

L I T E R A T U R E R E V I E W

Burnout and post-traumatic stress disorder in frontline nurses during the COVID-19 pandemic: a systematic literature review and meta-analysis of studies published in 2020

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Abstract. *Background and aim:* Burnout and post-traumatic stress disorder (PTSD) among frontline nurses working with COVID-19 patients during the initial phase of the pandemic (2020) have been described by several studies. Therefore, this study aimed to systematically synthesize evidence regarding burnout and PTSD among nurses engaged in the frontline during the COVID-19 pandemic, highlighting their risk and protective factors. *Methods:* A systematic review was performed (PROSPERO: CRD42021227939), searching literature published in 2020 on Pubmed, Scopus, CINAHL, and PsycInfo. We quantitatively pooled means of included studies measuring burnout and PTSD with the same tools. *Results:* Twenty-five studies were included in this review. Seven (3766 nurses) were included in the meta-analysis for estimating means of depersonalization and emotional exhaustion assessed using the Maslach Burnout Inventory, respectively: 7,40 (95%CI=6,00-8,80) and 22,82 (95%CI=19,24-26,41). Likely, 12 studies were used to estimate two pooled means for PTSD, one for six studies adopting the Impact of Event Scale-Revised (1551 nurses), and six adopting the PTSD Scale for DSM-5 (8547 nurses). The main risk and protective factors of both outcomes were female sex and younger age, work-related variables, and physical and mental factors, such as concerns, skin lesions from wearing personal protective equipment. *Conclusions:* This systematic review portrayed the situation described in literature during 2020 on nurses' burnout and PTSD during the COVID-19 pandemic. Although the outcomes' levels described in the included studies are diverse, the broad situation appears alarming, and supportive multi-level strategies, considering individual and system-level, should be planned to decrease the described worsening scenario within the clinical settings avoid middle and long-term negative consequences.

Keywords: burnout; COVID-19; depersonalization; emotional exhaustion; healthcare workers

Introduction

On 11 March 2020, the World Health Organization (WHO) declared the spreading of the Coronavirus-Disease-2019 (COVID-19) as a pandemic (1). Globally, as of 20 January 2021, almost 100 million COVID-19 confirmed cases, and more than two million deaths had been reported (2). The COVID-19

pandemic has revolutionized care scenarios and posed significant challenges to healthcare workers (HCWs). For instance, since the beginning of the COVID-19 outbreak in Italy, roughly 100 thousand COVID-19 cases have been diagnosed among HCWs (median age equal to 47 years) (3). The risk of being infected was not the only burden for HCWs; in fact, poor mental health outcomes have been detected as relevant

among HCWs worldwide (4–6). In particular, front-line HCWs are the most at-risk professionals (5,7), and although all HCWs currently experience a psychological toll, nurses have been previously recognized to report higher risks of burnout and post-traumatic stress disorder (PTSD) (8).

The global nursing workforce is equal to 27.9 million nurses, and 19.3 million are professional nurses, confirming that they are the largest occupational group in the healthcare sector, accounting for approximately 59% of HCWs globally (9). During the current COVID-19 pandemic, nurses have been recognized to play a pivotal role in managing clinical and organizational challenges (10), providing direct care in close physical proximity to positive patients (11). Besides, nurses often face a substantial workload, acknowledging the frequent nurse's unbalanced ratio per patient (in some contexts higher than ten patients to one nurse) and increased clinical complexity of inpatients (12). This challenging situation can jeopardize their mental health, as described by several empirical studies that have already described as alarming the burnout and PTSD levels in nurses during the current COVID-19 pandemic (8,13,14).

More precisely, among HCWs, nurses have been described as the most exposed professional group to burnout (15). Without preventive and supportive strategies, burnout could have severe consequences for patients, other HCWs, healthcare organizations, as it could negatively affect patient safety and the overall quality of care (15). Previous evidence demonstrated that during critical situations, such as influenza pandemics, nurses are at risk of developing psychological distress (16), triggering emotional exhaustion and depersonalization, which are components of burnout (17). In addition, previous research showed that PTSD symptoms in HCWs (including nurses) were detected with rates ranging from 11 to 73.4% during outbreaks (18), and these symptoms lasted after 1-3 years in 10-40% of cases (19).

Although a recent systematic review summarized the evidence regarding mental health outcomes in HCWs during the COVID-19 pandemic, highlighting increased levels of burnout (ranging from 3.1 to 43.0%) and PTSD (ranging from 7.4 to 37.4%) (20), the specific literature on nurses' mental health out-

comes still remains not synthesized. This gap contributes to limit the up-to-date understanding of the estimates regarding burnout levels and PTSD among nurses (11). Considering that nurses represent more than half of all HCWs globally (9), a specific focus on summarizing literature regarding their burnout and PTSD levels could help frame an updated appraisal on the current global scenario. This appraisal could be useful to inform decision-makers for planning supportive and preventive strategies for sustaining nurses' mental health in a middle and long term perspective.

Aim

This study sought to systematically synthesize evidence regarding burnout and PTSD among nurses engaged in the frontline during the COVID-19 pandemic, highlighting their risk and protective factors.

Materials and methods

Design

This study was a systematic review with meta-analysis to estimate the pooled means of burnout and PTSD; as reported in **Supplementary File 1**, the Preferred Reporting System for Systematic Reviews (PRISMA) statement guided the study reporting (21). The research questions used to operationalize the study aim were: (a) What is the impact of the SARS-CoV-2 pandemic on burnout and post-traumatic stress disorder among nurses working at the frontline? (b) What are the risk factors for burnout and post-traumatic stress disorder among frontline nurses during the COVID-19 pandemic? (c) What factors could mitigate the psychological impact of the COVID-19 pandemic on the well-being of frontline nurses?

Search strategy

We performed a systematic search of the literature, consulting PubMed, CINAHL, Scopus, and PsycINFO databases in December 2020 and January 2021. We also considered Google Scholar for performing a citation tracking of the included studies as a secondary data source. The search process was performed independently by two authors, who followed the PRISMA flowchart phases: identification, screening, eligibility,

and inclusion. In the identification phase, the queries for performing the electronic searches in the different databases were developed and adopted to perform the searches. After identifying all the potential records and excluding the duplicates, the screening phase was based on each title/abstract's reading for excluding the articles that did not meet the systematic review's inclusion/exclusion criteria. The remained records were considered eligible; thus, the articles were retrieved in full-text and evaluated following the pre-identified strategy of the quality appraisal. All the articles showing moderate/good quality were included in this systematic review.

The queries developed in the identification phase are described in **Supplementary File 2**. A consensus discussion between two authors was performed for each phase of the PRISMA flowchart. The following inclusion criteria were considered: (a) empirical research among nurses working against COVID-19, (b) published in English, (d) between March and December 2020, (e) containing an indexed abstract, and (f) measuring burnout and/or PTSD with valid and reliable tools. The low-quality appraisal in the eligibility phase was the only exclusion criteria.

Study selection process

As described in **Figure 1**, the electronic searches identified 1027 records from the developed queries (n=714 in PubMed; n=227 in Scopus; n=71 in CINAHL; n=15 in PsycINFO) and 16 additional records derived from the citation tracking of the eligible studies. After removing the duplicates (n=129), two authors screened 914 titles and abstracts. In this phase, 869 records were excluded as they did not measure burnout and/or PTSD. From the remaining 45 articles, two authors verified from the abstract if inclusion criteria were met, and 20 articles were excluded due to (a) 13 articles did not present data about nurses, (b) one study did not measure burnout and/or PTSD, (c) five measured other mental health outcomes, and (d) one study was not referred to the burnout or PTSD referred to the COVID-19 pandemic. The 25 eligible articles (ten focused on burnout and 15 on PTSD) were then retrieved in full-text and evaluated for their content and quality by following the strategy described in the quality appraisal section. Accordingly, all the 25

eligible studies were included in this systematic review.

However, only seven out of the ten studies reporting burnout have presented mean and variance of the burnout sub-scales measured with the same tool (emotional exhaustion and depersonalization, assessed using the Maslach Burnout Inventory, MBI). For this reason, these seven studies were included in a meta-analysis, while the remaining studies were narratively synthesized. Likely, six studies measured PTSD using the Event Scale-Revised (IES-R), and six other studies measured PTSD using the PTSD checklist for DSM-5 (PCL). For this reason, pooling the means of studies adopting IES-R and means of those adopting PC was feasible in two meta-analysis models. The remaining three studies on PTSD and the risk and protective factors of burnout and PTSD were narratively synthesized.

Data extraction, quality appraisal, and risk of bias

Two authors extracted the relevant data from the articles or contacting the author of reference of the eligible studies throughout a structured extraction form. The following extraction format was adopted: first author/year/country, aim, sample/setting, study design, study period, measurement tools, study design, results. A consensus discussion was adopted to solve any disagreements between authors in the phase.

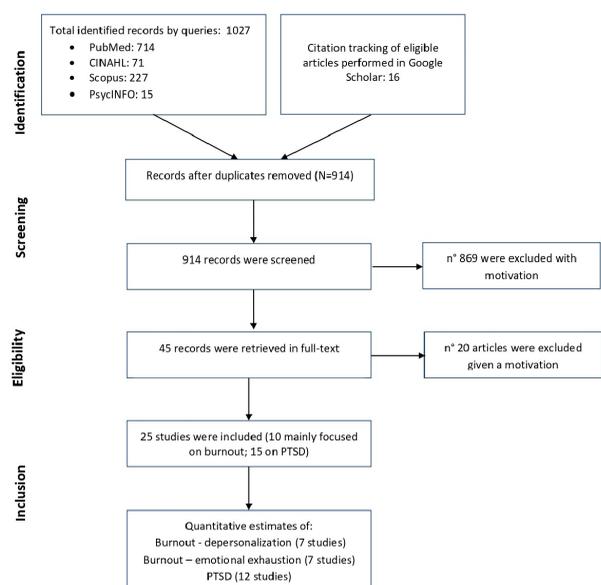


Figure 1. PRISMA flowdiagram

The STROBE checklist for observational studies was used to evaluate the selected studies' methodological quality (22). Two authors performed the methodological evaluation, and the Fleiss' kappa was employed to determine the agreement between raters. In case of disagreement (low values of Fleiss' kappa), a consensus discussion was planned to align possible different views in performing the evaluation. The evaluation of the methodological quality is reported in **Supplementary File 3**. However, the STROBE is not an adequate tool for assessing the risk of bias, as it was developed to evaluate the methodological and reporting quality. For this reason, once study with moderate and high quality was included in this systematic review, as per previous studies, we used the adapted Newcastle Ottawa Scale (NOS) to assess their risk of bias (23), considering an overall rating equal to or higher than five as a moderate risk of bias, and higher than six as a low risk of bias.

