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Burnout syndrome and its determinants among healthcare workers during the first wave of the Covid-19 outbreak in Italy: a cross-sectional study to identify sex-related differences

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Abstract

Introduction: *Several studies described burnout levels of healthcare workers (HCWs) during the COVID-19 pandemic; however, sex-related differences remain poorly investigated. Objective: To describe sex-related differences in burnout and its determinants among HCWs during the first pandemic wave of the COVID-19 in Italy.* ***Methods:*** *A cross-sectional study was performed between April and May 2020. The framework given by the Job Demands Resources (JD-R) model was used to assess burnout determinants (risk and protective factors).* ***Results:*** *Male HCWs (n=133) had higher levels of depersonalization than female HCWs (P=0,017) and female HCWs (n=399) reported greater emotional exhaustion rates (P=0,005). Female nurses were the most exposed to burnout (OR=2,47; 95%CI=1,33-4,60; P=0,004), emotional exhaustion (OR=1,89; 95% CI=1,03-3,48; P=0,041), and depersonalization (OR=1,91; 95% CI=1,03-3,53; P=0,039). Determinants of burnout differed between sexes, and some paradoxical associations were detected: the score of job demands was a protective factor in females for burnout, emotional exhaustion, and depersonalization, resilience was a risk factor for males.* ***Conclusions:*** *This study reveals that the stressors in male and female HCWs tended to be associated with burnout differently. Both sexes showed alarming burnout levels, even if the weights of emotional exhaustion and depersonalization acted in different ways between the sexes. The revealed paradoxical effects in this study could reflect the study's cross-sectional nature, highlighting that more resilient and empathic individuals were more consciously overwhelmed by the challenges related to the COVID-19 pandemic, thus reporting higher scores of emotional exhaustion and burnout. Future in-depth and longitudinal analyses are recommended to further explore sex-related differences in burnout among HCWs.*

Introduction

The COVID-19 pandemic impact on healthcare workers' (HCWs) wellbeing and mental health has been dramatic (1). The COVID-19 pandemic triggered several demands, such as increased workload, fear of being infected and becoming potential spreaders of the disease within the own families,

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frequent adjustments of clinical protocols, and increased emotional demands in delivering care for critical patients (2–5). This challenging situation has amplified stressors within every healthcare system worldwide, and the levels of burnout among HCWs in response to increasingly stressful demands have been documented as alarming (1, 2, 4). In this regard, a recent literature review described that more than one HCW out of four presented anxiety, depression, and burnout (6). Furthermore, it seems that nurses, female workers, frontline healthcare workers, younger medical staff, and workers in areas with higher infection rates reported higher levels of unfavorable mental health outcomes (7). Additionally, an increased rate of sleep problems and distress by HCWs during the ongoing COVID-19 pandemic has been detected as associated with emotional distress (8).

The literature has already described that during other infectious disease epidemics, such as severe acute respiratory syndrome (SARS) and the Middle East respiratory syndrome (MERS), a considerable number of HCWs suffered from significant emotional distress that lead to burnout (9, 10). Burnout is a prolonged response to extended emotional and interpersonal stressors on the job, conceptualized by the interplay of emotional exhaustion, depersonalization, and diminished personal accomplishment (11). Although the available evidence describing HCWs burnout during previous pandemics is relevant (9, 10), the challenges that the COVID-19 pandemic brought to every healthcare system have distinctive aspects, such as the massive pressure placed on hospitals and alarming epidemiologic features given the highly interconnected daily life (12). Accordingly, this global situation can potentially expose many HCWs to an unprecedented situation (8). For instance, HCWs, who were not involved in critical care before the COVID-19 pandemic, can be asked to cover shifts in critical settings, working under severe pressures without sufficient training or experience of coping with these stressors (13).

In the last two decades, the study of burnout was facilitated by some theoretical frameworks, and the Job Demands Resources (JD-R) model is one of the most adopted frameworks to study burnout as it helps to monitor workplace settings so as to increase work engagement and prevent burnout (14). The JD-R model relies on considering that every job includes demands (risk factors of burnout) and resources (protective factors of burnout) (14): the higher balance between job demands and job resources, the higher individual's wellbeing. In the current research, the relationships from job demands and job resources to burnout were explored by considering the influence of variables that can mitigate or amplify the effects of job demands and job resources on burnout, such as empathy and orientation to engagement (15). Thus, the JD-R model allows researchers to identify burnout determinates, which can be used to inform the planning, implementation, and evaluation of psychosocial and organizational interventions. This approach is particularly meaningful in the current pandemic situation. In this complex scenario, beyond the need to describe the associations from job demands and job resources to burnout, understanding the individual-level determinants of burnout is strategic to provide evidence for designing proper psychosocial interventions (16,17).

Personal resources given by the theorization of the JD-R model are the individuals' characteristics that might contribute to individuals' optimal functioning. Among these characteristics, the orientation to patient engagement, resilience, and empathy have been recently described as strategic (18). Resilience and empathy have been described as significant predictors of healthcare workers' psychological wellbeing in some studies (19, 20). A similar association was described considering the professionals' orientation toward patients' psychosocial needs and engagement (namely orientation to patient engagement) (21). However, how these personal characteristics act in determining symptoms of burnout might differ in the extraordinary situation given by the first pandemic wave in countries, such as Italy, where HCWs started to face between March and June 2020 the challenges of an unknown disease that brought hospital overload with an unprecedented volume of patient demands. In this context, the associations of some personal resources and symptoms of burnout and burnout could be theoretically different from the well-rec-

ognized associations given by the negative relationships between positive personal characteristics (e.g., high orientation to patient engagement or high reliance) and burnout. In other terms, it is reasonable to theorize that HCWs with higher levels of some positive personal resources (e.g., high orientation to patient engagement) might experience burnout symptoms earlier than HCWs with lower personal resources, even if, theoretically, HCWs with more positive personal resources have more chance to effectively face with the stressors brought by the pandemic over time.

