, L.A.P., L.C.S., B.R. and S.F.G.; supervision, L.A.P. and S.F.G.; project administration, L.A.P. and L.C.S.; funding acquisition, L.A.P. All authors have read and agreed to the published version of the manuscript.

**Funding:** This research was funded by NIH/NICHD, grant number R01 HD093680 (PI: Laura A. Payne).

**Institutional Review Board Statement:** The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board of Partners Healthcare (protocol 2020P002578; approved 25 August 2020).

Informed Consent Statement: Patient consent was waived due to the anonymous nature of the study.

**Data Availability Statement:** The current approved institutional mechanism for data sharing is by individual data use agreements executed between the interested parties.

Conflicts of Interest: The authors declare no conflict of interest.

# References

- McGinty, E.E.; Presskreischer, R.; Anderson, K.E.; Han, H.; Barry, C.L. Psychological Distress and COVID-19-Related Stressors Reported in a Longitudinal Cohort of US Adults in April and July 2020. JAMA 2020, 324, 2555–2557. [CrossRef]
- Pierce, M.; Hope, H.; Ford, T.; Hatch, S.; Hotopf, M.; John, A.; Kontopantelis, E.; Webb, R.; Wessely, S.; McManus, S.; et al. Mental health before and during the COVID-19 pandemic: A longitudinal probability sample survey of the UK population. *Lancet Psychiatry* 2020, 7, 883–892. [CrossRef]
- Hammarberg, K.; Tran, T.; Kirkman, M.; Fisher, J. Sex and age differences in clinically significant symptoms of depression and anxiety among people in Australia in the first month of COVID-19 restrictions: A national survey. *BMJ Open* 2020, 10, e042696. [CrossRef]