Statistical analysis

Based on the availability of the descriptive data derived from the same measurement tool for assessing burnout (MBI) and PTSD (IES-R and PCL), a quantitative mean pooling of emotional exhaustion (six studies), depersonalization (six studies), PTSD measured by IES-R (six studies), and PTSD measured by PCL (six studies), was feasible. Accordingly, the means of the original studies aggregated per tool specific-outcomes were quantitatively pooled and reported using a pooled mean values as the effect size of the model with 95% confidence intervals (95% CIs). Given that the included studies had an observational design, we assumed a high potential for statistical heterogeneity between studies, and accordingly, a random-effects model was used to calculate the pooled effects. Heterogeneity was assessed by the random effect model of the inverse variance, and its magnitude was estimated by chi-squared (Q) and I-square statistics (I²). As evaluating the publication bias using the comparison-adjusted funnel plot was used could be misleading in analyses with few included studies, we assumed a moderate risk of publication bias beyond a funnel-plot evaluation. Analyses were run using the Comprehensive Meta-Analysis software (version 2.2.057, Biostat, Englewood, USA).

Results

Description of the included studies

This systematic review included 25 observational studies: 10 studies (24,25,34–43,26,44–48,27–33) were mainly focused on burnout and 15 studies (26–29,32,40,42,45,48) were mainly referred to PTSD (24,25,39,41–43,46,47,30,31,33–38). The majority of the included studies (n=14) were performed in Asia (12 studies in China, one in Singapore, one in South Korea) (24,28,44,46–48,29,30,32–36,39), followed by eight studies conducted in Europe (three studies in Italy, one in Germany, one in Turkey, one in Spain, one in Finland, and one in Poland) (25–27,31,38,41–43), two in North America (one in the United States of America, one in Canada) (37,45), and one in the Middle East (Iran) (40).

Notably, **Table 1** shows a summary of the main characteristics and results of the included studies. The studies measuring burnout (emotional exhaustion and depersonalization) using the same tool (MBI) and reporting means and variances were seven (26–29,32,45,48), including a total of 3766 nurses. Six studies measured PTSD using PCL in 8547 nurses (30,33,36,43,46,47) and six studies assessed PTSD with IES-R in 1551 nurses (24,25,31,34,35,41). Three studies measured PTSD with other tools enrolling a total of 1435 nurses (39,42,45).

Risk of bias in included studies

Table 2 describes the evaluation of the risk of bias. The sample's representativeness, the adoption of valid and reliable tools, and the adopted statistical tests were considered adequate in all the included studies. The sample size was justified in seven studies (31,32,34,40,45–47). The response rate was justified and adequate in 18 studies (24,25,40,43–48,26,27,30–34,37). Overall, 19 studies reported a moderate risk of bias (24,25,37–44,48,26–30,33,35,36), and six studies showed low risk of bias (31,32,34,40,45–47).

Pooled means of depersonalization and emotional exhaustion (burnout)

The model for quantitatively pooling the means of the seven studies measuring depersonalization using MBI showed moderate heterogeneity

Table 1. Synopsys of the included studies

| Author, year; Country | Aim | Sample, setting | Study design, Study period and Measurement tools | Results |
|---|--|---|--|--|
| Barello et al. (2020), Italy | To describe professionals' BO levels and physical symptoms of Italian frontline HCWs and the relationship between professionals' BO and negative health symptom. | HCWs: n=376 --> nurses: n=271; hospital unit workers: n=307 (81.6%). | Cross-sectional study. MBI | 1/3 --> high score of EE; 1/4 high levels of Dp. 15% --> low levels of PG. Mean, SD: EE -->22,7 (12,1); Dp --> 6,1 (5,7); PA --> 37,5 (7,6). 45% --> at least one physical symptom in the previous 4 weeks. Females --> higher levels of EE than male. |
| Zerbini et al. (2020), Germany | To explore psychosocial strain of HCWs working in COVID-19 wards and nurses and physicians pandemic affection; to investigate individual reasons and perceptions of psychosocial burden. | HCWs: n=110 --> nurses: n=75 (45 COVID-19 wards vs. 30 regular wards); physicians: 35 (17 COVID-19 wards vs. 18 regular wards). | Cross-sectional study (March– April 2020). PHQ, German version of MBI. | COVID-19 wards nurses --> higher EE, depressive mood, lower levels of work-related fulfillment compared to their colleagues; Mean, SD: EE= 18,16 (8,45); Dp= 7,89 (4,20). No differences in physicians' score. Most common causes for burden: job strain (37,5%), uncertainty about the future (30%). Important resources --> Psychosocial support and leisure time. |
| Ruiz-Fernández et al. (2020), Spain | To analyse ProQoL and PS in HCWs facing the COVID-19 pandemic. | HCWs: n=506 --> nurses: n = 398 (working at primary care centres and in ED, ICUs, specific COVID-19 units). | Descriptive cross-sectional online study (March– April 2020). ProQol (Spanish version), PSS-14. | ProQoL --> high levels of CF, medium to high levels of CS and BO. Mean, SD: PS --> 29,3 (5,8). Physicians --> Mean, SD: CF --> 21,6 (8,6), BO --> 26,2 (6,6). Nurses --> Mean, SD: CS --> 39,9 (5,9), BO --> 24,3 (5,7). PS similar in both occupations. CF and BO --> higher in COVID-19 units and ED HCWs; CS and PS --> similar. Multiple linear regression model for BO: risk factors --> CF, CS. |
| Sarbooji Hoseinabadi et al. (2020), Iran | To assess and compare BO level between frontline and other nurses during COVID-19 pandemic and to identify influencing factors. | Nurses: n= 245 nurses --> 151 (61.63%) COVID-19 infection exposure group and 94 (38.37%) non-exposure group. | Cross-sectional study (March– April 2020). OLB, JSQ | Mean, SD: COVID-19 related job stress --> 3,2 (0,9) vs. 2,8 (0,7); COVID-19 related BO --> 2,61 (0,27) vs. 2,51 (0,23). Univariate linear regression: risk factors for COVID-19-related BO --> employment type, experience in taking care of pts with COVID-19 infection, hospital resources. |
| Chen et al. (2020), China | To assess the occurrence of trauma, BO, and PST growth among nurses involved in the COVID-19 pandemic and the associated factors. | Nurses: n= 12596, CCUS= 28,4%, COVID-19 hospitals= 52.3% , provided direct care to positive pts= 7.1%. | Multi-site, Large-scale cross-sectional study (April 2020). TSQ, MBI-GS, PTGI-SF. | TSQ ≥ 6 --> 13.3%, PTGI-SF ≥ 60th percentile --> 39.3%. Mean, SD: EE --> 19,1 (10,0); Dp --> 5,5 (4,6); PA --> 19,0 (8,4). Nurses caring for Covid-19 positive pts --> Mean, SD: EE= 18,7 (9,5); Dp= 5,2 (4,4), Lack PA=17,6 (8,2). Logistic regression analysis: EE, Dp --> greater in those working in critical area units, COVID-19 hospital, COVID-19 department. Being a woman --> risk factor for EE; + never caring for pts with COVID-19 --> factors influencing lack of PA. |
| Hu et al. (2020), China | To examine BO, anxiety, depression, and fear and its associated factors among frontline nurses who were caring for COVID-19 pts. | Nurses: n= 2014 | Multi-site, large-scale cross-sectional, descriptive, correlational study (February 2020). MBI-HSS, SAS, SDS, FS-HPs (Chinese versions). SLS, GSS, CD-RISC-10, MSPSS | Moderate/high --> EE= 60,5%, Dp= 42,3%, PA= 60,6%, anxiety= 14,3%, depression= 10,7%, fear= 91,2%. One or more skin lesion --> 94,8%. Mental health outcomes --> positively correlated with skin lesion, negatively correlated with self-efficacy, resilience, social support, and frontline work willingness. |
| Guixia et al. (2020), China | To examine nurses' level of BO and to investigate its influencing factors during COVID-19 pandemic. | Nurses: n=92 --> 63,04% (non-COVID-19 wards), 13,04% (COVID-19 ICU), 23,91% (COVID-19 general ward) | Descriptive cross-sectional study (February 2020). MBI, SAS, SDS. | Moderate/high --> BO= 43,5%-62,0%. Multiple regression analyses: anxiety + working years --> 26,8% of the variation in BO --> positively correlated with anxiety and negatively with working years. |