Thus far, several studies and literature reviews on the burnout levels of HCWs during the COVID-19 pandemic have been performed (2, 4, 5, 12, 22). Although several studies showed sex-related differences in the rates of emotional exhaustion and depersonalization, studies designed to specifically address the sex-related differences in burnout levels and its determinants are still lacking in the research regarding burnout among HCWs facing the COVID-19 pandemic challenges (23). This lack of evidence explicitly addressing the sex -related differences in the rates of burnout among HCWs and describing sex-related differences in its determinants could significantly undermine optimal psychosocial support planning for HCWs (24). Understanding some sex-specific patterns in the associations from personal resources (e.g., orientation to engagement, resilience, and empathy), job demands to burnout symptoms and burnout might be highly strategic to frame specific theoretical hypotheses for further in-depth research and orient organizations supporting HCWs. Research aimed at describing these associations could be particularly required as the COVID-19 pandemic might have triggered unusual relationships between personal resources and job demand perception with burnout (24). A recent meta-analysis revealed that sex-related differences in burnout should be in-depth considered in empirical research on burnout as females seemed to report higher levels of emotional exhaustion than males, and males higher levels of depersonalization (25). For these reasons, this study sought to describe sex -related differences in burnout and its determinants among HCWs during the first pandemic wave of COVID-19 in Italy.

Methods

Design

This study is part of a larger international (Italy and Brasil) research project (protocol "COPE", approved by the Institutional Review Board of the Catholic University of Milan) to specifically identify sex-related differences in burnout and its determinants among HCWs in Italy during the first pandemic wave of COVID-19 in Italy (April-May 2020). The study had an observational design, collecting data cross-sectionally and via web-survey. The 'STrengthening the Reporting of OBservational studies in Epidemiology' (STROBE) checklist for cross-sectional studies was used to guide the study's reporting (see Supplementary file 1).

Procedure

A web-based survey was created in March 2020, during phase one of the COVID-19 outbreak in Italy, and was disseminated using the online platform Qualtrics® in April and May, which were the months of the first epidemic peak of the COVID-19 outbreak in Italy. The survey was distributed by email and social network invitations and by asking medical directors of several healthcare facilities to disseminate further the invitation to participate in the study using their internal networks (emails). This approach was consistent with the snowball sampling method (26). Once participants accepted to participate in the study, the online form contained information regarding the study aims, data management policy, and publication policy. Thus, respondents had to fill initially a self-assessment check of eligibility (inclusion criteria were being employed as HCW and speak/read fluently Italian) before proceeding with the measurements regarding burnout and its determinants. An online consent form was requested to be filled, and an opt-out link was available for HCWs who were not willing to proceed with the data collection.

Study subjects

Table 1 shows the participants' characteristics and the comparisons between sexes (males = 133

Table 1. Sociodemographic and professional characteristics

	Males (N=133)		Females (N=399)		*p*
	No.	%	No.	%	
Nationality					
Italy	128	96.2	384	96.2	0.172
Other	5	3.8	15	3.8	
Marital Status					
Unmarried	44	33.1	176	44.1	0.025
Married	89	66.9	223	55.9	
Siblings					
Yes	75	56.4	168	42.1	0.004
Family caregiver					
Yes	16	12	68	17	0.170
Suffering chronic condition					
Yes	27	20.3	76	19.3	0.751
Profession					
Physician	43	32.3	63	15.8	<0.001
Nurse	69	51.9	258	64.7	
Allied health professionals	21	15.8	78	19.5	
Provenance (first wave)					
Red zone	100	75.2	317	79.4	0.301
Other zones (northern It)	33	24.8	82	20.6	
Age					
Years	42.94*	11.55**	40.43*	10.97**	0.025
Work experience					
Years (mean; SD)	17.13*	11.96**	15.90*	11.97**	0.313

*Mean; **SD

HCWs; females = 399 HCWs). The majority of HCWs in both sub-samples were Italians. Rates of married HCWs and the presence of at least one child were reported slightly higher among males (respectively: 66.9% *vs*. 55.9%, P=0.025; 56.5% *vs*. 42.1%, P=0.004). In both sexes, roughly two HCWs out of ten reported assisting a relative as a family caregiver (P=0.174), and two participants out of ten reported having a chronic disease (P=0.751). Rates of nurses were higher among female HCWs than male HCWs (P<0.001). No differences were detected considering respondents from red zones who represented more than 75% of HCWs in both sexes (P=0.301). Female HCWs were slightly younger than male HCWs [40.43(±10.97) vs. 42.94(±11.55) years; P=0.025], even if no differences were reported in years of work experience (P=0.313).

Measurements

This study comprised two main sections. The first section included socio-demographic and professional data, and the second included self-report measurements of burnout and its possible determinants.

Socio-demographic and professional data were nationality (Italian vs. other), marital status (unmarried vs. married), the presence of siblings (yes vs. no), the need to act as a family caregiver for at least one frail relative (yes vs. no), the presence of chronic disease (yes vs. no), profession (physicians, nurses, allied health professionals), residence (red zones vs. non-red zones), and work experience (years).

The burnout was assessed using the Maslach Burnout Inventory, Italian version (MBI) (27). As per previous research regarding sex-related differences in burnout (25), we used as outcomes the two sub-scales of the MBI for measuring emotional exhaustion and depersonalization. Both sub-scales asked HCWs to rate their feelings using a 7-points-Likert scale, ranging from never having those feelings to having those feelings a few times a week. Emotional exhaustion included nine items, depersonalization comprised five items; both sub-scales previously showed high internal consistency (27). We also considered the levels of personal accomplishment (7 items) in both sexes; this sub-scale previously showed evidence of validity and reliability as well (27).

To assess burnout's self-report determinants, we considered the JD-R model as a framework for developing ad hoc items for measuring job demands, job resources. The JD-R model considers the need to measure constructs that theoretically could modulate the strengths of associations from job demands and job resources to burnout (14, 17). The selection of these distinct constructs from job demands and job resources was based on previous research (17, 28, 29), and we considered the following constructs: orientation to patient engagement, resilience, and empathy (14, 17). In this study, we

needed to develop *ad hoc* self-report measures for assessing job demands, job resources, and HCWs' orientation to engagement, as no tools were available in the literature specifically focuses on the COVID-19 challenges. In contrast, valid and reliable self-report scales were available for assessing resilience (30) and empathy (31), and both the constructs did not require adaptations to increase their fit with the COVID-19 pandemic challenges due to their theoretical adaptation to every stressful situation was clear enough, even without the need of presenting contextual situations.