- 4. Laughlin, L.; Wisniewski, M. Women Represent Majority of Workers in Several Essential Occupations. Available online: https://www.census.gov/library/stories/2021/03/unequally-essential-women-and-gender-pay-gap-during-covid-19.html (accessed on 31 March 2021).
- Magee, L.A.; Benetou, V.; George-Carey, R.; Kulkarni, J.; MacDermott, N.E.; Missmer, S.A.; Morroni, C.; Vidler, M.; Kennedy, S.H. Editorial: COVID-19 and Women's Health. *Front. Glob. Women's Health* 2022, *3*, 861315. [CrossRef] [PubMed]
- Critchley, H.O.D.; Babayev, E.; Bulun, S.E.; Clark, S.; Garcia-Grau, I.; Gregersen, P.K.; Kilcoyne, A.; Kim, J.J.; Lavender, M.; Marsh, E.E.; et al. Menstruation: Science and society. *Am. J. Obstet. Gynecol.* 2020, 223, 624–664. [CrossRef] [PubMed]
- Office on Women's Health. Your Menstrual Cycle and Your Health. Available online: https://www.womenshealth.gov/ menstrual-cycle/your-menstrual-cycle-and-your-health (accessed on 31 March 2021).
- 8. Valsamakis, G.; Chrousos, G.; Mastorakos, G. Stress, female reproduction and pregnancy. *Psychoneuroendocrinology* **2019**, 100, 48–57. [CrossRef] [PubMed]
- 9. Ozimek, N.; Velez, K.; Anvari, H.; Butler, L.; Goldman, K.N.; Woitowich, N.C. Impact of Stress on Menstrual Cyclicity during the Coronavirus Disease 2019 Pandemic: A Survey Study. *J. Womens Health* **2022**, *31*, 84–90. [CrossRef]
- Takmaz, T.; Gundogmus, I.; Okten, S.B.; Gunduz, A. The impact of COVID-19-related mental health issues on menstrual cycle characteristics of female healthcare providers. *J. Obstet. Gynaecol. Res.* 2021, 47, 3241–3249. [CrossRef]
- 11. Demir, O.; Sal, H.; Comba, C. Triangle of COVID, anxiety and menstrual cycle. *J. Obstet. Gynaecol.* **2021**, *41*, 1257–1261. [CrossRef]
- Phelan, N.; Behan, L.A.; Owens, L. The Impact of the COVID-19 Pandemic on Women's Reproductive Health. *Front. Endocrinol.* 2021, 12, 642755. [CrossRef]
- 13. Wang, L.; Wang, X.; Wang, W.; Chen, C.; Ronnennberg, A.G.; Guang, W.; Huang, A.; Fang, Z.; Zang, T.; Wang, L.; et al. Stress and dysmenorrhoea: A population based prospective study. *Occup. Environ. Med.* **2004**, *61*, 1021–1026. [CrossRef] [PubMed]
- 14. Aolymat, I.; Khasawneh, A.I.; Al-Tamimi, M. COVID-19-Associated Mental Health Impact on Menstrual Function Aspects: Dysmenorrhea and Premenstrual Syndrome, and Genitourinary Tract Health: A Cross Sectional Study among Jordanian Medical Students. *Int. J. Environ. Res. Public Health* **2022**, *19*, 1439. [CrossRef] [PubMed]
- Maher, M.; Keeffe, A.O.; Phelan, N.; Behan, L.A.; Collier, S.; Hevey, D.; Owens, L. Female Reproductive Health Disturbance Experienced during the COVID-19 Pandemic Correlates with Mental Health Disturbance and Sleep Quality. *Front. Endocrinol.* 2022, 13, 838886. [CrossRef] [PubMed]
- 16. Pagé, M.G.; Lacasse, A.; Dassieu, L.; Hudspith, M.; Moor, G.; Sutton, K.; Thompson, J.M.; Dorais, M.; Janelle Montcalm, A.; Sourial, N.; et al. A cross-sectional study of pain status and psychological distress among individuals living with chronic pain: The Chronic Pain & COVID-19 Pan-Canadian Study. *Health Promot. Chronic Dis. Prev. Can.* **2021**, *41*, 141–152. [CrossRef]