Table 1. Synopsys of the included studies

| Author, year, Country | Aim | Sample, setting | Study design, Study period and Measurement tools | Results |
|--|---|--|--|--|
| Zhang et al. (2020), China | To identify stressors and BO among nurses who cared for COVID-19 pts and to explore coping strategies and perceived effective support factors to address stressors. | Nurses: n= 107 (91.59% worked in quarantine areas). COVID-19 pts and to explore coping strategies and perceived effective support factors to address stressors. | Prospective observational survey study (March 2020). MBI. | Mean, SD: EE= 12.27 (7.14), Dp= 2.07 (2.78), PA= 16.44 (8.36). Moderate/severe --> EE= 21.5%, Dp= 7.5%, Lack of PA= 81%. Longer working hours in COVID-19 units--> higher EE and Dp; younger age--> higher EE--> decreased with increasing working experience years. |
| Sagherian et al. (2020), United States | To describe and quantify levels of insomnia, fatigue and intershift recovery, and psychological well-being among hospital nursing staff during the COVID-19 pandemic, and to examine differences based on work-related characteristics. | Nurses and nurses assistants: n= 587 (68.23% provided nursing care to pts with COVID-19). | Observational cross-sectional study (May- June 2020). MBI-HSS, SPRINT. | Mean, SD: EE= 33.36 (11.39), Dp= 11.98 (7.05), PA= 32.95 (7.90), SPRINT= 16.11 (6.87). EE--> related to worked hours per week and 30-min breaks. Dp--> related to work status, shift length and years of experience. Post-traumatic stress--> related to work hours per week and 30- min breaks. |
| Tan et al. (2020), Singapore | To examine BO and associated factors among HCWs. | HCWs: n= 3075 (Doctors= 14.9%, nurses= 45.3%, AHPs= 15.7%, support staff= 16.0%, and administrative staff= 8.0%). | Multi-site, cross-sectional survey study (May- June 2020). SAQ, OLB, HADS. | Mean, frequencies: Disengagement= 2.38 (79.7%) , Exhaustion= 2.50 (75.3%); both= 68.2%. Mean: Exhaustion--> highest for nurses (2.52), lowest for support staff (2.44). No difference in scores among HCW roles. Multivariate regression analysis: Chinese or Malay ethnicity, HADS anxiety or depression scores >8, shifts lasting >8 hours, education level, being redeployed--> associated with higher OLB. |
| Song et al. (2020), China | To assess the mental health of emergency department medical staff during the COVID-19 pandemic. | HCWs: n= 14825 (physicians= 41.1%, nurses= 58.9%). | Cross-sectional (February-March 2020). PSS, CES-D, PCL-5 (Chinese versions) | Depressive symptoms= 25.2%, PTSD= 9.1%. Men, middle-age--> associated with depressive symptoms and PTSD. Lower levels of social support--> associated with risk of negative outcomes. Prevalence of PTSD in nurses--> higher than in physicians. Shifts lasting >9 hours, few years of employment--> higher risk of depressive symptoms and PTSD. Local medical staff in the Hubei Province--> higher risk of depressive symptoms and PTSD. |
| Wang, Y.X. et al. (2020), China | To investigate PCL-C scores and the incidence of PTSD in nurses exposed to COVID-19, to analyse influencing factors of PTSD and to explore the correlation between the PCL-C scores, positive and negative coping. | Nurses: n=202 (exposed to COVID-19). | Cross-sectional and correlational study (February-March 2020). PCL-C (Chinese version), SCSQ. | Median, IQR: PCL-C= 27.00 (21.00-34.00), Avoidance= 9.50 (7.00-13.25). PTSD= 16.83%. Median, IQR: SCSQ positive coping= 22.00 (15.00-25.25), negative coping= 9.00 (6.00-11.00). Multivariable stepwise linear regression: job satisfaction, gender--> associated with PCL-C scores (18% of all PCL-C variation). PCL-C--> negatively correlated with positive coping, positively correlated with negative coping. |
| Si et al. (2020), China | To investigate the presence of adverse psychological outcome, anxiety, depression and PTS, in HCWs during the COVID-19 outbreak and assess the associated factors. | HCWs: n=863 (physicians= 43.7%, nurses= 24.4%, other=31.9%). Frontline HCWs= 16.8%. | Cross-sectional study (February- March 2020). IES-6, DASS, PSSS (Chinese versions), SCSQ. | Mean, SD: IES-6= 8.54 (4.87), PTSD= 40.2%, PTS symptoms= 97.9%. Extremely severe symptoms: depression= 13.6%, anxiety= 13.9%, stress= 8.6%. Bivariate correlation: being nurses, having chronic diseases, with high concern to the outbreak, with confirmed cases among relatives and friends--> higher risk to have PTS symptoms. Tobacco users--> lower risk have PTS symptoms. Perceived threat and passive coping strategies--> positively related to PTS. |

Table 1. Synopsys of the included studies

| Author, year, Country | Aim | Sample, setting | Study design, Study period and Measurement tools | Results |
|-------------------------------|--|--|--|---|
| Li et al. (2020), China | To evaluate psychological well-being and factors associated with PTSD of front-line nurses during the COVID-19 pandemic. | Nurses: n=356 (frontline). | Multi-site, predictive study design, at two time points (before and after nurses worked at COVID19 units). (January- March 2020). PSS, PCL-5, CD-RISC. | PTSD: prior to working in COVID-19 units= 1.6%; after working at COVID-19 units= 62%. Univariate model: being married, working in Covid-19 unit--> risk factors for PTSD. Age, education level, working experience (≥ 6 years), professional level, being a nurse specialist--> protective factors for PTSD. |
| Nowicki et al. (2020), Poland | To investigate the level of PTS, perceived social support, opinions on positive and negative consequences of the pandemic, sense of security and of meaning among nurses during the COVID-19 pandemic. | Nurses: n=325 (exposed to COVID-19= 46.46%) | Cross-sectional study (May 2020). IES-R, MSPSS, CIOQ, SEQ, MLQ. | Mean, SD: IES-R= 1.78 (0.65), avoidance= 1.86 (0.73), hyperarousal= 1.8 (0.78), intrusion= 1.74 (0.83), positive psychological changes= 18.56 (4.04), MLQ= 5.33 (0.87)--> higher score if married and had children. Positive correlation between work experience and the Intrusion dimension. |
| Cai et al. (2020), China | To evaluate the nurses' psychological status and the risk factors in different periods of the COVID-19 pandemic. | Nurses: n= 1330 (outbreak period= 53.3%, stable period= 46.7%). Nurse: n= 81 from the Wuchang Fangcang shelter hospital, enrolled in the second survey | Longitudinal study (January-February 2020; February 2020). PHQ-9, GAD-7, ISI, IES-R. | Outbreak period: 1/3 had symptomatic depression, anxiety, and insomnia, 1/5 presented PTSD symptoms. Diagnosed PTSD= 33.3%. Stable period--> psychological problems decreased significantly. Worse physical condition and uncertainty about pandemic--> risk of psychological problems. Nurses from Fangcang shelter hospitals--> higher risk of psychological problems. |
| Wang, Y. et al. (2020), China | To assess HCWs' acute psychological effects experienced during the early period of the COVID-19 outbreak and the related risk factors among HCWs. | HCWs: n=1897 (physicians= 29.7%, nurses= 70.3%, health care workers= 39.1%) | Survey-based cross-sectional study (January- February 2020). PHQ-9, GAD-7, IES-R. | HCWs: Depression= 21.7%, anxiety= 38.5%, PTSD= 15.4%. Nurses: PTSD= 10.9%. Univariate logistic regression--> being females, having insufficient training for protection--> higher risk for PTSD. Working in Hubei Province (except Wuhan) or other provinces--> lower risk for PTSD. Binary logistic regression--> being a nurse, having an intermediate technical title, working at the frontline, and lack of confidence in protection measures--> risk factors for PTSD. Not worrying about infection--> protective factor for PTSD. |
| ahin et al. (2020), Turkey | To evaluate the prevalence of depression, anxiety, distress, and insomnia and related factors in HCWs during the COVID-19 outbreak. | HCWs: n=939 (nurses= 27.1%), working on the frontline= (60.6%) | Online survey study (April-May 23 2020). PHQ-9, GAD-7, ISI, IES-R. | HCWs: Depression= 77.6%, anxiety= 60.2%, insomnia= 50.4%, distress 76.4% (higher in females than in males). Insomnia and distress symptoms--> higher in nurses. Nurses: PTSD= 81.2%. Being female, having history of psychiatric illness and having been tested for COVID-19--> risk factors for distress symptoms. |
| Leng et al. (2020), China | To quantify the severity of nurses' PTSD symptoms and stress and to explore the influencing factors of their psychological health when caring for pts with COVID-19 in an ICU. | Nurses: n=90 nurses | Cross-sectional survey study (March 2020). PTSD-PCL-C, PPS (Chinese versions). | Mean, SD: PTSD= 24.62 (6.68), CPSS: 19.33 (7.21). significant level of PTSD= 56.6%. Nurses from ED--> the lowest on PTSD symptoms. Pearson correlation analysis--> correlation between nurses' CPSS and PCL-C. |