Empathy was measured using an adapted version of the Jefferson Scale of Empathy (JSE), comprising 20 items to measure empathy in healthcare contexts (31, 32). The JSE has a three-factor solution underpinning its scoring to determine perspective-taking (ten items), compassionate care (eight items), and standing in the patient's shoes (two items). Each item has to be answered on a seven-point Likert scale. The resilience was measured using the Brief Resilience Scale (BRS) for evaluating an HCW's ability to cope successfully despite substantial adversity (30); it encompasses six items showing mono-dimensionality (30).

The self-report measures for assessing job demands, job resources, and HCWs' orientation to engagement were developed considering the literature about stress and burnout in previous infectious disease pandemics (9, 10) and following methodological recommendations to develop *ad hoc* self-report measures (33). These scales were developed using a five-point Likert scale for answering each item.

The scale of job demands (20 items) showed adequate evidence of validity (dimensionality) and reliability considering a four-factor dimensionality: $\chi^2_{(166)}$ = 365.226, p < 0.001; χ^2/df=2.2; RMSEA = 0.066, 90% CI [0.057–0.075]; CFI = 0.908; TLI = 0.895; and SRMR = 0.069 (see data analysis paragraph). The four dimensions of job demands were labeled as interference (5 items), emotional demands (4 items), uncertainty (4 items), and risk perception (7 items). More details regarding the items' wording and the factor loadings are shown in the supplemeary file.

The scale of job resources (10 items) showed adequate evidence of validity if we consider a two-fact solution to explain its latent structure: $\chi^2_{(185)}$ = 282.820, p < 0.001; χ^2/df=1.5; RMSEA = 0.045, 90% CI [0.034–0.056]; CFI = 0.955; TLI = 0.927; and SRMR = 0.032 (see data analysis paragraph). The two dimensions of job resources were labeled as organization emotional support (5 items) and organizational orientation towards patient engagement (5 items). More details regarding the items' wording and the factor loadings are shown in the supplementary file.

The scale of HCWs' orientation to engagement was developed considering published frameworks to conceptualize items and theoretical dimensionality (28, 29). It comprised of 12 items and its conceptualized three-factor dimensionality was confirmed by the preliminary analysis of this study: $\chi^2_{(33)}$ = 62.269, p < 0.001; χ^2/df=1.9; RMSEA = 0.059, 90% CI [0.036–0.081]; CFI = 0.951; TLI = 0.903; and SRMR = 0.035 (see data analysis paragraph). The three domains were labeled as: relationships as a value (6 items), engagement as a barrier [to adequately perform working tasks] (3 items), orientation to empowerment (3 items). More details regarding the items' wording and the factor loadings are shown in the supplementary file.

Statistical analysis

Data were preliminarily checked for possible missing information, errors, or outliers by analyzing frequency distribution. Quantitative variables were initially assessed for normality using skewness and kurtosis evaluation, followed by the Kolmogorov–Smirnov test, and synthesized using mean (±standard deviation, SD) if appropriate (normally-distributed variables). Numbers and percentages have been employed for summarizing categorical variables. Missing values were managed using the pairwise deletion: this procedure cannot include a specific variable when it had a missing value, but it can use the case when analyzing other variables with non-missing values.

As preliminary analyses, we provided evidence of validity for each *ad hoc* developed scale (see measurements), i.e., job demands, job resources, and HCWs' orientation to patient engagement. We em-

ployed exploratory factor analysis (EFA) models by extracting the number of latent factors considering the analysis of the eigenvalues, the scree test, and the adopted literature's framework to develop the scales (9, 10, 28, 29). The models were run using a robust maximum likelihood estimator (MRL), and an oblique rotation (Geomin) was adopted to maximize the interpretation of the relationships from latent factors to items. We further considered the following fit indices to evaluate each model fit to data: χ^2 and χ^2/degrees of freedom (df); the comparative fit index (CFI) (values >0.90 indicated a good fit); the root mean square error of approximation (RMSEA) (values <0.06 indicated a good fit); the standardized root mean square residual (SRMR) (values <0.08 indicated a good fit). Accordingly, the most suitable factor solution for the scale of job demands showed four factors, the most plausible factor solution for the scale of job resources showed two factors, and orientation to patient engagement showed a three-factor solution. Although this study's focus was not related to providing psychometric evidence of newly developed tools, the methodological validation of *ad hoc* developed scales could reduce the study's measurement bias; for this reason, the fit of these models are reported in the measurement section. These preliminary analyses were run in Mplus 8.1.

A comparison of the socio-demographic and professional data, and the self-report measures, was performed between males and females. According to the nature of each variable, the comparison was performed using the χ^2 test (or Fisher exact test when appropriate) and the Student's t-test. These comparisons were also adopted to explore which possible determinant of burnout had to be included in regression analyses by considering significant differences and theoretical determinants to select the regression models' independent variables.

When evaluating the relationship between symptoms of burnout (emotional exhaustion and depersonalization) with other outcomes (e.g., health-related outcomes), the ideal approach is given by considering the measurements of the symptoms as continuous data. However, a suggested practical approach to highlight associations between theoretical determinants with symptoms of burnout and overall burnout is to report categorized results separately using established definitions of specifically described for each context (e.g., high cutoff scores versus lower scores) for each domain and the overall burnout assessment, even if this approach is not standard in managing data derived from the MBI (18). Thus, considering that previous research suggested cutoffs for identifying high emotional exhaustion (scores≥24) and depersonalization (scores≥9) in the Italian context (34), we employed these cutoffs for dichotomizing the two dependent variables. Although this approach is not included in the recent version of the MBI manual, it is supported by Maslach for those cases where dichotomizing symptoms of burnout and the overall burnout might enhance the interpretability of the association between predictors and burnout, as an individual may be considered clinically burned out when a high emotional exhaustion score is present in combination with either a high depersonalization score or a low personal accomplishment score (18). For this reason, a variable labelled as overall burnout was also computed by summing emotional exhaustion and depersonalization scores and subtracting four minus personal accomplishment (18). The obtained overall score was dichotomized in high burnout levels vs moderate/low levels following the normative published statistics available in the first edition of the Maslach Burnout Inventory manual (35). Then, separate logistic regression (LR) models were employed in male and female sub-samples to explore associations from determinants to dependent variables (emotional exhaustion, depersonalization, and burnout). Statistical significance was evaluated using Wald's χ^2 and likelihood ratio test, and the goodness-of-fit measures were the omnibus test (χ^2), the Hosmer–Lemeshow test, and the analysis of pseudo-R^2 of Nagelkerke. The determinants of each model were entered simultaneously into the equation. The personal accomplishment was not included in the regression analyses as a determinant due to it might theoretically act as a determinant (e.g., higher personal accomplishment might determine lower emotional exhaustion and depersonalization) and as a consequence (low lower emotional exhaustion and depersonalization might trigger higher personal accomplishment). Associations were reported as adjusted odds ratio (OR) and

