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Posttraumatic stress disorder symptoms in healthcare workers after the peak of the COVID-19 outbreak: A survey of a large tertiary care hospital in Wuhan

Hongyi Zhang\textsuperscript{a,d}, Yuqin Shi\textsuperscript{b}, Ping Jing\textsuperscript{c,d}, Peiyan Zhan\textsuperscript{c,d}, Yue Fang\textsuperscript{c,d,\textsuperscript{**}}, Fang Wang\textsuperscript{c,d,\textsuperscript{*}}

\textsuperscript{a} Department of Pediatric Surgery, Tongji Hospital, Wuhan 430030, China
\textsuperscript{b} Department of Epidemiology and Health Statistics, School of Public Health, Medical College, Wuhan University of Science and Technology, Wuhan 430030, China
\textsuperscript{c} Department of Neurology, The Central Hospital of Wuhan, Wuhan 430030, China
\textsuperscript{d} Tongji Medical College and Huazhong University of Science and Technology, Wuhan 430030, China

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\textbf{ABSTRACT}

This study examined the prevalence of posttraumatic stress disorder (PTSD) symptoms and assessed mental illness via an online survey among healthcare workers (HCWs) at the Central Hospital of Wuhan after the peak of the COVID-19 outbreak. PTSD symptoms were measured using the PTSD Checklist Civilian Version (PCL-C), with a cutoff score of 50. Among the 642 HCWs, the prevalence of probable PTSD was 20.87%. Additionally, 88.88%, 82.09%, 100%, and 95.52% of HCWs with probable PTSD reported varying degrees of anxiety, depression, somatic symptoms, and insomnia, respectively. HCWs with probable PTSD scored higher on the Hospital Anxiety and Depression Scale (HADS), Patient Health questionnaire-15 (PHQ-15), and Insomnia Severity Index (ISI) than non-PTSD HCWs (all $p<0.05$). Multivariate regression analysis revealed that HCWs with negative COVID-19 tests (OR, 0.35; 95% CI, 0.21–0.58; $p<0.00$), those with high Social Support Self-Rating Scale (SSRS) scores (OR, 0.30; 95% CI, 0.17–0.52; $p<0.00$), and HCWs whose family members tested negative (OR, 0.64; 95% CI, 0.42–0.96; $p=0.03$) were less likely to have probable PTSD. This study found a high prevalence of probable PTSD and severe mental illness among local HCWs. Our finding emphasizes the need to provide mental health support for HCWs.

\section{Introduction}

The coronavirus disease 2019 (COVID-19) first emerged during the end of December 2019 in Wuhan, and subsequently became a global pandemic (Pan et al., 2020; Aborsu et al., 2020). Healthcare workers (HCWs) paid a heavy price in the battle against COVID-19, among whom the daily rate of cases (130.5 per million people) was higher than that in the general population (41.5 per million people) (Pan et al., 2020). In China, a total of 3387 (4.4%) of the 77,262 patients with COVID-19 were either medical professionals or worked in medical facilities. As of April 3, 2020, 18 medical professionals died from COVID-19 in Wuhan (Zhan et al., 2020).

Previous studies on severe acute respiratory syndrome (SARS) reported that the onset of highly contagious viral pneumonia is associated with significant challenges and shock to HCWs, causing mental illness and leading to posttraumatic stress disorder (PTSD) (Hong et al., 2009; Lancee et al., 2008; Chan and Huak, 2004; Wu et al., 2009; Maunder et al., 2006). COVID-19 is a new type of mass trauma due to its unfamiliarity and uncontrollability. The months-long COVID-19 outbreak, during which HCWs were continuously exposed to the trauma, could increase the adverse mental health impact of the COVID-19 outbreak (Rajkumar, 2020; Zhang et al., 2020; Kang et al., 2020; Cai et al., 2020).

In this study, we performed an online survey among HCWs at the Central Hospital of Wuhan to assess the prevalence of PTSD symptoms and identify predictive factors associated with PTSD. The Central Hospital of Wuhan was the first and hardest hit hospital by COVID-19 among the 27 tertiary hospitals in Wuhan. In January 2020, the hospital discharged its last group of recovered COVID-19 patients and reopened as a non-COVID-19 patient care facility.
after thorough disinfection. All hospital staff underwent COVID-19 screening tests before serving non-COVID-19 patients. During the battle against the virus, more than 285 of the 4300 HCWs at the Central Hospital of Wuhan were infected with COVID-19, compared to a total of 1496 confirmed cases in local HCWs (Zhan et al., 2020; Pan et al., 2020). The hospital suffered more staff deaths than any other hospital in Wuhan. High psychological burdens and PTSD morbidity were expected. This study examined the levels of PTSD symptoms among HCWs at the Central Hospital of Wuhan. The morbidity and severity of anxiety and depression, somatic symptoms, and insomnia were also assessed. We hope that our findings will increase our understanding of the psychological impact of COVID-19 and improve the psychological well-being of local HCWs.