Table 1. Synopsys of the included studies

| Author, year; Country | Aim | Sample, setting | Study design, Study period and Measurement tools | Results |
|----------------------------------|---|--|---|---|
| Jo et al. (2020), South Korea | To evaluate the stress and psychological impacts experienced by HCWs during the COVID-19 outbreak and the effect of telephone-based psychiatric consultations on screened high-risk participants. | HCWs: n=253 (27 doctors, 149 nurses, 42 allied health professionals, 35 auxiliary staff members). | Cross-sectional study, IES-R, MINI (Korean versions), CGI-S. | HCWs--> Mean, SD: IES-R= 13.2 (13.8). Women--> higher IES-R scores. Nurses--> mean, SD: IES-R= 13.67 (13.10). Kruskal-Wallis test--> significant difference in the total IES-R scores between occupational groups: physicians--> lower IES-R scores than nurses and auxiliary health professionals. 15 of 54 high-risk participants (IES-R scores >25) responded to the IES-R and CGI-S after two weeks of telephone-based psychiatric consultations--> IES-R scores decreased by 13.67 (16.15 points), CGI-S scores decreased by 1.00 (0.74) points. |
| Nie et al. (2020), China | To report the prevalence and the risk factors of psychological distress among nurses working in the frontline during the COVID-19 pandemic. | Nurses: n=263 (frontline) | Cross-sectional study (February 2020). GHQ-12, PSSS, SCSQ, IES-R (Chinese versions) | Mean, SD: positive coping style= 1.68 (0.60), negative coping style= 0.97 (0.51), PSSS= 58.76 (13.41), IES-R= 28.05 (14.79). Stress symptoms= 73.8%; psychological distress= 25.1%. Multiple logistic regression analysis --> working years, concern for own, negative coping style--> risk factors for stress symptom. Positive coping style--> protective factor for this outcome. |
| Gorini et al. (2020), Italy | To evaluate mental health outcomes among HCWs during the second month of the COVID-19 outbreak. | HCWs: n=650 (physicians= 177, nurses= 214, allied health professionals= 217, administrative staff=42); exposed to COVID-19= 60.8%. | Multicenter cross-sectional study (April- May 2020). PHQ-4, IES-R | Women--> overall higher scores than men. Physicians--> lower scores in anxiety, depression and psychological distress than the other workers. Nurses--> moderate/severe level of psychological distress= 58.9%. Regression analysis--> male less suffered the pandemic impact. Nurses--> suffered this impact more than both physicians and other health professionals. |
| Bassi et al. (2021), Italy | To investigate the contribution of positive mental health to PTSD development among HCWs and socio-demographic and work-related factors. | HCWs: n=653 (nurses and midwives= 318, frontline=261) | Cross-sectional web-based study (April- May 2020). PCL-5, MHC-SF | PTSD= 39.8%. Flourishing= 33.4%, moderate mental health= 57.7%, languishing= 8.9%. Being women, nurses and midwives--> higher risk of PTSD; odds of inpatient frontline workers--> 2.01 times higher than those of outpatient & services second-line workers. Flourishing participants--> lower risk of PTSD, languishing participants--> higher risk of PTSD. |
| Haravuori et al. (2020), Finland | To assess the well-being of the HCWs. | HCWs: n=4804 (nurses= 62.4%, doctors= 8.9%) | Baseline online survey study (June 2020). MHI-5, ISI, PHQ-2, PC-PTSD-5, OASIS | PTEs related to the COVID-19--> more common among the personnel exposed to COVID-19 (43.4% vs. 21.8% among the others); 27.8% of participants presented PTEs. 23-24%--> presented high risk of PTSD. Being nurses and exposed to COVID-19--> positively associated with psychological distress. |
| Crowe et al. (2020), Canada | To examine the mental health of Critical Care nurses providing direct patient care during the initial phase of the COVID-19 pandemic. | Nurses: n= 109 (ICU or the High Acuity Unit); 15 participated in a semi-structured interview. | Convergent parallel mixed-method study, IES-R, DASS-21 | Mean, SD: mild to severe depression= 57%, anxiety= 67%, stress= 54%. PTSD symptoms= 50.4%. Interviews: psychological distress (anxiety, worry, distress, fear)--> related to rapidly changing policy and information, overwhelming and unclear communication, meeting patient care needs, managing home and personal commitments to self and family. |

Table 2. Adapted Newcastle-Ottawa Scale (NOS) for assessing the risk of bias of nonrandomised studies

| First author (year) | Reviewer | Selection | | | | Comparability based on design and analysis | Outcome | | | Total |
|-------------------------|----------|----------------------------------|-------------|-----------------|---|--|-----------------------|------------------|------------|-------|
| | | Representativeness of the sample | Sample size | Non-respondents | Demonstration that outcome of interest was measured with valid and reliable tools | | Assessment of outcome | Statistical test | Follow-ups | |
| ahin et al. (2020) | RC | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 7 |
| | CA | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 7 |
| Leng et al. (2020) | RC | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 6 |
| | CA | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 6 |
| Jo et al. (2020) | RC | 1 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 6 |
| | CA | 1 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 6 |
| Nie et al. (2020) | RC | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 6 |
| | CA | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 6 |
| Gorini et. al (2020) | RC | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 6 |
| | CA | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 6 |
| Bassi et al. (2021) | RC | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 6 |
| | CA | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 6 |
| Haravuori et al. (2020) | RC | 1 | 0 | 0 | 1 | 1 | 1 | 1 | 0 | 5 |
| | CA | 1 | 0 | 0 | 1 | 1 | 1 | 1 | 0 | 5 |
| Crowe et al. (2020) | RC | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 5 |
| | CA | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 5 |

($I^2=36,46\%$). The forest plot of the model is depicted in **Figure 2**. The model's overall effect size showed that depersonalization on the 3766 nurses enrolled in the seven studies has a pooled mean of 7,40 (95%CI=6,00-8,80) (26-29,32,45,48).

The model for quantitatively pooling the means of the seven studies measuring emotional exhaustion using MBI showed low heterogeneity ($I^2=11,99\%$). The forest plot of the model is depicted in **Figure 2**. The model's overall effect size showed that emotional exhaustion on the 3766 nurses enrolled in the seven studies has a pooled mean of 22,82 (95%CI=19,24-26,41) (26-29,32,45,48).

Pooled means of PTSD

The model for quantitatively pooling the means of the six studies measuring PTSD using IES-R showed moderate heterogeneity ($I^2=54,7\%$). The forest plot of the model is depicted in **Figure 3**. The model's over-

all effect size showed that PTSD on the 1551 nurses enrolled in the six studies has a pooled mean of 23,99 (95%CI=20,77-27,21) (24,25,31,34,35,41).

The model aimed at pooling the means of the six studies measuring PTSD using PCL showed low heterogeneity ($I^2=4,6\%$). The forest plot of the model is depicted in **Figure 3**. The model's overall effect size showed that PTSD on the 8547 nurses enrolled in the six studies has a pooled mean of 29,43 (95%CI=26,23-32,64) (24,25,31,34,35,41).

Risk and protective factors of burnout

The main risk factors associated with burnout (depersonalization and emotional exhaustion) were sex, age, education, work-related variables, and physical and mental factors, as described in **Table 3**. Considering the heterogeneity of risk factors in the included studies, a quantitative pooled analysis for estimating their effects on burnout was not feasible. Three

Burnout: Pooled means and 95% CIs

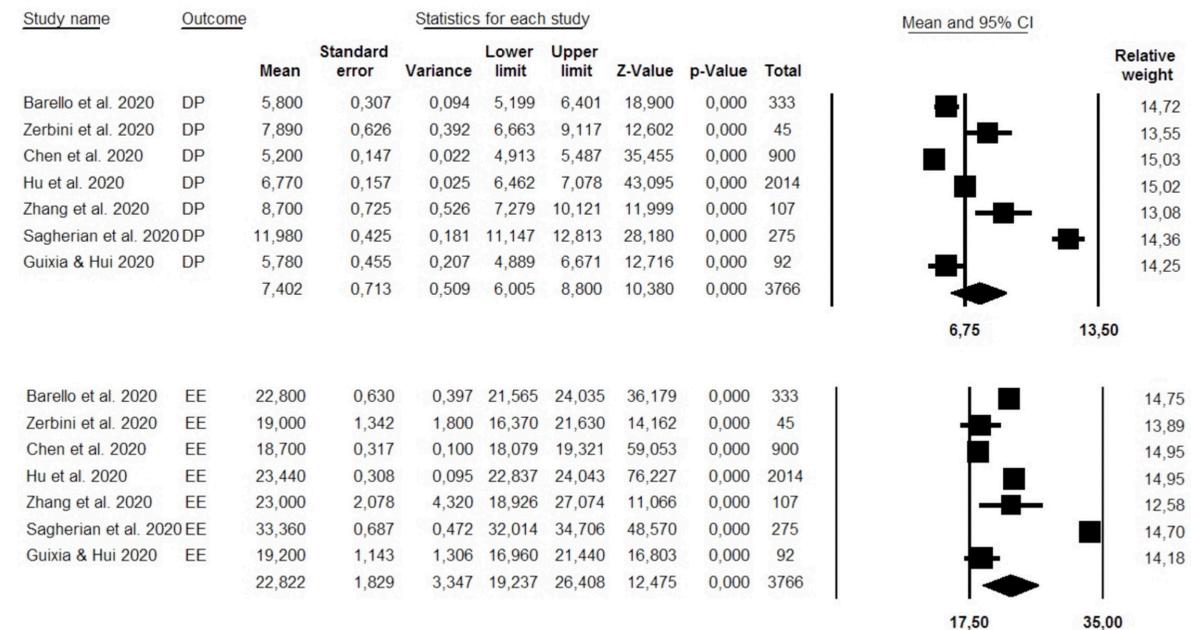


Figure 2. Pooled means of depersonalization and emotional exhaustion

PTSD : Pooled mean and 95% CI

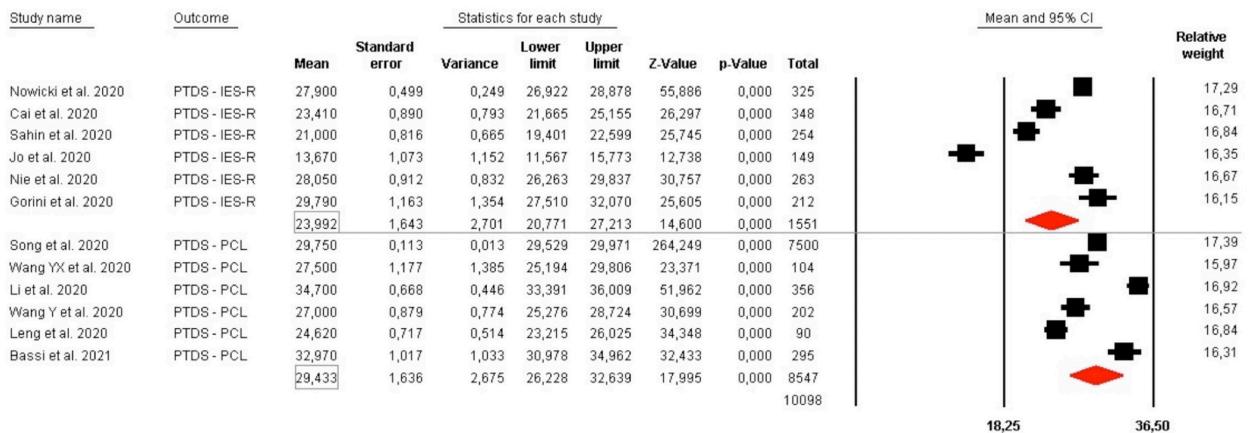


Figure 3. Pooled means of PTSD

studies reported that female nurses showed higher levels of emotional exhaustion (27,32,44). One study showed that nurses under 30 years were more likely to experience burnout (29). Higher educated nurses' role was uncertain in influencing burnout; however, it seems that nurses with higher education (practitioners) reported slightly higher levels of burnout (44). One study reported that among work-related risk fac-

tors, higher employment time, higher time spent with positive patients, and lower availability of resources for treating patients were associated with higher burnout levels (40). Likely, working in COVID-19 hospitals and intensive care units were described as risk factors of burnout (32). Another risk factor was given by the organization's need underpinning the necessity to relocate a nurse to a new ward to face the challenges