95% confidence interval (CI). To corroborate the differences in the associations from determinants to dependent variables between males and females, we employed three LR models (one for each dependent variable) on the overall sample, testing whether sex modified the association between any independent and dependent variables, including interactions between sex and the independent variables. All the tests had a two-tailed null hypothesis with type I error = 5%. Statistics were run using IBM SPSS® Statistics for Windows version 22 (IBM Corp., Armonk, NY, USA) and the add-in "R essentials for Statistics" for SPSS.

Results

The scores of job demands, job resources, and orientation to patient engagement are reported in Table 2. In the job demands scale, female HCWs had significantly higher mean scores for emotional demands [mean(±SD) = 4.93 (±0.95) *vs.* mean(±SD) = 4.56 (±1.14); P<0.001], uncertainty [mean(±SD) = 4.26 (±1.08) *vs.* mean(±SD) = 3.77 (±1.34); P<0.001], and job demands total mean scores [mean(±SD) = 4.40 (±0.79) *vs.* mean(±SD) = 4.11 (±0.90); P<0.001]. No differences were detected in the mean scores of job resources. In the orientation to patient engagement, no differences were found in the sub-scales of relationship as a value (P=0.189) and empowerment (P=0.664); besides, the perception of engagement as a barrier to adequately perform working tasks was higher in the descriptive statistics in male HCWs [2.94 (±1.13) *vs.* 2.72 (±1.18); P=0.054] even if the inferential test was borderline.

The mean (±SD) scores of emotional exhaustion, depersonalization, and personal accomplishment are described in Table 3. Although the overall rates of burnout did not differ between sexes (almost 3 HCWs out of ten reported high burnout; P=0.571), emotional exhaustion mean scores were higher in female HCWs [mean(±SD) = 23.42 (±11.83) *vs.* mean(±SD) = 19.96 (±12.57); P<0.001], and depersonalization mean scores were higher in male

Table 2. Job demands, resources, and engagement between males and females

	Males		Females		*p*
	mean	SD	mean	SD	
Job demands					
Interference	4.04	1.36	4.28	1.31	0.079
Emotional demands	4.56	1.14	4.93	0.95	<0.001
Uncertainty	3.77	1.34	4.26	1.08	<0.001
Risk perception	4.10	1.01	4.30	0.98	0.054
Total	4.11	0.90	4.40	0.79	<0.001
Job resources					
Organisation emotional support	4.05	1.31	4.14	1.18	0.499
Organisational orientation towards engagement	3.70	1.36	3.77	1.31	0.611
Total	3.91	1.23	3.99	1.13	0.512
Orientation to Engagement					
Relationships	4.74	0.75	4.83	0.73	0.189
Engagement as a barrier	2.94	1.13	2.72	1.18	0.054
Empowerment	3.60	1.30	3.65	1.32	0.664

Table 3. Burnout between males and females

	Males		Females		P
	mean	SD	mean	SD	
Burnout (score)					
Emotional Exhaustion (EE)	19.96	12.57	23.42	11.83	0.005
Depersonalization (DP)	6.93	5.99	5.49	5.76	0.017
Personal Accomplishment (PA)	38.32	7.37	37.59	7.61	0.341
	No.	%	No.	%	
Emotional exhaustion					
High	56	42.10	173.00	43.40	
Moderate	32	24.10	112.00	28.10	0.014
Low	45	33.80	114.00	28.60	
Depersonalisation					
High	46	34.60	100	25.1	
Moderate	43	32.30	117	29.3	0.026
Low	11	33.10	182	45.6	
Personal Accomplishment					
High	18	13.50	55	13.8	
Moderate	35	26.30	118	29.6	0.746
Low	80	60.20	226	56.6	
Burnout					
High	33	24.80	109	27.3	0.571

HCWs [mean(±SD) = 6,93 (±5.99) *vs.* mean(±SD) = 5.49 (±5.76); P<0.001]. No differences were reported in the sub-scale of personal accomplishment (P=0.341). The differences between males and females in mean scores of emotional exhaustion and depersonalization were reflected in the variable categorizations (high, moderate, and low levels) using the available normative cutoffs.

Table 4 shows the sex-related differences in determinants of high burnout, high emotional exhaustion, and high depersonalization.

In determining high burnout in male HCWs, each additional point of perspective-taking decreased by 88% the odds of reporting high burnout (OR = 0.123; 95% CI = 0.020–0.740; P = 0.022). Conversely, each additional point of compassionate care increased by roughly nine times the odds of reporting high burnout (OR = 9.646; 95% CI = 1.996–16.610; P = 0.005). Likely, each additional point of resilience increased by roughly four times the odds of reporting high burnout (OR = 4.407; 95% CI = 2.115–16.610; P < 0.001). In determining high burnout in female HCWs, each additional point of perspective-taking decreased by 88% the odds of reporting high burnout (OR = 0.123; 95% CI = 0.020–0.740; P = 0.022). Conversely, each additional point of relationship perceived as a value (orientation to engagement) increased by roughly two times the odds of reporting high burnout (OR = 2.311; 95% CI = 1.536–3.477; P < 0.001). Likely, being a nurse compared to being a physician increased by roughly two times the odds of reporting high burnout (OR = 2.470; 95% CI = 1.325–4.604; P = 0.004). Each additional point of job demands decreased by roughly 69% the odds of reporting high burnout (OR = 0.316; 95% CI = 0.210–0.477; P < 0.001). The model performed on the overall sample, including the interaction of sex in the associations from determinants and high burnout, confirmed that sex interacted with job demands (P=0.010) and perspective-taking (P=0.007) in determining high burnout.