2. Methods

2.1. Study design

This cross-sectional study was conducted online between June 6, 2020 and June 13, 2020. The study was designed to survey the levels of PTSD and psychological distress among the staff of the Central Hospital of Wuhan. We recruited participants via WeChat using app-based, self-administered questionnaires. The questionnaires were forwarded to different WeChat hospital staff groups to recruit participants. People who completed the questionnaire were also encouraged to forward the survey to others. Ethics approval was obtained from the Institutional Review Board of the Central Hospital of Wuhan (CHW-IRB-2020-041). All participants were informed of the purpose of the study before completing the online questionnaires. To protect the privacy of respondents, the survey was conducted anonymously.

2.2. Participants

Inclusion criteria: (1) staff of the Central Hospital of Wuhan, (2) WeChat users, (3) volunteers for the survey, and (4) people who could submit survey responses using the same IP address only once. Exclusion criteria: (1) completion of the questionnaires within three minutes, (2) the existence of a medical history of PTSD, depressive disorders, or sleep disorders; (3) the existence of a history of mental disorder; or those receiving pharmacological or psychological treatments; (4) the existence of a history of unstable medical illness such as uncontrolled cardiac disease, hypertension, severe headaches, glaucoma, or seizures within the last year; and (5) the existence of one of the following conditions after April 6, 2020: respondents or their family members (HCWs’ spouse, parents, siblings, and children) being COVID-19 positive, being hospitalized for COVID-19, working at a fever clinic, or being under quarantine.

The participants’ medical histories of PTSD, mental disorder, pharmacological or psychological treatments, and unstable medical illness were collected via self-report during the online survey. History of a positive COVID-19 test was also collected via self-report. Participants were considered to be positive for COVID-19 if they had a positive result for SARS-CoV-2 virus by real-time reverse transcription-polymerase chain reaction assay or high-throughput sequencing of nasal and pharyngeal swab specimens (Lai et al., 2020; Pan et al., 2020).

2.3. Measurements

2.3.1. Posttraumatic stress disorder (PTSD)

Probable PTSD was assessed using the PTSD Checklist Civilian Version (PCL-C), with one item anchored to each of the 17 key symptoms required for determination of PTSD from the Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition) (DSM-IV) (Sonis et al., 2009). It requires respondents to indicate the degree to which they have been affected during the past month by the PTSD symptoms. The 17 items of the PCL-C include three factors: reexperiencing, avoidance and numbing, and hyperarousal (Table 1). Probable PTSD was considered when an HCW had a total PCL-C score ≥50 (Wilberforce et al., 2010; Schlenger et al., 2002; Forbes et al., 2001). We used the term probable PTSD because the PCL-C, despite its excellent evaluation properties, is not a diagnostic interview (Sonis et al., 2009).

2.3.2. Depression and anxiety

The Hospital Anxiety and Depression Scale (HADS) is valid for the measurement of depression and anxiety (Falk et al., 2020). It excludes somatic symptoms of emotional distress that could be caused by the illness itself. It is composed of 14 items to which participants respond through a four-point scale (0–3) referring to overt symptoms within the last week. It is composed of two scales: anxiety (seven items) and depression (seven items). A summary score was calculated for both the anxiety and depression subscales. A score of 8 is indicative of anxiety or depression.

2.3.3. Somatization symptoms

The Patient Health Questionnaire-15 (PHQ-15) is one of the well-established and most frequently used instruments to identify people at risk for somatization (Kocalevent et al., 2013). It assesses the presence and severity of common somatic symptoms using 15 items. A summary score reflects the self-rated symptom burden, with higher scores indicating higher burden.

2.3.4. Subjective sleep quality

The Insomnia Severity Index (ISI), a valid self-report questionnaire of sleep, is used to measure the current perception in terms of symptom severity, stress, and impairment within the last two weeks (Morin et al., 2011). The ISI consists of seven sleep-related questions ranked on a five-point Likert scale. A summary score of the ISI ranges from 0 to 28. A score above or below the cutoff score of 8 is indicative of insomnia.