Table 3. Risk and protective factors of burnout

| Risk factors | Study | Association, 95% CI | P-value |
|---|------------------------------------|---|--|
| Sex | | | |
| Female | Barello et. al (2020) | F1.312=12.444; η^2 =.038. M(female)= 24.05 \pm 11.57; M(male)=18.74 \pm 12.65 | p<.001 |
| | Chen et al. (2020) | OR(EE): 1.30 (1.09-1.54) | P= .003 |
| | Tan et. al (2020) | β = 0.03 (0.00-0.07) | P= .051 |
| Age, years | | | |
| \leq 30 years | Zhang et al. (2020) | OR(EE): 2.96 (0.11-5.82) | p=0.042 |
| Education | | | |
| Low vs. High | Tan et. al (2020) | β Degree= 0.10 (0.04-0.16); β Diploma= 0.09 (0.03-0.16) | p=.001; p=.003 |
| Work-related variables | | | |
| Employment Type | Sarbooji Hoseinabadi et al. (2020) | β = 0.128 (0.00-0.034) | p=.047 |
| Experience in caring for Covid-19 infection | Sarbooji Hoseinabadi et al. (2020) | β = 0.175 (0.027-0.164) | p=.006 |
| Hospital resource for treatment of Covid-19 | Sarbooji Hoseinabadi et al. (2020) | β = -0.128 (-0.001-1.00) | p=.047 |
| Worked in a Covid-19 designed hospital | Chen et al. (2020) | OR(EE): 1.26 (1.17-1.36); OR (DP): 1.21(1.12-1.31) | P< .001; P<.001 |
| Worked in critical care units | Chen et al. (2020) | OR(EE):1.23 (1.12-1.33); OR (DP): 1.15 (1.06-1.25) | P< .001; P=.001 |
| Worked in a Covid-19- related department | Chen et al. (2020) | OR(EE): 1.16 (1.04-1.29); OR (DP): 1.20 (1.08-1.33) | P=.006; P=.001 |
| Professional title (junior) | Hu et al. (2020) | MEE(\pm SD): 23.82 (\pm 13.94), r/t = 2.116; MDP(\pm SD): 7.07 (\pm 7.22), r/t =3.395 | 0.01 \leq p<0.05; 0.001 \leq p < 0.01 |
| Wuhan as original working place (yes) | Hu et al. (2020) | MEE(\pm SD): 23.88 (\pm 13.58), r/t = 11.364; MDP(\pm SD): 7.42(\pm 7.19), r/t =5.988 | p< .001 |
| Working wards changed (yes) | Hu et al. (2020) | MEE(\pm SD): 22.65 (\pm 13.63), r/t = -1.965; MDP(\pm SD): 7.33(\pm 7.49), r/t =2.671 | 0.01 \leq p<0.05; 0.001 \leq p < 0.01 |
| Work experience, years | Sagherian et al. (2020) | M(\leq 2years): 11.68 (\pm 7.07); M(3-8years): 12.28 (\pm 6.89); M(9-14years): 11.70 (\pm 7.56); M(\geq 15years): 9.08 (\pm 6.70); F(DP): 5.11 | p=.002 |
| Working time in quarantine areas (\geq 20 hours) | Zhang et al. (2020) | OR(EE):2,72 (0.02-5.42); OR(DP): 1.14 (0.10-2.19) | p= 0.049; p= 0.033 |
| Average worked hours per week in the past month | Sagherian et al. (2020) | M(\leq 40h): 31.89 (\pm 12.14); M(>40h):34.38 (\pm 11.24); t(EE): -1.97 | p=.050 |
| Duration of shift, hours | Tan et. al (2020) | β 8 to<12= 0.06 (0.01-0.10); β >12= 0.16 (0.10-0.23) | p=.015; p<.001 |
| | Sagherian et al. (2020) | M(extended): 11.55 (\pm 7.04); M(traditional): 9.16 (\pm 6.94); t(DP): 2.36 | p=.019 |
| Work status | Sagherian et al. (2020) | M(Full time): 10.93 (\pm 6.93); M(Part Time): 13.04 (\pm 7,78); t(DP): -2.09 | p=.037 |
| 30-min breaks | Sagherian et al. (2020) | M(rarely/never): 35.05 (\pm 11.79); M(sometimes): 33.36 (\pm 11.62); M(often/always): 30.60 (\pm 11.80); F(EE): 5.37 | p=.005 |
| Un-confidence in caring for Covid-19 patients | Hu et al. (2020) | MEE(\pm SD): 28.12 (\pm 13.43), r/t =12.782; MDP(\pm SD): 7.94(\pm 7.13), r/t =6.020 | p< .001 |
| Un-confidence in self-protection | Hu et al. (2020) | MEE(\pm SD): 28.36 (\pm 13.21), r/t =14.577; MDP(\pm SD): 8.06 (\pm 7.17), r/t =7.144 | p< .001 |

Table 3. Risk and protective factors of burnout

| Risk factors | Study | Association, 95% CI | P-value |
|---|------------------------------------|---|----------------------|
| Evaluation of working safety while caring for Covid-19 (Unsafe) | Hu et al. (2020) | MEE(\pm SD): 28.48 (\pm 13.18), r/t =14.651; MDP(\pm SD): 8.07 (\pm 7.24), r/t =7.019 | p< .001 |
| Not Believe in family's readiness to cope with the COVID-19 outbreak | Hu et al. (2020) | MEE(\pm SD): 29.88 (\pm 13.00), r/t =14.064; MDP(\pm SD): 8.27 (\pm 7.23), r/t =6.042 | p< .001 |
| Not Believe in colleagues' readiness to cope with the COVID-19 outbreak | Hu et al. (2020) | MEE(\pm SD): 31.33 (\pm 13.17), r/t =13.612; MDP(\pm SD): 8.80 (\pm 7.36), r/t =6.386 | p< .001 |
| Not Believe in hospital's readiness to cope with the COVID-19 outbreak | Hu et al. (2020) | MEE(\pm SD): 32.39(\pm 13.12), r/t =14.278; MDP(\pm SD): 9.01 (\pm 7.48), r/t =6.364 | p< .001 |
| Redeployed (vs. Offsite) | Tan et. al (2020) | β Onsite(low risk)= 0.18 (0.05-0.29); β Onsite(high risk)= 0.17 (0.05-0.28) | p=.007; p=.005 |
| Individual assessment of training quality (vs. good or better) | Tan et. al (2020) | β Neutral or worse= 0.25(0.16-0.35); β No training received= 0.24 (0.12-0.37) | p<.001 |
| Physical and mental factors | | | |
| Skin lesion | Hu et al. (2020) | r EE= 0.182 | p< .001 |
| Fear of infection | Zerbini et al. (2020) | ρ (MBI exhaustion): 0.33 | p=.0004 |
| Stress at work | Zerbini et al. (2020) | ρ (MBI exhaustion):0.62; ρ (MBI depersonalization): 0.21 | p<.0001; p=.0242 |
| Covid-19 related job stress | Sarbooji Hoseinabadi et al. (2020) | β = 0.350 (0.068-0.138) | p< .001 |
| Compassion fatigue | Ruiz-Fernández et al. (2020) | β = 0.576 (t= 18.643) | p<.0001 |
| Anxiety | Guixia et al. (2020) | β = 0.491(t= 5.409) | p=.000 |
| | Tan et. al (2020) | β score \geq 8= 0.25 (0.22-0.28) | p<.001 |
| | Hu et al. (2020) | r EE= 0.637; rDP= 0.417 | p<.001 |
| Depression | Hu et al. (2020) | r EE= 0.569; rDP= 0.406 | p<.001 |
| | Tan et. al (2020) | β score \geq 8= 0.23 (0.19-0.62) | p<.001 |
| Protective factors | | | |
| | Study | Association, 95% CI | P-value |
| Work-related variables | | | |
| Cared for patients with Covid-19 | Chen et al. (2020) | OR (Dp): 0.85 (0.72-0.99); OR (Lack PA): 0.50 (0.28-0.89) | P= 0.048; P= .019 |
| Willingness to participate in frontline work during the Covid-19 outbreak (Yes) | Hu et al. (2020) | MEE(\pm SD): 23.25(\pm 13.57), r/t =-6.279; MDP(\pm SD): 6.62 (\pm 6.99), r/t =-5.200 | p< .001 |
| Longer working years | Guixia et al. (2020) | β = -0.181(t= -1.997) | p=.049 |
| | Zhang et al. (2020) | OR(EE): -3.25(-6.11; -0.38) | p= 0.027 |
| Safety climate | Tan et. al (2020) | β percentage agree= - 0.03 (-0.07,-0.01) | p<.001; p=.002 |
| Job satisfaction | Tan et. al (2020) | β percentage agree= - 0.17 (-0.21,-0.13) | p<.001 |
| Physical and mental factors | | | |
| Compassion satisfaction | Ruiz-Fernández et al. (2020) | β = -0.332 (t= -10.746) | p<.0001 |
| Self-efficacy | Hu et al. (2020) | r EE= -0.193 | p< .001 |
| Resilience | Hu et al. (2020) | r EE= -0.325; rDP= -0.208 | p< .001 |
| Intra-family social support | Hu et al. (2020) | r EE= -0.170; rDP= -0.221 | p< .001 |
| Extra-family social support | Hu et al. (2020) | r EE= -0.234; rDP= -0.216 | p< .001 |