In determining high emotional exhaustion in male HCWs, having sons increased by seven times the odds of reporting high emotional exhaustion (OR = 7.054; 95% CI = 1.920–25.920; P = 0.003). Conversely, each additional point of job demands decreased by 58% the odds of reporting high emotional exhaustion (OR = 0.426; 95%CI = 0.207–0.873; P = 0.020), and each additional point of perspective-taking decreased by 83% the odds of reporting high emotional exhaustion (OR = 0.171; 95% CI = 0.032–0.903; P = 0.038). Each additional point of resilience increased by five times the odds of reporting high emotional exhaustion (OR = 5.220; 95% CI = 2.391–11.395; P < 0.001). In determining high emotional exhaustion in female HCWs, each additional point of job demands decreased by 74% the odds of reporting high emotional exhaustion (OR = 0.256; 95%CI = 0.175–0.374; P < 0.001). Conversely, each additional point of relationship perceived as a value (orientation to engagement) increased by roughly two times the odds of reporting high emotional exhaustion (OR = 1.706; 95% CI = 1.164–2.500; P = 0.006). Likely, being a nurse as compared to being a physician increased by roughly two times the odds of reporting emotional exhaustion (OR = 1.889; 95% CI = 1.026–3.478; P = 0.041). Each additional point of resilience increased by roughly 1,5 times the odds of reporting high emotional exhaustion (OR = 1.556; 95%CI = 1.173–2.063; P = 0.002). The model performed on the overall sample, including the interaction of sex in the associations from determinants and high emotional exhaustion, confirmed that sex interacted with profession (P=0.016), and job demands (P<0.001) in predicting the outcome.

In determining high depersonalization in male HCWs, each additional point of resilience increased by two times the odds of reporting high depersonalization (OR = 2.384; 95% CI = 1.397–4.068; P = 0.001). In determining high depersonalization in female HCWs, each additional point of job demands decreased by 50% the odds of reporting high depersonalization (OR = 0.496; 95% CI = 0.342–0.721; P < 0.001). Conversely, each additional point of compassionate care increased by roughly two times the odds of reporting high depersonalization (OR = 2.095; 95% CI = 1.029–4.262; P = 0.041). Likely, being a nurse compared to being a physician increased by roughly two times the odds of reporting depersonalization (OR = 1.909; 95% CI = 1.032–3.534; P = 0.039). The model performed on the overall sample, including the interaction of sex

Table 4. Sex-related differences in determinants of burnout. emotional exhaustion. and depersonalization

	Males				Females			
High burnout (outcome)								
Independent variables	OR	95%CI		P	OR	95%CI		P
Constant	0.005			0.089	1.150			0.933
Siblings (Yes)	2.36	0.705	7.898	0.163	0.541	0.289	1.012	0.055
Profession (aggregated)				0.453				**0.017**
Physicians	0.997	0.192	5.172	0.997	1.916	0.842	4.362	0.121
Nurses	0.486	0.112	2.104	0.334	**2.47**	**1.325**	**4.604**	**0.004**
Age	1.030	0.972	1.091	0.317	1.007	0.979	1.036	0.634
Job demands (overall score)	0.574	0.268	1.228	0.152	**0.316**	**0.210**	**0.477**	**<0.001**
Relationship (orientation to engagement)	0.834	0.333	2.090	0.698	**2.311**	**1.536**	**3.477**	**<0.001**
Perspective-taking (Empathy)	**0.123**	**0.020**	**0.740**	**0.022**	0.779	0.385	1.576	0.487
Compassionate care (Empathy)	**9.646**	**1.996**	**16.61**	**0.005**	1.276	0.623	2.615	0.505
Standing in the patient's shoes (Empathy)	1.428	0.512	3.985	0.496	1.224	0.705	2.124	0.473
Resilience	**4.407**	**2.155**	**9.010**	**<0.001**	1.103	0.814	1.494	0.528
Model fit	Pseudo- $\chi 2$	d.f.	P	R^2	Pseudo- $\chi 2$	d.f.	P	R^2
Hosmer-Lemeshow test	2.552	8	0.959	0.450	3.145	8	0.925	0.234
High emotional exhaustion (outcome)								
Independent variables	OR	95%CI		P	OR	95%CI		P
Constant	10.585			0.451	34.543			0.027
Siblings (Yes)	**7.054**	**1.920**	**25.92**	**0.003**	0.756	0.427	1.341	0.339
Profession (aggregated)				0.059				**0.021**
Physicians	0.986	0.199	4.887	0.986	0.88	0.402	1.923	0.748
Nurses	0.248	0.058	1.071	0.062	**1.889**	**1.026**	**3.478**	**0.041**
Age	1.006	0.951	1.064	0.831	1.005	0.979	1.031	0.720
Job demands (overall score)	**0.426**	**0.207**	**0.873**	**0.020**	**0.256**	**0.175**	**0.374**	**<0.001**
Relationship (orientation to engagement)	0.925	0.407	2.106	0.853	**1.706**	**1.164**	**2.500**	**0.006**
Perspective-taking (Empathy)	**0.171**	**0.032**	**0.903**	**0.038**	0.728	0.379	1.399	0.341
Compassionate care (Empathy)	3.41	0.751	15.483	0.112	1.027	0.513	2.059	0.939
Standing in the patient's shoes (Empathy)	0.758	0.261	2.204	0.611	0.97	0.565	1.665	0.913
Resilience	**5.22**	**2.391**	**11.395**	**<0.001**	**1.556**	**1.173**	**2.063**	**0.002**
Model fit	Pseudo-$\chi 2$	d.f.	P	R^2	Pseudo-$\chi 2$	d.f.	P	R^2
Hosmer-Lemeshow test	8.885	8	0.352	0.551	13.233	8	0.104	0.296
High depersonalization (outcome)								
Independent variables	OR	95%CI		P	OR	95%CI		P
Constant	0.012			0.081	0.297			0.457
Siblings (Yes)	1.323	0.507	3.452	0.567	0.772	0.416	1.432	0.412
Profession (aggregated)				0.247				0.091
Physicians	1.311	0.357	4.82	0.684	1.261	0.569	2.797	0.568
Nurses	0.562	0.178	1.773	0.326	**1.909**	**1.032**	**3.534**	**0.039**
Age	1.034	0.989	1.081	0.143	1.011	0.983	1.04	0.439
Job demands (overall score)	0.839	0.494	1.427	0.517	**0.496**	**0.342**	**0.721**	**<0.001**
Relationship (orientation to engagement)	0.818	0.394	1.696	0.589	**1.899**	**1.274**	**2.829**	**0.002**
Perspective-taking (Empathy)	0.71	0.194	2.598	0.605	0.543	0.269	1.097	0.089
Compassionate care (Empathy)	2.949	0.887	9.81	0.078	**2.095**	**1.029**	**4.262**	**0.041**
Standing in the patient's shoes (Empathy)	0.763	0.321	1.81	0.539	1.211	0.702	2.087	0.492
Resilience	**2.384**	**1.397**	**4.068**	**0.001**	0.904	0.668	1.221	0.510
Model fit	Pseudo-$\chi 2$	d.f.	P	R^2	Pseudo-$\chi 2$	d.f.	P	R^2
Hosmer-Lemeshow test	12.925	8	0.114	0.238	7.119	8	0.524	0.15