2.3.5. Social support

The Social Support Self-Rating Scale (SSRS) is one of the most commonly used instruments for measuring social support in China (Xiao, 1994). The high reliability and validity of this tool was proven in previous studies (Dai et al., 2016; Liu et al., 2018). It comprises of 10 items, which measure three subscales of social support: three items that assess objective support, four items that assess subjective support, and three items that assess social support availability. Higher scores indicate higher individual social support. High social support was defined as a total SSRS score ≥30 (Liu et al., 2018).

2.4. Statistical method

Percentages and standard deviations were calculated during descriptive analysis. Enumeration data were compared using the Chi-square test, and measurement data were compared using the Student’s t-test. Multiple regression analyses were used to examine the relationship between the predictor variables and PTSD. Statistical analysis was conducted using SPSS 22.0 (SPSS Inc., Chicago, IL). The significance level was set at p < 0.05.

3. Results

3.1. Demographic characteristics

A total of 721 hospital staff participated in the online survey. However, 43 respondents were excluded from the study because they fulfilled at least one exclusion criteria. Among them, 16 completed the questionnaires within three minutes; 19 had a medical history of sleep disorders; and 13 respondents or their family members were COVID-19 positive, were hospitalized for COVID-19, were working at a fever clinic, or were under quarantine after April 6, 2020.
The 678 respondents included 174 (25.66%) doctors, 468 (69.03%) nurses, 20 (3.10%) medical technicians, and 16 (2.21%) administrative staff. The data of 642 doctors and nurses (healthcare workers, HCWs) were analyzed in this study (Table 2). Of the HCWs, 96 (14.95%) were males and 546 (85.05%) were females; 274 (42.68%) were <30 years old; 299 (44.86%) were between 30 and 40 years old; 69 (12.46%) were 40 years or older; 421 (65.58%) respondents were frontline HCWs directly engaged in diagnosing, treating, or caring for patients with or suspected to have COVID-19; 335 (52.18%) were previously quarantined, 90 (14.02%) tested positive for COVID-19, and 330 HCWs (51.40%) reported that their family members were diagnosed with COVID-19.

### 3.2 Prevalence of probable PTSD

The entire study population was divided into two subgroups: "high-scoring respondents" at increased risk of probable PTSD (PTSD group, scores ≥50; n = 134), and "low-scoring respondents" (non-PTSD group, scores <50; n = 508).

Among the 642 HCWs, the prevalence of probable PTSD was 20.87%. The symptoms were considered severe if they were assigned a score of 4 or 5. Of the 314 HCWs with probable PTSD, five hyperarousal symptoms were most frequently assigned scores of 4 or 5 (items #13–17: 76.12%, 60.44%, 59.64%, 57.46%, and 47.02%, respectively), suggesting hyperarousal was the most common severe PTSD symptom (Table 1).

The 508 (79.13%) HCWs of the non-PTSD group scored less than 50. These HCWs also reported some PTSD symptoms, although they scored lower than 50 (Table 1). It is worth noting that cutoff scores of 30 and 44 have been used to screen PTSD (Walker et al., 2002; Sonis et al., 2009).

We chose a cutoff value of 50 because of its high specificity and sensitivity in predicting a clinical diagnosis of PTSD. If the cutoff PCL-C score had been decreased to 44, 240 (37.38%) HCWs would have been identified as PTSD cases. Moreover, the females with PTSD had significantly lower subscale scores for objective support (7.18 ± 2.66 vs. 8.39 ± 3.07), subjective support (10.38 ± 1.98 vs. 11.20 ± 1.95), and utilization of social support (7.00 ± 1.56 vs. 7.54 ± 1.60) than non-PTSD females (all p < 0.00).