Table 4. Risk and protective factors of PTSD

| Risk factors | Study | Association, 95% CI | P-value |
|--|---------------------------|--|---------|
| Socio-demographic data | | | |
| Sex | | | |
| Male | Song et al. (2020) | OR: 1.75 (1.51-2.03) | ? |
| | Wang, Y. X. et al. (2020) | β : 0.229 (t = 3.566) | P<.001 |
| Female | Wang, Y. et al. (2020) | OR:1.73 (1.08-2.78) | p=0.022 |
| | ahin et al. (2020) | OR: 1.77 (1.30-2.42) | p<.001 |
| | Jo et al. (2020) | M(female): 14.11 (\pm 14.09); M(male): 8.56(\pm 11.86) | p=.02 |
| | Bassi et al. (2021) | OR: 1.62 (1.07-2.44) | p=0.02 |
| | Chen et al. (2020) | OR: 1.48 (1.12-1.97) | p=0.006 |
| Age | Song et al. (2020) | OR(26-30y): 1,48 (1.18-1.86); OR(31-40y): 1.34 (1.02-1.77) | ? |
| Marital status | Li et al. (2020) | OR(married): 9.71 (5.33-17.7) | p<.001 |
| | Nowicki et al. (2020) | M(Married): 1.85 \pm 0.61 | p=0.047 |
| Having offspring | Nowicki et al. (2020) | M(yes): 1.81 \pm 0.78 | p=0.035 |
| Work-related variables | | | |
| Work experience, years | Song et al. (2020) | OR(16-20y): 1,57 (1.17-2.11); OR(11-15y): 1.73 (1.20-2.48); OR(<10y): 1.62 (1.11-2.36) | ? |
| | Nowicki et al. (2020) | r = 0.144 | p=0.01 |
| | Nie et al. (2020) | OR: 1.536 (1.120-2.106) | p=.008 |
| Working in Covid-19 unit | Li et al. (2020) | OR(inpatient ward): 21.9 (5.08-94.5) | p<.001 |
| Worked in a Covid-19 designed hospital | Chen et al. (2020) | OR: 1.24 (1.11-1.38) | p<.001 |
| Worked in critical care units | Chen et al. (2020) | OR: 1.20 (1.06-1.35) | p=.004 |
| Technical title | Wang, Y. et al. (2020) | OR: 1.88 (1.32-2.67) | p<.001 |
| Frontline workers | Wang, Y. et al. (2020) | OR: 2.27 (1.63-3.17) | p<.001 |
| | Bassi et al. (2021) | OR(Inpatient frontline): 2.01 (1.18-3.43) | p=.01 |

given by the re-organization of the shifts and units (48). The time spent in quarantine areas was described as a risk factor of burnout as well (29). Overall, the unconfidence in the organization's ability to respond adequately to the changing challenges was described as an important risk factor (48). Among physical and mental factors, skin lesions due to wearing personal protective equipment (48), fear of infection (26), work-related stress (26,40), compassionate fatigue (42), anxiety (28,44,48), and depression (44,48) were reported to be associated with burnout.

The protective factors of burnout were work-related variables, physical and mental factors. Among work-related variables, in contrast with other included findings (32), caring for positive patients was described as a possible protective factor in one study (32), and the higher working experience seemed to be a protec-

tive factor in two other studies (28,29). The perceptions of safety and adequate job satisfaction were considered as a protective factor in one study (44). Among physical and mental factors, the roles of compassion satisfaction, self-efficacy, resilience, intra-family and extra-family social support were considered as strategic protective factors (42,48).

Risk and protective factors of PTSD

The main risk factors associated with PTSD were sociodemographic characteristics (sex, age, marital status, offspring), work-related variables, and physical and mental factors, as described in **Table 4**. Considering the risk factors heterogeneity in the included studies, a quantitative pooled analysis for estimating their effects on PTSD was not feasible. The role of sex was uncertain as four studies described male nurses with

Table 4. Risk and protective factors of PTSD

| Risk factors | Study | Association, 95% CI | P-value |
|---|---------------------------|--|-------------------|
| Duration of shift, hours | Song et al. (2020) | OR(9-10h): 1.36 (1.18-1.56); OR(11-12h): 1.69 (1.43-2.01); OR(>12h): 2.42 (1.96-2.99) | ? |
| Average worked hours per week in the past month | Sagherian et al. (2020) | M(\leq 40h): 14.84 (\pm 7.28); M(>40h): 16.43(\pm 6.33); <i>t</i> : -2.25 | p=.026 |
| Enough training for protection | Wang, Y. et al. (2020) | OR: 1.56 (1.14-2.14) | p=0.006 |
| Clinical setting | Leng et al. (2020) | M(paediatrics): 27.20(\pm 8.67); M(operating room): 29.50(\pm 9.19); M(obstetrics and gynecology): 31.20 (\pm 8.87); <i>t/F</i> = 2.53 | p=.003 |
| 30-min breaks | Sagherian et al. (2020) | M(rarely/never): 17.43(\pm 6.66); M(sometimes): 14.42 (\pm 6.66); M(often/always): 14.49 (\pm 7.22); <i>F</i> = 7.91 | p<.001 |
| Location | Song et al. (2020) | OR(Hubei province): 1.43 (0.92-2.21) | ? |
| Social support | Song et al. (2020) | OR(Moderate): 2.73 (2.42-3.07); OR(Low): 5.49 (4.04-7.45) | ? |
| Degree of job satisfaction | Wang, Y. X. et al. (2020) | β : 0.354(<i>t</i> = 5.520) | P<.001 |
| Confirmed cases among relatives and friends | Si et al. (2020) | β = 3.045 | P=.039 |
| Perceived threat | Si et al. (2020) | β = 0.342 | P=.000 |
| Sufficient protection conditions | Cai et al. (2020) | OR: 1.813 (1.243-2.644) | P=0.002 |
| Confidence in protection measures | Wang, Y. et al. (2020) | OR: 1.73 (1.23-2.43) | p=0.002 |
| Physical and mental factors | | | |
| Have chronic diseases | Si et al. (2020) | β = 1.800 | P=.010 |
| Levels of concern to the outbreak | Si et al. (2020) | β = 1.704 | P=.000 |
| | Si et al. (2020) | β =0.234 | P=.000 |
| Negative coping style | Nie et al. (2020) | OR: 5.400 (2.544-11.462) | p<.001 |
| | Wang, Y. X. et al. (2020) | <i>r</i> : 0.154 | P<.05 |
| Physical condition change worse | Cai et al. (2020) | OR: 1.567 (1.66-2.107) | p= 0.003 |
| Value of online psychological information | Cai et al. (2020) | OR: 1.556 (1.155-2.097) | p=0.004 |
| A history of psychiatric illness | ahin et al. (2020) | OR: 1.85 (1.25-2.75) | p=0.002 |
| Taking the Covid-19 test | ahin et al. (2020) | OR: 1.46 (1.07-1.99) | p=0.015 |
| Self-concern | Nie et al. (2020) | OR: 4.481 (2.383-8.427) | p= .001 |
| Perceived stress | Leng et al. (2020) | <i>r</i> =0.506 | p< 0.1 |
| Mental Health | Bassi et al. (2021) | OR(Languishing): 3.00 (1.56-5.77) | p= .001 |
| Protective factors | | | |
| Socio-demographic data | | | |
| Sex | Gorini et. al (2020) | β man: -0.45 (<i>t</i> = -3.38) | P= 0.0008 |
| Age, years | Li et al. (2020) | OR:0.73 (0.68-0.78) | p<.001 |
| Unmarried | Song et al. (2020) | OR: 0.76 (0.64-0.91) | ? |
| Educational level | Song et al. (2020) | OR(university): 0.83 (0.72-0.97); OR(graduate school): 0.81(0.63-1.05) | ? |
| | Li et al. (2020) | OR(Bachelor): 0.42 (0.22-0.79); OR(Masters and above): 0.12(0.03-0.54) | p=.007; p=.004 |

Table 4. Risk and protective factors of PTSD

| Risk factors | Study | Association, 95% CI | P-value |
|---|---------------------------|---|------------------------------|
| Work-related variables | | | |
| COVID-19 units | Song et al. (2020) | OR(other department): 0.71 (0.55-0.91) | ? |
| Location | Wang, Y. et al. (2020) | OR(Hubei except Wuhan): 0.56 (0.38-0.83); OR(Other provinces): 0.54 (0.36-0.81) | p=.003 |
| Working experience | Li et al. (2020) | OR(6-10 years): 0.10 (0.01-0.75); OR(11-20 years): 0.004 (0.001-0.03); OR(>20 years): 0.004 (0.001-0.04) | p= .03; p<.001; p<.001 |
| Professional level | Li et al. (2020) | OR(Senior nurses): 0.08 (0.02-0.35); OR(Nurse managers/supervisors): 0.01 (0.003-0.05); OR(Deputy chief nurse): 0.01 (0.001-0.04) | p=.001; p<.001; p<.001 |
| Being a Nurse specialist | Li et al. (2020) | OR: 0.12 (0.04-0.38) | p<.001 |
| Working non-frontline | Cai et al. (2020) | OR: 0.690 (0.514-0.927) | P=.014 |
| Certainty of fighting against the epidemic | Cai et al. (2020) | OR: 0,371 (0.277-0.497) | p<.001 |
| Physical and mental factors | | | |
| Positive coping style | Wang, Y. X. et al. (2020) | r: - 0.151 | P<.05 |
| | Nie et al. (2020) | OR: 0.3850 (0.220-0.673) | p=.001 |
| Current tobacco user | Si et al. (2020) | β = -1.426 | P=0.024 |
| Resilience (CD-RISC) | Li et al. (2020) | OR: 0.96 (0.93-0.99) | p=.02 |
| Worry about infection (No) | Wang, Y. et al. (2020) | OR: 0.03 (0.01-0.23) | p= .001 |
| Impact of Psychiatric intervention on IES-R | Jo et al. (2020) | M(pre-intervention scores): 32.33 (\pm 13.40); M(post-intervention score): 18.67(\pm 23.46) | p<.01 |
| Mental Health | Bassi et al. (2021) | OR(Flourishing):0.26 (0.17-0.39) | p< .001 |

higher odds of reporting PTSD (31,33,36,46), while three studies reported higher odds of PTSD in female nurses (32,35,43). Younger nurses seemed to experience higher levels of PTSD (36), as well as married nurses and those with offsprings (41,47). Considering work-related variables, lower work experience, working in proximity to positive patients, in the frontline, with shifts lasting more than 9 hours, working more than 40 hours per week, in red zones, with confirmed cases among relative and friends, were the main risk factors associated with higher PTSD (24,30,47,32-34,36,39,41,45,46). Likely, having a chronic disease, higher concerns about the pandemic, dysfunctional coping mechanisms, un-optimal physical condition, previous psychiatric illness, higher stress, and poor mental health status were associated with PTSD as well (24,30,31,33,34,39,43).