Note: Bold values represent significant associations

in the associations from determinants and high depersonalization, confirmed that sex interacted with compassionate care (P=0.011).

Discussion

We report significant HCWs' sex-related differences in emotional exhaustion rates, depersonalization, and their determinants during the epidemic peak of the first wave of COVID-19 in Italy (April-May 2020). Understanding sex-related differences in the field of burnout studies could be pivotal to plan tailored psychosocial preventive and supportive interventions (16, 24, 36). We found that female HCWs reported higher emotional exhaustion than male HCWs, while males reported greater depersonalization levels. Given that at the beginning of the 2000s, burnout was gendered in the social perception of the phenomenon, due to research often associated burnout as a female experience (11), our findings confirmed that both sexes experienced burnout, but differently: male HCWs tended to reach high burnout levels through depersonalization, while female HCWs tended to reach high burnout levels through emotional exhaustion. These results confirmed previous research and open to several reflections, especially considering the different strengths in the associations from determinants to burnout, emotional exhaustion, and depersonalization between male and female HCWs (25, 37).

In determining burnout, we found relevant differences between sexes: in male HCWs, the perspective-taking (a domain of empathy) was a protective factor, while compassionate care (another domain of empathy) and resilience were risk factors; in females HCWs, the job demands (overall score) was a protective factor, while being a nurse and considering clinician-patient relationships as a value (orientation to engagement) were risk factors. The first reflection is that the predictors were different between sexes in determining burnout. More in-depth, it was surprising and paradoxical that resilience in males and the perception of clinician-patient relationships as a value (orientation to engagement) in females acted as risk factors, in contrast with the current evidence suggesting them as protective factors (30). The role of job demands in decreasing the odds of burnout seemed to be paradoxical as well, considering that job demands usually predict higher burnout (14,38). This association might portray the extraordinary situation of that period where people with higher internal resources (resilience) were more challenged by the situation and developed before people with lower resilience a sense of being burned out, as they were probably overwhelmed by the challenges in facing the unknown disease at that time. The cross-sectional nature of data collection could explain these results, as it is theoretically plausible that people with higher resilience over time recovered from distress earlier than people with low resilience.

In fact, these results represent a specific moment in the life of the enrolled HCWs where these paradoxical effects could reflect the high frustration of HCWs who potentially had abilities to cope with a stressful situation. Besides, they were overwhelmed by the challenges brought by the COVID-19 pandemic, especially in the initial period of uncertainty of every possible way-out strategy. However, further longitudinal studies should confirm this hypothesis by considering the measurement of frustration to test its effects on resilience and orientation to engagement. On the other hand, it was not surprising that female nurses had a greater risk of burnout than previous studies (6, 25). The paradoxical detected effect of job demands in female HCWs could reflect that a higher perception of tasks required to take care of patients (job demands) seemed to increase the likelihood of a self-perception of being useful during the pandemic's initial phase. However, the prolonged experience of job demands without enhanced organizational support can theoretically exacerbate burnout. We do not believe that these observed paradoxical associations "call into question" the theoretically sound traditional relationship between risk factors (e.g., job demands) and burnout, but they likely return a particular situation of the most hectic weeks experienced by HCWs in the clinical contexts. It is plausible that those professionals who were asked to do more in those weeks (higher perception of job demands) had greater satisfaction given by a possible feeling of doing something worthwhile.

Some relevant differences between sexes were also found in relationship to determinants of emo-

tional exhaustion: in male HCWs, having siblings and resilience were risk factors, and job demands and perspective-taking (empathy) were protective factors; in females HCWs, the overall score of job demands was a protective factor, while being a nurse, considering clinician-patient relationships as a value (orientation to engagement), and resilience were risk factors. The presence of siblings in males as a risk factor could reveal a gendered perception of the parental role, identifying males as the protectors of their families and relatives, thus exacerbating emotional exhaustion (39). The other relationships could be explained in line with the reflections mentioned earlier regarding burnout determinants (paradoxical effects of job demands, resilience, and orientation to engagement).

We also found sex-related differences in determining depersonalization: in male HCWs, resilience was a risk factor; in female HCWs, the job demands (overall score) acted protective factors while being a nurse, and compassionate care (empathy) were risk factors. Again, in the specific period where data were collected, job demands had probably delayed the individual-level stress processing temporarily, returning the observed paradoxical effect that a greater perception of job demands was associated with less depersonalization. This association likely does not contradict the theoretically positive association between job demands and burnout symptoms, but it reflects the peculiarity of the most demanding weeks experienced by HCWs in the wards. As per the presented earlier reflections, job demand in females was a constant protective factor, reflecting the possible role of job demand in enhancing the self-perception of being useful during the initial phases of the COVID-19 pandemic.