- 17. Asquini, G.; Bianchi, A.E.; Borromeo, G.; Locatelli, M.; Falla, D. The impact of COVID-19-related distress on general health, oral behaviour, psychosocial features, disability and pain intensity in a cohort of Italian patients with temporomandibular disorders. *PLoS ONE* **2021**, *16*, e0245999. [CrossRef] [PubMed]
- Mun, C.J.; Campbell, C.M.; McGill, L.S.; Aaron, R.V. The Early Impact of COVID-19 on Chronic Pain: A Cross-Sectional Investigation of a Large Online Sample of Individuals with Chronic Pain in the United States, April to May, 2020. *Pain Med.* 2021, 22, 470–480. [CrossRef]
- 19. Cankurtaran, D.; Tezel, N.; Ercan, B.; Yildiz, S.Y.; Akyuz, E.U. The effects of COVID-19 fear and anxiety on symptom severity, sleep quality, and mood in patients with fibromyalgia: A pilot study. *Adv. Rheumatol.* **2021**, *61*, 41. [CrossRef]
- 20. Koppert, T.Y.; Jacobs, J.W.G.; Lumley, M.A.; Geenen, R. The impact of COVID-19 stress on pain and fatigue in people with and without a central sensitivity syndrome. *J. Psychosom. Res.* **2021**, *151*, 110655. [CrossRef]
- Hruschak, V.; Flowers, K.M.; Azizoddin, D.R.; Jamison, R.N.; Edwards, R.R.; Schreiber, K.L. Cross-sectional study of psychosocial and pain-related variables among patients with chronic pain during a time of social distancing imposed by the coronavirus disease 2019 pandemic. *Pain* 2021, *162*, 619–629. [CrossRef]
- Harris, P.A.; Taylor, R.; Minor, B.L.; Elliott, V.; Fernandez, M.; O'Neal, L.; McLeod, L.; Delacqua, G.; Delacqua, F.; Kirby, J.; et al. The REDCap consortium: Building an international community of software platform partners. *J. Biomed. Inform.* 2019, 95, 103208. [CrossRef]
- Harris, P.A.; Taylor, R.; Thielke, R.; Payne, J.; Gonzalez, N.; Conde, J.G. Research electronic data capture (REDCap)—A metadatadriven methodology and workflow process for providing translational research informatics support. *J. Biomed. Inform.* 2009, 42, 377–381. [CrossRef]
- Breivik, E.K.; Björnsson, G.A.; Skovlund, E. A comparison of pain rating scales by sampling from clinical trial data. *Clin. J. Pain* 2000, 16, 22–28. [CrossRef] [PubMed]
- Dworkin, R.H.; Turk, D.C.; Farrar, J.T.; Haythornthwaite, J.A.; Jensen, M.P.; Katz, N.P.; Kerns, R.D.; Stucki, G.; Allen, R.R.; Bellamy, N.; et al. Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. *Pain* 2005, 113, 9–19. [CrossRef] [PubMed]
- Chen, C.X.; Kwekkeboom, K.L.; Ward, S.E. Self-report pain and symptom measures for primary dysmenorrhoea: A critical review. *Eur. J. Pain* 2015, 19, 377–391. [CrossRef] [PubMed]
- 27. Chen, C.X.; Ofner, S.; Bakoyannis, G.; Kwekkeboom, K.L.; Carpenter, J.S. Symptoms-Based Phenotypes among Women with Dysmenorrhea: A Latent Class Analysis. *West. J. Nurs. Res.* **2018**, *40*, 1452–1468. [CrossRef]
- Rogers, S.K.; Rand, K.L.; Chen, C.X. Comparing dysmenorrhea beliefs and self-management techniques across symptom-based phenotypes. J. Clin. Nurs. 2021, 30, 2015–2022. [CrossRef]