### Table 1.

#### The 17-item PCL-C checklist scale.

| Item | PTSD (PCL-C scores ≥50) n = 134 | Non-PTSD (PCL-C scores <50) n = 508 |
|------|-------------------------------|-----------------------------------|
| No. (and%) of respondents | No. (and%) of respondents |
| 1. Re-experiencing memories, thoughts, or images | 0 (5.80) 78 (36.15) 15 (11.22) 120 (23.62) 54 (30.31) | 1 (0.00) 223 (44.89) 154 (21.17) |
| 2. Repeated dreams | 0 (12.81) 30 (11.86) 168 (22.88) 101 (11.86) | 0 (1.27) 22 (44.78) 21 (21.78) |
| 3. Sudden acting or feeling as if a stressful experience were happening again | 1 (1.77) 21 (36.81) 5 (3.54) | 0 (0.00) 21 (44.78) 12 (21.78) |
| 4. Feeling very upset at reminders | 1 (5.80) 81 (45.60) 21 (11.22) 5 (3.54) | 0 (0.00) 21 (44.78) 12 (21.78) |
| 5. Physical reactions to reminder | 4 (7.00) 71 (11.22) 24 (5.80) | 0 (0.00) 22 (44.89) 15 (21.17) |
| 6. Avoiding/avoidance/emotional numbness | 6 (4.48) 69 (51.40) 7 (5.80) | 0 (0.00) 22 (44.89) 15 (21.17) |
| 7. Avoid activities or situations | 6 (25.66) 61 (26.16) 31 (13.43) | 0 (0.00) 22 (44.89) 15 (21.17) |
| 8. Trouble remembering important parts | 12 (35.82) 64 (17.62) 17 (5.80) | 0 (0.00) 22 (44.89) 15 (21.17) |
| 9. Loss interest | 6 (25.66) 73 (27.62) 14 (5.80) | 0 (0.00) 22 (44.89) 15 (21.17) |
| 10. Feeling distant or cut off from others | 0 (0.00) 187 (72.87) 15 (5.80) | 0 (0.00) 22 (44.89) 15 (21.17) |
| 11. Feeling emotionally numb | 0 (0.00) 27 (10.24) 23 (8.27) | 0 (0.00) 22 (44.89) 15 (21.17) |
| 12. Feeling as if your future will somehow be cut short | 0 (0.00) 27 (10.24) 23 (8.27) | 0 (0.00) 22 (44.89) 15 (21.17) |
| 13. Trouble falling or staying asleep | 0 (0.00) 25 (9.70) 32 (12.02) | 0 (0.00) 22 (44.89) 15 (21.17) |
| 14. Feeling irrelevant or having angry outbursts | 0 (0.00) 25 (9.70) 32 (12.02) | 0 (0.00) 22 (44.89) 15 (21.17) |
| 15. Difficulty concentrating | 0 (0.00) 25 (9.70) 32 (12.02) | 0 (0.00) 22 (44.89) 15 (21.17) |
| 16. Being super alert or watchful on guard | 0 (0.00) 25 (9.70) 32 (12.02) | 0 (0.00) 22 (44.89) 15 (21.17) |
| 17. Feeling jumpy or easily startled | 0 (0.00) 25 (9.70) 32 (12.02) | 0 (0.00) 22 (44.89) 15 (21.17) |

PTSD, Posttraumatic stress disorder; PCL-C, PTSD Checklist Civilian Version; Re-experiencing: items #1–5; Avoidance/emotional numbness: items # 6–12; Hyperarousal: items # 13–17.

Respondents rate each item from 1 to 5 (1, never; 2, rarely; 3, occasionally; 4, frequently; 5, constantly) to indicate the degree to which they have been bothered by the symptom over the past month.
1.85 vs. 7.29

3.3. Factors associated with probable PTSD

To elucidate the relationship among outbreak event exposures, risk perception, and level of PTSD, logistic regression analyses were conducted (Table 3). Negative COVID-19 tests among the HCWs were found to be negatively correlated with PTSD levels. The adjusted odds ratio

was 0.35 (95% CI, 0.21–0.58; p < 0.00). Negative COVID-19 tests among the family members of HCWs were also protective against high PTSD levels in HCWs (OR, 0.64; 95% CI, 0.42–0.96; p = 0.03). Moreover, high social support scores were also found to be an independent protective factor against high PTSD levels (OR, 0.30; 95% CI, 0.17–0.52; p < 0.00). Multivariable logistic regression analysis revealed that the HCWs who tested negative for COVID-19 or those whose family members tested negative and those with high social support were less likely to have probable PTSD (Table 3).

### 3.4. Prevalence of anxiety and depression

With regards to HADS, 119 (88.88%) and 110 (82.09%) of the HCWs with probable PTSD had scores of 8 or higher for anxiety and depression symptoms, respectively. In the non-PTSD group, fewer HCWs exhibited anxiety (156, 30.71%, p = 0.01) and depression symptoms (362, 71.26%; p < 0.01) (Table 4).