In this study, empathy showed contradictory predictive performance, as compassionate care (a domain of empathy) was a risk factor of depersonalization in female HCWs, while perspective-taking (another domain of empathy) was a protective factor of burnout and emotional exhaustion in male HCWs. These contradictory results are consistent with previous research (15). In fact, empathy is the ability of HCWs' to sense another person's feelings, identifying, understanding, and communicating another person's feelings from an objective stance (15). In particular, previous research showed that empathy acted as a protective factor of burnout or, on the contrary, in some cases, a risk factor (40, 41). There is room for a solid rationale for explaining both effects: in some cases, low empathy could trigger depersonalization, which is an aspect of burnout syndrome; in other cases, high levels of empathy, especially the compassionate care, could trigger emotional exhaustion as empathy can enhance the compassionate fatigue of HCWs (40–42).

Limitations

This study has several limitations. First, the convenience sample suggests that the inferential analyses have to be generalized with caution. Second, the study used a cross-sectional data collection, and the trajectory over time of the explored associations remain unknown. This limit could explain some paradoxical associations that might be specific to the time point we adopted for data collection. For instance, it is plausible that those professionals who were asked to do more in weeks of the initial answers to the first epidemic wave in Italy had greater satisfaction to their work given by a possible feeling of being useful in that particular situation; it is also plausible that high job demands might have triggered higher levels of burnout symptoms over time; unfortunately, we have collected data only cross-sectionally. Third, some possible confounders (e.g., frustration) were not assessed, and analyses could reflect the lack of control for possible psychological variables acting as confounders. Fourth, the inferential analysis generalization could be undermined as the study was performed in Italy; accordingly, cross-national research is required to overcome this limit. Fifth, the *ad hoc* developed scales could lack in psychometric propriety as they were newly developed, even if a rigorous preliminary psychometric analysis carefully managed this limit. Furthermore, our analyses used dichotomous scores. Although this approach could facilitate the interpretation of the associations between independent variables and outcomes (considering that the associations are reported as ORs), the dichotomization is an implicit limit in the data management as it reduces the available information captured by scores. In this regard,

the adopted cutoffs were based on the research of Sirigatti et al. (34) reporting normative cutoffs for HCWs in the Italian context; however, the available evidence supporting the adequacy of these cutoffs in relationship to their sensitivity and specificity are still limited, and the dichotomization of burnout symptoms is not recommended when it is needed to evaluate the relationship between symptoms of burnout (emotional exhaustion and depersonalization) and other outcomes (e.g., health-related outcomes). In this study, within the perimeter of the limitations brought by dichotomizing continuous data, the dichotomizing has been considering suitable for simplifying the reporting of the associations from theoretical determinants to symptoms of burnout and overall burnout by using ORs. For this reason, the reported associations are intended to support some insights and hypotheses for future in-depth research and results have to be generalized with high caution and referred only to the period of data collection. In other words, consistently with other studies, job demands are expected to be positively associated with burnout symptoms, and personal resources (e.g., resilience) are expected to be negatively associated with burnout. Finally, other possible influencing variables describing work conditions were not collected in this study, such as the provided training and resources; having these variables in future studies could allow researchers to perform multi-level analyses for describing organizational features that can influence an individual's level of stress and burnout.

Conclusions

This study revealed that male HCWs during the initial phase of the COVID-19 pandemic had higher depersonalization levels than female HCWs. Conversely, female HCWs reported greater emotional exhaustion rates, and female nurses were the most exposed to the likelihood of reporting emotional exhaustion. Some paradoxical effects in determining burnout, emotional exhaustion, and depersonalization were found in males and females regarding the role of job demands, resilience, and orientation to engagement. These effects could reflect the extraordinary impact of the COVID-19 on HCWs' mental health: more resilient individuals were more consciously overwhelmed by the challenges of COVID-19, thus reporting higher scores of emotional exhaustion and burnout as an individual contextual response to face unprecedented challenges. Future research should investigate these associations using longitudinal designs.

Currently, we have to consider that the strong mandate to protect and promote HCWs' mental health and wellbeing, even more so in times of health emergencies, could be strategic for achieving positive performance at individual and organizational levels. The attention toward HCWs' mental health could reflect a concrete strategy for improving patients' health quality of care. In such context, our findings are of fundamental importance to plan, implement and monitor interventions to keep into account the possible sex-related differences in expressing burnout: male HCWs should be sustained to prevent and manage depersonalization primarily, female HCWs should be primarily sustained to prevent and manage emotional exhaustion.

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Supplementary file

Job demands – Exploratory factor analysis (MLR estimator, geomin rotation)

		Interference (McDonald's omega = 0.697)	**Emotional demands** (McDonald's omega = 0.717)	**Uncertainty** (McDonald's omega = 0.620)	**Risk perception** (McDonald's omega = 0.701)
1	My work rates have increased significantly	**0.833**	0.071	-0.069	0.013
2	I spend more hours at work than I should	**0.808**	-0.055	0.006	0.003
3	The number of patients I care for on a daily basis has increased	**0.632**	0.171	-0.106	0.011
4	I spend so much energy on work that my private life is being affected	**0.772**	0.241	0.083	0.029
5	Since the Covid-19 emergency began, I am no longer able to spend enough time with my loved ones	**0.654**	0.057	0.027	0.204
6	My work does not allow me to enjoy time with family life	-0.109	**0.759**	-0.134	0.175
7	The Covid-19 emergency forces me to deal with emotionally difficult situations	0.033	**0.748**	0.086	-0.036
8	The Covid-19 emergency puts me in more frequent contact with the suffering of other people	0.063	**0.670**	-0.036	-0.047
9	The Covid-19 emergency puts me in the situation of having to make difficult decisions in my work	-0.032	0.302	**0.711**	0.224
10	I often feel compelled to hide my emotions while I work	0.012	**0.698**	0.287	0.152
11	In my job, I often have to do things that I don't want to do	-0.256	0.207	**0.553**	0.210
12	I find it hard to tolerate the unpredictability of the emergency situation linked to Covid-19	0.053	-0.790	**0.867**	-0.013
13	It is difficult to know if my efforts are beneficial for the health of patients	0.007	0.079	**0.814**	-0.009
14	The uncertainty in the patient care with Covid-19 makes me uneasy	0.033	0.087	0.158	**0.362**
15	My job is putting me at serious risk	0.135	-0.110	0.167	**0.852**
16	The health risk I am taking from my job is unacceptable	0.121	0.097	-0.038	**0.783**
17	Accepting the risk of contracting COVID-19 is part of my job	0.121	0.097	-0.038	**0.351**
18	I don't feel safe for my health when I go to work	0.242	-0.003	0.140	**0.641**
19	People close to me are at risk of contracting COVID-19 because of my work	0.052	0.111	0.050	**0.573**
20	People close to me are worried about my health	0.161	-0.005	0.074	**0.477**