- Scherrer, K.H.; Ziadni, M.S.; Kong, J.T.; Sturgeon, J.A.; Salmasi, V.; Hong, J.; Cramer, E.; Chen, A.L.; Pacht, T.; Olson, G.; et al. Development and validation of the Collaborative Health Outcomes Information Registry body map. *Pain Rep.* 2021, *6*, e880. [CrossRef]
- 30. Brummett, C.M.; Bakshi, R.R.; Goesling, J.; Leung, D.; Moser, S.E.; Zollars, J.W.; Williams, D.A.; Clauw, D.J.; Hassett, A.L. Preliminary validation of the Michigan Body Map. *Pain* **2016**, *157*, 1205–1212. [CrossRef]
- Landis, J.R.; Williams, D.A.; Lucia, M.S.; Clauw, D.J.; Naliboff, B.D.; Robinson, N.A.; van Bokhoven, A.; Sutcliffe, S.; Schaeffer, A.J.; Rodriguez, L.V.; et al. The MAPP research network: Design, patient characterization and operations. *BMC Urol.* 2014, 14, 58. [CrossRef]
- Harle, C.A.; Listhaus, A.; Covarrubias, C.M.; Schmidt, S.O.; Mackey, S.; Carek, P.J.; Fillingim, R.B.; Hurley, R.W. Overcoming barriers to implementing patient-reported outcomes in an electronic health record: A case report. *J. Am. Med. Inform. Assoc.* 2016, 23, 74–79. [CrossRef]
- 33. Hoang, N.S.; Hwang, W.; Katz, D.A.; Mackey, S.C.; Hofmann, L.V. Electronic Patient-Reported Outcomes: Semi-Automated Data Collection in the Interventional Radiology Clinic. J. Am. Coll. Radiol. 2019, 16, 472–477. [CrossRef] [PubMed]
- 34. Rosenberg, G.M.; Shearer, E.J.; Zion, S.R.; Mackey, S.C.; Morris, A.M.; Spain, D.A.; Weiser, T.G. Implementation Challenges Using a Novel Method for Collecting Patient-Reported Outcomes after Injury. J. Surg. Res. 2019, 241, 277–284. [CrossRef] [PubMed]
- 35. Taylor, S.; Landry, C.A.; Paluszek, M.M.; Fergus, T.A.; McKay, D.; Asmundson, G.J.G. Development and initial validation of the COVID Stress Scales. *J. Anxiety Disord.* 2020, 72, 102232. [CrossRef] [PubMed]
- Enlow, P.T.; Phan, T.T.; Lewis, A.M.; Hildenbrand, A.K.; Sood, E.; Canter, K.S.; Vega, G.; Alderfer, M.A.; Kazak, A.E. Validation of the COVID-19 Exposure and Family Impact Scales. J. Pediatr. Psychol. 2022, 47, 259–269. [CrossRef] [PubMed]
- Kazak, A.E.; Alderfer, M.; Enlow, P.T.; Lewis, A.M.; Vega, G.; Barakat, L.; Kassam-Adams, N.; Pai, A.; Canter, K.S.; Hildenbrand, A.K.; et al. COVID-19 Exposure and Family Impact Scales: Factor Structure and Initial Psychometrics. *J. Pediatr. Psychol.* 2021, 46, 504–513. [CrossRef] [PubMed]
- Sullivan, M.J.; Bishop, S.R.; Pivik, J. The pain catastrophizing scale: Development and validation. *Psychol. Assess.* 1995, 7, 524. [CrossRef]
- Fitzmaurice, G.; Davidian, M.; Verbeke, G.; Molenberghs, G. (Eds.) Longitudinal Data Analysis, 1st ed.; Chapman and Hall: London, UK; CRC Press: Boca Raton, FL, USA, 2008. [CrossRef]
- 40. Liang, K.-Y.; Zeger, S.L. Longitudinal data analysis using generalized linear models. Biometrika 1986, 73, 13–22. [CrossRef]
- 41. Hardi, G.; Evans, S.; Craigie, M. A possible link between dysmenorrhoea and the development of chronic pelvic pain. *Aust. N. Z. J. Obstet. Gynaecol.* **2014**, *54*, 593–596. [CrossRef]
- 42. Westling, A.M.; Tu, F.F.; Griffith, J.W.; Hellman, K.M. The association of dysmenorrhea with noncyclic pelvic pain accounting for psychological factors. *Am. J. Obstet. Gynecol.* **2013**, 209, 422.e1–422.e10. [CrossRef]
- 43. Zondervan, K.T.; Yudkin, P.L.; Vessey, M.P.; Jenkinson, C.P.; Dawes, M.G.; Barlow, D.H.; Kennedy, S.H. Chronic pelvic pain in the community–symptoms, investigations, and diagnoses. *Am. J. Obstet. Gynecol.* **2001**, *184*, 1149–1155. [CrossRef]
- 44. Wong, L.P. Premenstrual syndrome and dysmenorrhea: Urban-rural and multiethnic differences in perception, impacts, and treatment seeking. *J. Pediatr. Adolesc. Gynecol.* **2011**, 24, 272–277. [CrossRef]