The protective factors of PTSD were socio-demographic variables, work-related variables, and physical and mental factors. Female (25) and younger (47) nurses have been described to experience higher PTSD than those with lower educational backgrounds

(36,47). In contrast with some studies describing the work with positive patients as a risk factor, other authors found the working in the COVID-19 units during the first epidemic peak in China was a protective factor to PTSD in a short term perspective (36,46). In another study, non-frontline nurses, were described as associated with lower levels of PTSD than frontline nurses (34). Considering physical and mental factors, having functional coping mechanisms, smoking tobacco, higher resilience, lower concerns of being infected, and higher mental health were associated with lower levels of PTSD (24,33,35,43,46,47).

Discussion

This systematic review estimated the means of depersonalization and emotional exhaustion (burnout) measured using the MBI and means of PTSD measured using IES-R and PCL in nurses working during the COVID-19 pandemic in 2020. This study also narratively synthesized their risk and protective factors

leading to burnout and/or PTSD. For this reason, the results of this systematic review could represent a strategic ground to boost the understanding of the impact of the COVID-19 pandemic on the nurses' mental health, highlighting the current gaps in knowledge, increasing the accessibility to complex and diverse evidence by decision-makers and researchers.

As expected, burnout levels varied across the included studies. Burnout is a work-related stress syndrome resulting from prolonged exposure to job stress and clinically manifested as depersonalization, emotional exhaustion, and reduced personal accomplishment (49), leading to worse quality of care, increased intention to leave the profession, and decreased organizational capacity to deliver safe care (50). In the included studies, the means of depersonalization ranged from 5,2 to 12,0, and ones of emotional exhaustion ranged from 19,00 to 33,36. Our analysis showed an estimated pooled mean of depersonalization equal to 7,40 within a 95%CI ranging from 6,01 to 8,80; further, the estimated pooled mean of emotional exhaustion was equal to 22,82 within 95%CI ranging from 19,24 to 26,41.

These results suggest that, as expected, depersonalization and emotional exhaustion could vary significantly between different settings, as several factors influence burnout, and their overall estimates in nurses during 2020 have to be considered as alarming. Despite there is no consensus in defining equal and valid cut-off for identifying clinically relevant symptoms of depersonalization and emotional exhaustion (51), some results from normative data can help to interpret the obtained estimates: depersonalization scores ranging from 4 to 8 and emotional exhaustion scores ranging from 15 to 23 indicate moderate levels of symptoms (52–55). *De facto*, this systematic review highlighted that depersonalization is moderately clinically relevant in nurses working during the COVID-19 pandemic in 2020, while emotional exhaustion seemed highly relevant as a clinical symptom of burnout. These results, suggesting that the support for emotional exhaustion followed by support for depersonalization are highly needed, could be explained by the higher female rates within the nursing profession, as a previous meta-analysis showed that emotional exhaustion levels tend to be higher among females, while depersonali-

zation tends to be higher in males (56). However, as our narrative synthesis on the risk factor of burnout showed, the sex-related differences in burnout are still uncertain and should be addressed by specific research projects (57).

PTSD was detected in this systematic review to be moderately alarming as well, considering the pooled mean values reported for the two tools that were most frequently adopted during 2020 for assessing PTSD. A traumatic event, such as dealing with the challenges brought by the COVID-19 pandemic, could trigger fear, helplessness, or horror (58). Frontline nurses who have been exposed to such challenging situations are at increased risk for PTSD. This syndrome can enhance the likelihood of major depression, panic disorder, generalized anxiety disorder, and substance abuse compared with those who have not experienced traumatic situations. The prolonged exposure to the COVID-19 challenges could also lead to nonspecific symptoms such as insomnia, unexplained pain, palpitations, shortness of breath, tremor, nausea, mood swings, and previous research suggested that PTSD could trigger nonadherence to treatment as a manifestation of avoidance (52,59). Given the depicted scenario, a system-level re-organization to manage middle and long-term effects of PTSD on nurses is highly required, such as integrating the psychological support for individuals with the organizational support for facilities that have to provide nurses with PTSD the time to recover, drafting strategies to avoiding the social stigma of poor mental health. These strategies should consider to decrease risk factors of PTSD and burnout and enhance protective factors.

As expected, we found several common risks and protective factors of PTSD and burnout. Although the role of socio-demographic characteristics is still uncertain, it seems that younger, female, less educated nurses (in several countries, the entry-level to be a registered nurse could be inferior to the university education) were the most exposed ones to both the negative outcomes. However, the associations between socio-demographic characteristics, work-related variables, and physical and mental factors have to be considered with caution as the data currently available have been cross-sectionally collected; thus, these associations' longitudinal features are still mainly unknown.

Conclusions

This systematic review included 25 studies representing the up-to-date evidence regarding burnout and PTSD among nurses engaged in the frontline during the COVID-19 pandemic, highlighting their risk and protective factors. This systematic review presents limitations that require to be discussed. Firstly, the samples for each included study were diverse, considering education and socio-demographic data, and with limited sizes for allowing researchers to perform further in-depth analysis, such as subgroup analysis for each outcome or the meta-analyses on risk and protective factors. Furthermore, the pooled analyses' estimates were based on cross-sectional data, undermining the possibility to describe the trajectory of burnout and PTSD over time. Although we sought to identify all relevant studies to summarize the evidence regarding burnout and PTSD, the limited publication period could influence the search's comprehensiveness, even if this study represents the portrait of published research during 2020 on the investigated topics. In the estimates of the pooled means, strength was given by the inclusion of studies measuring burnout (depersonalization and emotional exhaustion) and PTSD with the same tool for allowing a summary of the estimates. The emerging scenario is diverse and broadly alarming. Middle and long-term multi-level strategies involving regulators, researchers, managers, and multi-stakeholders are required to avoid further negative consequences for the nurses' health and, in a public health perspective, for the overall quality and safety of the healthcare systems. These strategies should be supported by a continuous deepening of the understanding of factors associated with burnout and PTSD among HCWs in general, and specifically focused on each professional group for identifying profession-specific patterns that could be susceptible to supportive strategies. For this reason, research should longitudinally describe the clinical trajectory of symptoms characterizing burnout, PTSD, and the broad mental health of nurses. In conclusion, we invite decision-makers to increase their attention towards the wellbeing of nurses within each healthcare system worldwide, as nurses in health can add value within each clinical context.

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Supplementary materials.**Supplementary file 1.** Prisma statement

| Section/topic | # | Checklist item | Reported on page # |
|------------------------------------|----|---|------------------------------------|
| TITLE | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | Title page |
| ABSTRACT | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 1 |
| INTRODUCTION | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 1-2 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 2-3 Supplementary File 1 |
| METHODS | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | 3 |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 3 Supplementary File 1 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 3-4 Supplementary File 1 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | 3-4 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 3-4 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 5 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 4-5 |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | 5-6 |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 5-6 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis. | 5-6 |
| Section/topic | # | Checklist item | Reported on page # |
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | 6 |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | Na |
| RESULTS | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | Figure 1 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | 4 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | Supplementary File 2 and page 5 |

| | | | |
|-------------------------------|----|--|---------------------------------|
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | Figures 2 and 3 |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | 8-9 |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | Supplementary File 2 and page 7 |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | NA |
| DISCUSSION | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 10-11 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 12 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 12-14 |
| FUNDING | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | Title page |

Supplementary file 2. Queries

Pubmed:

1° November 2020:

((Nurse [MesH] OR Personnel, Nursing OR Nursing Personnel OR Registered Nurse* OR Nurse*, Registered) AND (COVID-19 [Supplementary Concept] OR 2019 novel coronavirus disease OR COVID19 OR COVID-19 pandemic OR SARS-CoV-2 infection OR COVID-19 virus disease OR 2019 novel coronavirus infection OR 2019-nCoV infection OR coronavirus disease 2019 OR coronavirus disease-19 OR 2019-nCoV disease OR COVID-19 virus infection)) AND (Burnout [MesH] OR Professional Burnout OR Occupational Burnout OR Burnout, Occupational OR Career Burnout OR Burnout, Career OR Psychological Burnout OR Burn-out Syndrome OR Burn out Syndrome OR Burnout Syndrome OR Burn-out OR Burn out OR Psychological Burn-out OR Burn-out, Psychological OR Psychological Burn out)

2° November 2020:

((Nurse [MesH] OR Personnel, Nursing OR Nursing Personnel OR Registered Nurse* OR Nurse*, Registered) AND (COVID-19 [Supplementary Concept] OR 2019 novel coronavirus disease OR COVID19 OR COVID-19 pandemic OR SARS-CoV-2 infection OR COVID-19 virus disease OR 2019 novel coronavirus infection OR 2019-nCoV infection OR coronavirus disease 2019 OR coronavirus disease-19 OR 2019-nCoV disease OR COVID-19 virus infection)) AND (PTSD OR Stress Disorder, Post Traumatic OR Neuroses, Posttraumatic OR Posttraumatic Neuroses OR Posttraumatic Stress Disorder* OR Stress Disorder*, Posttraumatic OR Neuroses, Post-Traumatic OR Neuroses, Post Traumatic OR Post-Traumatic Neuroses OR Post-Traumatic Stress Disorder* OR Post Traumatic Stress Disorders OR Stress Disorder, Post-Traumatic OR Moral Injury OR Injury, Moral OR Moral Injuries OR Delayed Onset Post-Traumatic Stress Disorder OR Delayed Onset Post Traumatic Stress Disorder OR Acute Post-Traumatic Stress Disorder OR Acute Post Traumatic Stress Disorder OR Chronic Post-Traumatic Stress Disorder OR Chronic Post Traumatic Stress Disorder)