The mean HADS scores of female HCWs with probable PTSD were significantly higher (anxiety: 10.66 ± 4.72 vs. 6.33 ± 2.98; p < 0.00; depression: 9.52 ± 2.19 vs. 8.45 ± 1.89; p < 0.00; total HADS score: 20.18 ± 4.54 vs. 14.79 ± 3.79; p < 0.00) than those of non-PTSD HCWs, confirming the higher prevalence of more severe anxiety and depression in female HCWs with PTSD (Table 5). In male HCWs, higher anxiety scores (9.55 ± 2.91 vs. 4.95 ± 2.54; p < 0.00) and higher total HADS scores (18.55 ± 4.46 vs. 13.36 ± 3.35; p < 0.00) were observed in PTSD HCWs than in those without PTSD. However, their depression scores (9.00 ± 2.10 vs. 8.41 ± 1.75; p = 0.31) were not significantly different (Table 5).

### 3.5. Prevalence of somatic symptoms

Of the respondents with probable PTSD, 134 (100%) had scores of 5 or higher and were considered to have positive somatic symptoms. Fewer HCWs (91.14%) in the non-PTSD group had positive somatic symptoms (p < 0.00) (Table 4). Among both female and male HCWs, the PHQ-15 score of the PTSD group was higher than that of the non-PTSD group (female, 19.41 ± 5.01 vs. 13.07 ± 5.42, p < 0.00; male, 17.09 ± 4.09 vs. 8.67 ± 4.40, p < 0.00) (Table 5). These results suggest higher rates of somatic symptoms and more severe somatic illness in HCWs with probable PTSD.

### 3.6. Sleep quality

Sleep quality and its components are reported in Table 4. According to the ISI score, 95.52% of HCWs with probable PTSD, compared with 40.16% of the non-PTSD respondents, reported poor sleep quality (ISI score > 7) (p < 0.00). Moreover, more HCWs with probable PTSD were considered to have clinical insomnia (44.03% with moderate insomnia...
An independent-samples \( t \)-test was conducted to compare the scores between PTSD and non-PTSD HCWs with the same gender. The scores for depression and anxiety, somatization symptoms, subjective sleep quality, and social support were sub-grouped by gender.

| Table 4. Prevalence of anxiety, depression, somatic symptoms, and insomnia. |
|--------------------------------|-----------|-----------|------------------|
| PTSD (n = 134) Non-PTSD (n = 508) P value |
| No. (and%) of respondents | Chi-square test |
| HADS Anxiety |
| Normal (0–7) | 15(11.12) | 352(69.29) | 0.00* |
| Borderline abnormal (8–10) | 63(47.01) | 118(23.23) | |
| Abnormal (11–21) | 56(41.87) | 38(7.48) | |
| Depression |
| Normal (0–7) | 24(17.91) | 146(28.74) | 0.01b |
| Borderline abnormal (8–10) | 73(54.48) | 295(58.07) | |
| Abnormal (11–21) | 37(27.61) | 67(13.19) | |
| PHQ-15 |
| No somatic symptom (0–4) | 0(0.00) | 45(8.86) | 0.00c |
| Somatic symptom | 134 | 463(91.14) | |
| Mild symptom (5–9) | 4(2.98) | 107(21.06) | |
| Moderate symptom | 19(14.18) | 173(34.06) | |
| Severe symptom (≥15) | 111(82.84) | 183(36.02) | |
| ISI |
| No clinically significant insomnia (0–7) | 6(4.48) | 304(59.84) | 0.00d |
| Insomnia |
| Subthreshold insomnia (8–14) | 128(95.52) | 204(40.16) | |
| Moderate clinical insomnia (15–21) | 54(40.30) | 167(32.87) | |
| Severe clinical insomnia (22–28) | 15(11.19) | 3(0.60) | |

HADS, Hospital Anxiety and Depression Scale; PHQ-15, Patient Health Questionnaire-15; ISI, Insomnia Severity Index.

Two-tailed \( P \) value was calculated using Chi-square test; PTSD, Posttraumatic stress disorder.

In this study, the female sex and marital status were not predictive of high levels of PTSD symptoms. These findings are inconsistent with previous studies that examined the mental health effects of the SARS outbreak (Mak et al., 2010; Hong et al., 2009; Sim et al., 2010). This might be explained by the fact that majority of the HCWs in this study were female (85.05%) and married (60.28%). Moreover, 52.18% of HCWs were quarantined at government-designated quarantine hotels. Complete separation reduced their fear of spreading the virus to their family members (Pan et al., 2020). Previous experience with SARS was not helpful in reducing the prevalence of probable PTSD. Although HCWs who were involved in the management of SARS patients knew how to protect themselves, they seemed to be overwhelmed by the impact of COVID-19.