- Wong, L.P.; Khoo, E.M. Menstrual-Related Attitudes and Symptoms among Multi-racial Asian Adolescent Females. Int. J. Behav. Med. 2011, 18, 246–253. [CrossRef]
- Zelaya, C.E.; Dahlhamer, J.M.; Lucas, J.W.; Connor, E.M. NCHS Data Brief. In *Chronic Pain and High-Impact Chronic Pain among* U.S. Adults, 2019; National Center for Health Statistics: Hyattsville, MD, USA, 2020; Volume 390.
- 47. Nahin, R.L. Estimates of pain prevalence and severity in adults: United States, 2012. J. Pain 2015, 16, 769–780. [CrossRef]
- 48. Ahn, H.; Weaver, M.; Lyon, D.E.; Kim, J.; Choi, E.; Staud, R.; Fillingim, R.B. Differences in Clinical Pain and Experimental Pain Sensitivity between Asian Americans and Whites with Knee Osteoarthritis. *Clin. J. Pain* **2017**, *33*, 174–180. [CrossRef]
- Kim, H.J.; Yang, G.S.; Greenspan, J.D.; Downton, K.D.; Griffith, K.A.; Renn, C.L.; Johantgen, M.; Dorsey, S.G. Racial and ethnic differences in experimental pain sensitivity: Systematic review and meta-analysis. *Pain* 2017, 158, 194–211. [CrossRef]
- Ostrom, C.; Bair, E.; Maixner, W.; Dubner, R.; Fillingim, R.B.; Ohrbach, R.; Slade, G.D.; Greenspan, J.D. Demographic Predictors of Pain Sensitivity: Results From the OPPERA Study. J. Pain 2017, 18, 295–307. [CrossRef]
- 51. Austin, M.P.; Leader, L. Maternal stress and obstetric and infant outcomes: Epidemiological findings and neuroendocrine mechanisms. *Aust. N. Z. J. Obstet. Gynaecol.* 2000, 40, 331–337. [CrossRef]
- 52. Casey, M.L.; MacDonald, P.C.; Mitchell, M.D. Despite a massive increase in cortisol secretion in women during parturition, there is an equally massive increase in prostaglandin synthesis. A paradox? *J. Clin. Investig.* **1985**, 75, 1852–1857. [CrossRef] [PubMed]
- 53. Wadhwa, P.D.; Dunkel-Schetter, C.; Chicz-DeMet, A.; Porto, M.; Sandman, C.A. Prenatal psychosocial factors and the neuroendocrine axis in human pregnancy. *Psychosom. Med.* **1996**, *58*, 432–446. [CrossRef] [PubMed]
- Geva, N.; Defrin, R. Opposite Effects of Stress on Pain Modulation Depend on the Magnitude of Individual Stress Response. J. Pain 2018, 19, 360–371. [CrossRef] [PubMed]
- 55. Vincent, K.; Warnaby, C.; Stagg, C.J.; Moore, J.; Kennedy, S.; Tracey, I. Dysmenorrhoea is associated with central changes in otherwise healthy women. *Pain* **2011**, *152*, 1966–1975. [CrossRef] [PubMed]
- 56. Payne, L.A.; Seidman, L.C.; Sim, M.-S.; Rapkin, A.J.; Naliboff, B.D.; Zeltzer, L.K. Experimental evaluation of central pain processes in young women with primary dysmenorrhea. *Pain* **2019**, *160*, 1421–1430. [CrossRef] [PubMed]

- Edelman, A.; Boniface, E.R.; Benhar, E.; Han, L.; Matteson, K.A.; Favaro, C.; Pearson, J.T.; Darney, B.G. Association between Menstrual Cycle Length and Coronavirus Disease 2019 (COVID-19) Vaccination: A U.S. Cohort. *Obstet. Gynecol.* 2022, 139, 481–489. [CrossRef] [PubMed]
- Edelman, A.; Boniface, E.R.; Male, V.; Cameron, S.T.; Benhar, E.; Han, L.; Matteson, K.A.; Van Lamsweerde, A.; Pearson, J.T.; Darney, B.G. Association between menstrual cycle length and covid-19 vaccination: Global, retrospective cohort study of prospectively collected data. *BMJ Med.* 2022, *1*, e000297. [CrossRef]
- 59. Gibson, E.A.; Li, H.; Fruh, V.; Gabra, M.; Asokan, G.; Jukic, A.M.Z.; Baird, D.D.; Curry, C.L.; Fischer-Colbrie, T.; Onnela, J.P.; et al. COVID-19 vaccination and menstrual cycle length in the Apple Women's Health Study. NPJ Digit. Med. 2022, 5, 165. [CrossRef] [PubMed]

**Disclaimer/Publisher's Note:** The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.