3° January 2021:

((Nurse [MesH] OR Personnel, Nursing OR Nursing Personnel OR Registered Nurse* OR Nurse*, Registered) AND (COVID-19 [Supplementary Concept] OR 2019 novel coronavirus disease OR COVID19 OR COVID-19 pandemic OR SARS-CoV-2 infection OR COVID-19 virus disease OR 2019 novel coronavirus infection OR 2019-nCoV infection OR coronavirus disease 2019 OR coronavirus disease-19 OR 2019-nCoV disease OR COVID-19 virus infection)) AND (Burnout [MesH] OR Professional Burnout OR Occupational Burnout OR Burnout, Occupational OR Career Burnout OR Burnout, Career OR Psychological Burnout OR Burn-out Syndrome OR Burn out Syndrome OR Burnout Syndrome OR Burn-out OR Burn out OR Psychological Burn-out OR Burn-out, Psychological OR Psychological Burn out) OR (PTSD OR Stress Disorder, Post Traumatic OR Neuroses, Posttraumatic OR Posttraumatic Neuroses OR Posttraumatic Stress Disorder* OR Stress Disorder*, Posttraumatic OR Neuroses, Post Traumatic OR Post-Traumatic Neuroses OR Post-Traumatic Stress Disorder* OR Post Traumatic Stress Disorders OR Stress Disorder, Post-Traumatic OR Moral Injury OR Injury, Moral OR Moral Injuries OR Delayed Onset Post-Traumatic Stress Disorder OR Delayed Onset Post Traumatic Stress Disorder OR Acute Post-Traumatic Stress Disorder OR Acute Post Traumatic Stress Disorder OR Chronic Post-Traumatic Stress Disorder OR Chronic Post Traumatic Stress Disorder) Filters: in the last 1 year, Adult: 19+ years

Supplementary file 2. Queries

Pubmed:

4° January 2021:

((Nurse [MesH] OR nurs* OR "Personnel, Nursing" OR "Nursing Personnel" OR "Registered Nurse*" OR "Nurse*, Registered")) AND ("severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[All Fields] OR "ncov"[All Fields] OR "2019 ncov"[All Fields] OR "covid 19"[All Fields] OR "sars cov 2"[All Fields] OR ("coronavirus"[All Fields] OR "cov"[All Fields]) AND 2019/11/01:3000/12/31[Date - Publication])) AND ((Burnout [MesH] OR burnout OR "Professional Burnout" OR "Occupational Burnout" OR "Burnout, Occupational" OR "Career Burnout" OR "Burnout, Career" OR "Psychological Burnout" OR "Burnout Syndrome" OR "Burnout Syndrome" OR "Burnout Syndrome OR Burnout" OR "Psychological Burnout" OR "Burnout, Psychological" OR "Psychological Burnout" OR ("PTSD" OR "Stress Disorder, Post Traumatic" OR "Neuroses, Posttraumatic" OR "Posttraumatic Neuro*" OR "Posttraumatic Stress Disorder*" OR "Stress Disorder*, Posttraumatic" OR "Neuroses*, Posttraumatic" OR "Neuroses*, Post Traumatic" OR "Posttraumatic Neuroses*" OR "Posttraumatic Stress Disorder*" OR "Post Traumatic Stress Disorder*" OR "Stress Disorder*, Posttraumatic" OR "Moral Injury" OR "Injury, Moral" OR "Moral Injuries" OR "Delayed Onset Post-Traumatic Stress Disorder" OR "Delayed Onset Post Traumatic Stress Disorder" OR "Acute Posttraumatic Stress Disorder" OR "Acute Post Traumatic Stress Disorder" OR "Chronic Posttraumatic Stress Disorder" OR "Chronic Posttraumatic Stress Disorder*"))

CINAHL

1° December 2020:

((Covid-19 OR (corona virus disease 2019) OR 2019 novel coronavirus disease) OR SARS-CoV-2) AND nurs*) AND burnout

2° December 2020:

((Covid-19 OR (corona virus disease 2019) OR 2019 novel coronavirus disease) OR SARS-CoV-2) AND (nurs*) AND (PTSD OR post traumatic stress disorder)

Scopus

1° December 2020:

Covid-19 OR corona virus disease 2019 OR 2019 novel coronavirus disease OR SARS-CoV-2 AND nurs* AND burnout

2° December 2020:

Covid-19 OR corona virus disease 2019 OR 2019 novel coronavirus disease OR SARS-CoV-2 AND nurs* AND PTSD

PsycInfo

1° December 2020:

((Covid-19 OR (corona virus disease 2019) OR 2019 novel coronavirus disease) OR SARS-CoV-2) AND nurs*) AND burnout

2° December 2020:

((Covid-19 OR (corona virus disease 2019) OR 2019 novel coronavirus disease) OR SARS-CoV-2) AND (nurs*) AND (PTSD OR post traumatic stress disorder)

Supplementary file 3. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) for evaluating reporting and methodological qualities of the eligible articles

| Study | Reviewer | Item 1 a | Item 1 b | Item 2 | Item 3 | Item 4 | Item 5 | Item 6 | Item 7 | Item 8 | Item 9 | Item 10 | Item 11 | Item 12a | Item 12b | Item 12c | Item 12d | Item 12e | Item 13a | Item 13b | Item 13c | Item 14 | Item 15 | Item 16a | Item 16b | Item 16c | Item 17 | Item 18 | Item 19 | Item 20 | Item 21 | Item 22 | Fleiss' K | Overall | | |
|------------------------------|----------|----------|----------|--------|--------|--------|--------|--------|--------|--------|--------|---------|---------|----------|----------|----------|----------|----------|----------|----------|----------|---------|---------|----------|----------|----------|---------|---------|---------|---------|---------|---------|-----------|---------|---------|---------|
| Barello et al. (2020) | RC | ? | + | + | + | + | + | + | + | + | ? | ? | + | + | + | + | - | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 0,98 | Include | |
| Zerbini et al. (2020) | CA | ? | + | + | + | + | + | + | + | + | ? | ? | + | + | + | + | - | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 1 | Include |
| Ruiz-Fernández et al. (2020) | RC | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 1 | Include |
| Sarbozi | CA | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 1 | Include |
| Hoseinabadi et al. (2020) | RC | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 1 | Include |
| Chen et al. (2020) | RC | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 1 | Include |
| Hu et al. (2020) | CA | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 0,98 | Include |
| Guixia et al. (2020) | RC | - | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 0,98 | Include |
| Zhang et al. (2020) | CA | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 0,98 | Include |
| Sagherian et al. (2020) | RC | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 0,98 | Include |
| Tan et al. (2020) | CA | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 0,98 | Include |
| Song et al. (2020) | RC | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 1 | Include |
| Wang, Y. X. et al. (2020) | CA | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 0,98 | Include |
| Si et al. (2020) | RC | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 0,98 | Include |
| | CA | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 0,98 | Include |

Supplementary file 3. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) for evaluating reporting and methodological qualities of the eligible articles

| Study | Reviewer | Item 1 a | Item 1 b | item 2 | item 3 | item 4 | item 5 | item 6 | item 7 | item 8 | item 9 | item 10 | item 11 | item 12a | item 12b | item 12c | item 12d | item 12e | item 13a | item 13b | item 13c | item 14 | item 15 | item 16a | item 16b | item 16c | item 17 | Item 18 | item 19 | item 20 | item 21 | item 22 | Fleiss' K | Overall | | | |
|-------------------------|----------|----------|----------|--------|--------|--------|--------|--------|--------|--------|--------|---------|---------|----------|----------|----------|----------|----------|----------|----------|----------|---------|---------|----------|----------|----------|---------|---------|---------|---------|---------|---------|-----------|---------|---------|---------|---------|
| Li et al. (2020) | RC | + | + | + | + | + | + | - | + | + | - | + | + | + | - | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 0,98 | Include | | |
| Nowicki et al. (2020) | RC | + | + | + | + | + | + | + | + | + | - | + | + | + | - | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 0,98 | Include | |
| Cai et al. (2020) | RC | + | + | + | + | + | + | + | + | + | - | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 1 | Include | |
| Wang, Y. et al. (2020) | RC | + | + | + | + | + | + | + | + | + | - | + | + | + | - | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 0,98 | Include | |
| ahin et al. (2020) | RC | + | + | + | + | - | + | - | + | + | - | + | + | + | - | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 0,98 | Include | |
| Leng et al. (2020) | RC | + | + | + | + | + | + | + | + | + | - | + | + | + | - | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 1 | Include | |
| Jo et al. (2020) | RC | - | + | + | + | + | + | + | + | + | - | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 0,98 | Include | |
| Nie et al. (2020) | RC | + | + | + | + | + | + | + | + | + | - | + | + | + | - | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 0,98 | Include |
| Gorini et. al (2020) | RC | + | + | + | + | + | + | - | + | + | - | + | + | + | - | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 0,98 | Include |
| Bassi et al. (2021) | RC | + | + | + | + | + | + | + | + | + | - | + | + | + | - | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 0,98 | Include |
| Haravuori et al. (2020) | RC | + | + | + | + | + | + | - | + | + | - | + | + | + | - | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 0,98 | Include |
| Crowe et al. (2020) | RC | + | + | + | + | + | + | + | + | + | - | + | + | + | - | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 0,98 | Include |
| | CA | + | + | + | + | + | + | + | + | + | - | + | + | + | - | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 0,98 | Include |