Note: Bold values showed a coefficient higher than |0.35|. Estimates were reported as standardized coefficients (STDYX). The model shown adeguate fit to the sample statistics: $\chi 2(166) = 365.226$, $p < 0.001$; $\chi 2/df=2.2$; RMSEA = 0.066, 90% CI [0.057–0.075]; CFI = 0.908; TLI = 0.895; and SRMR = 0.069

Job resources – Exploratory factor analysis (MLR estimator, geomin rotation)

		Organization emotional support (McDonald's omega = 0.781)	**Organizational orientation towards patient engagement** (McDonald's omega = 0.802)
1	When I'm at work, I don't feel alone	**0.431**	0.141
2	When I am at work, I know I can share what worries me with my colleagues	**0352**	0.201
3	I am sure I will receive help and support from my colleagues in case of need	**0.722**	0.248
4	I am sure to get help and support from my superiors in case of need	**0.767**	0.085
5	I feel part of the group in which I work	**0.756**	0.241
6	My organization has in its mission the centrality of the patient even in emergency situations	0.210	**0.803**
7	My organization has activated psychological support initiatives for patients even at a distance	0.287	**0.665**
8	The team of professionals in which I work is oriented towards the centrality of the patient	0.112	**0.822**
9	My organization provides for the use of support for making therapeutic decisions for patients ("decision aids")	0.050	**0.606**
10	My organization provides specific training for healthcare professionals on the issues of patient involvement and patient-centred medicine	0.144	**0.661**

Note: Bold values showed a coefficient higher than |0.35|. Estimates were reported as standardized coefficients (STDYX). The model shown adeguate fit to the sample statistics: $\chi 2(185) = 282.820$, $p < 0.001$; $\chi 2/df=1.5$; RMSEA = 0.045, 90% CI [0.034–0.056]; CFI = 0.955; TLI = 0.927; and SRMR = 0.032

HCWs' orientation to engagement – Exploratory factor analysis (MLR estimator, geomin rotation)

		Relationships as a value (McDonald's omega = 0.796)	**Engagement as a barrier [to adequately perform working tasks]** (McDonald's omega = 0.816)	**Orientation to empowerment** (McDonald's omega = 0.755)
1	The active role of the patient in preventing or mitigating symptoms related to COVID-19 is crucial	**0.526**	0.216	-0.126
2	Despite the current situation, I can find alternative ways to relate to my patients	**0.709**	-0.013	0.169
3	Despite the current situation, I am able to build a relationship of trust with my patients	**0.801**	0.008	0.318
4	In this emergency situation, the alliance with the patient is a fundamental element for the management of care	**0.652**	-0.048	0.084
5	In this emergency situation, involving the patient in therapeutic decisions is an obstacle to the success of the treatment	-0.003	**0.679**	0.100
6	In this emergency situation, giving voice to patients' expectations is more of a hindrance than a help in the care process	-0.222	**0.647**	0.004
7	In this emergency situation, family members are often an obstacle to the care process	-0.191	**0.350**	0.223
8	In this emergency situation, it is important to empower patients and family members to share doubts or questions even if they are not explicitly asked	**0.504**	-0.014	0.025
9	In this emergency situation, patients and family members must be able to determine when to contact the healthcare professional and when they can manage their health independently	**0.402**	0.217	-0.013
10	In this emergency situation, the healthcare professional is the expert, and the patient must simply follow the instructions provided	-0.123	0.102	**-0.460**
11	In this emergency situation, it is risky to consider the patient's values in making decisions about the path of care	0.014	0.261	**-0.681**
12	In this emergency situation, it is risky to consider the values of family members in making decisions about the care path	-0.073	-0.009	**-0.937**

Note: Bold values showed a coefficient higher than |0.35|. Estimates were reported as standardized coefficients (STDYX). The model shown adeguate fit to the sample statistics $\chi^2_{(33)} = 62.269$, $p < 0.001$; $\chi^2/df=1.9$; RMSEA = 0.059, 90% CI [0.036–0.081]; CFI = 0.951; TLI = 0.903; and SRMR = 0.035

Correlations

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Age (1)	1															
Sex (2)	-.097*	1														
Siblings (3)	.552**	-.124**	1													
Profession (4)	-0.021	.142**	0.019	1												
JD_Overall (5)	-.107*	.152**	-0.016	0.058												
Relationships as a value (6)	-.087*	0.057	-.142**	.124**	0.018	1										
Engagement as a barrier (7)	0.027	-0.083	-0.013	.091*	.088*	-.203**	1									
Orientation to empowerment (8)	-.102*	0.019	0.004	-.139**	-0.028	.119**	-.522**	1								
Organization emotional support (JR) (9)	-0.023	0.029	-0.067	0.042	-.160**	.166**	-0.037	-.094*	1							
Perspective taking (10)	0.059	0.075	0.012	-0.006	.101*	.472**	-.297**	.269**	0.081	1						
Compassionate care (11)	0.028	.105*	-0.015	0.015	.092*	.498**	-.264**	.238**	0.062	.790**	1					
Walking in patients shoes (12)	0.037	0.068	-0.031	-0.021	0.039	.466**	-.192**	.145**	0.058	.649**	.714**	1				
Resiliance (13)	0.019	-.181**	-0.011	-.086*	-.279**	0.081	-0.065	0.058	.170**	0.019	0.023	0.047	1			
Emotional exhaustion (14)	-0.023	.124**	0.005	0.018	.467**	-0.072	0.046	-0.054	-.219**	0.054	0.034	0.029	-.368**	1		
Deporsonalization (15)	-.125**	-.107*	-0.061	-0.014	.209**	-.225**	.205**	-.107*	-.219**	-.145**	-.212**	-.190**	-.131**	.511**	1	
Personal accomplishment (16)	.118**	-0.041	0.028	-0.037	-0.04	.309**	-.107*	0.036	.209**	.248**	.296**	.342**	.190**	-.237**	-.344**	1