It is worth noting that working on the frontline was not predictive of probable PTSD. This suggests that both the frontline and second-line HCWs faced similar threats due to COVID-19 during the pandemic. The Central Hospital of Wuhan was among the first hospitals that dealt with COVID-19 cases. In the early weeks after the COVID-19 outbreak, the hospital was overcrowded with patients with fever or respiratory symptoms. Before the first announcement of human-to-human transmission on January 20, 2020, it was not unusual for fever patients to be admitted to ordinary wards for treatment of their underlying medical conditions (Pan et al., 2020). As a result, it is not surprising that seven hospital staff (6 HCWs and 1 administrative staff), who died in isolation wards or fever clinics, died from COVID-19 (Zhan et al., 2020). On the other hand, the frontline HCWs were better protected. They were provided with hospital-designated hotel rooms near the hospital. These measures reduced the mental burden of frontline HCWs.

A meta-analysis revealed that low social support was one of the most important risk factors among the 25 potential risk factors of PTSD (Trickey et al., 2012; Hong et al., 2009). In this study, we found that high social support was an independent predictive factor for lower levels of
PTSD symptoms. The findings suggest that adequate access to economic assistance, psychological intervention, and sufficient utilization of available social support might help alleviate PTSD symptoms in HCWs.

The epidemic situation in the Central Hospital of Wuhan was more serious than in other local hospitals. The prevalence of PTSD-related symptoms in HCWs was expected to be higher. A study by Lai et al., which involved 1257 HCWs who treated patients exposed to COVID-19 in multiple regions of China, revealed that HCWs reported symptoms of depression (50.4%), anxiety (44.6%), and distress (71.5%) (Lai et al., 2020). Another study surveyed 14,825 HCWs in 31 provinces of mainland China and found that the prevalence rates of depressive symptoms and PTSD were 25.2% and 9.1%, respectively. Working in the Hubei province was associated with a higher risk of depressive symptoms (Song et al., 2020). By using different measurement scales, we found that 642 HCWs reported symptoms of depression (73.52%) and anxiety (42.83%). In the study by Lai and our study, the seven-item ISI was used to measure the severity of insomnia. In our study, 51.71% of all HCWs, including 95.52% of the probable PTSD HCWs and 40.16% of the non-PTSD HCWs, reported insomnia, which is much higher than that reported by Lia et al. (51.71% vs. 34.0%).

5. Limitations and future direction

This study has several limitations. First, this is a cross-sectional study, therefore no causal relationship between risk perception and PTSD can be established. Second, the PCL-C evaluates the level of PTSD symptoms, but cannot be used to diagnose PTSD itself (Sonis et al., 2009). HCWs with PCL-C scores <50 also presented with PTSD symptoms. These HCWs may develop chronic PTSD and may need long-term follow-up. Third, the HCWs’ self-reports were prone to recall bias. Any self-reported information the participants provided might be incorrect despite their best effort to be honest and accurate. Moreover, the predominance of female nurses in the respondents could introduce some bias in the sample and reduce the generalizability of the results.

Future studies should involve a larger sample and multicenter randomized controlled trials and should use objective and quantitative measurements to investigate the long-term mental health effects of COVID-19. Studying the longitudinal trajectory of PTSD levels in HCWs will increase our understanding of the mental health impact of COVID-19.

6. Conclusions

This study highlighted several important findings. First, we found significant rates of probable PTSD (20.65%) in HCWs at the Central Hospital of Wuhan, about six months after the first local outbreak of COVID-19. Second, high levels of psychiatric and somatic illness and insomnia were associated with probable PTSD. Lastly, the HCWs with negative COVID-19 tests, those whose family members tested negative, and those with high social support were less likely to have probable PTSD. These factors must be understood in order to develop a theoretical account of PTSD in this population and to organize prevention programs that can help these HCWs cope with future epidemics.

Ethics approval

Ethics approval was obtained from the Institutional Review Board of the Central Hospital of Wuhan (CHW-IRB-2020-041).

Author statement

H.Z. collected all the data and wrote the paper. Y.S. performed the statistical analysis. P.J. and P.Z. helped supervise the project. Y.F. and F.W. conceived the original idea and supervised the project. All authors discussed the results and contributed to the final manuscript.

Declaration of Competing Interest

The authors declare that they have no conflicts of interest.

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