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Stress impact of COVID-19 in nurse managers

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ABSTRACT

Background: The COVID-19 pandemic has directly affected specially nurses, not only those on the front lines but also nurse managers.

Aims: To assess and compare stress levels of nurse managers before and during the pandemic, and to identify predictive factors.

Method: Cross-sectional studies were carried out in two moments, before and during pandemic. 102 manager nurses were recruited before the sanitary crisis (2018) and 87 during the health crisis (2020). Perceived stress was measured with the Perceived Stress Scale-14 and quality of professional life, job demands, motivation and managerial support were assessed with the Professional Quality of Life Questionnaire. Socio-demographic and job-related variables were also analysed. Statistical analysis was performed using student's t-test, correlations and multiple regression analysis.

Results: The majority of nurse managers were women, married, who worked the morning shift. 78.2% managed nursing personnel who worked with COVID patients. They suffered a significant increase in both job demands and perceived stress level in the pandemic. Job demands, working in shifts morning, being young and being unmotivated were predictors of perceived stress level according to multiple linear regression analysis.

Conclusion: Perceived stress was greatest during the COVID-19 pandemic. Both, before and during the pandemic, job demands are central predictors of nurse managers' general perceived stress. It is necessary to adapt the workplace to personal characteristics of the nurse manager and increase actions to enhance their motivation and reduce their job demands to prevent stress.

Introduction

The COVID-19 pandemic has caused an unprecedented impact around the world, placing extraordinary demands on health systems [1]. Spain is one of the most affected countries [2].

In Spain, at the beginning of the pandemic, the number of patients increased enormously in a few days. Many of them required hospitalization and, in a high proportion, ICU beds. In April–June 2020, approximately a third of hospital beds were occupied by COVID patients. At the time of the study, July 2020, the number of patients had decreased, strict confinement was ending, but hospitals

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still had 25% of beds occupied by COVID patients.

To face this pandemic, hospitals underwent a profound process of transformation in a few days. These changes were accompanied by the scarcity of resources, both in health professionals and in material resources, caused by uncontrolled contagion [3].

Previous studies on the SARS and Ebola epidemics show that the onset of a sudden and life-threatening illness could put extraordinary pressure on healthcare professionals [4,5]. Also, the desire of health workers to alleviate the suffering of patients may exceed their capacity in certain situations, which can cause them to experience negative emotions [6].

When people face with the pandemic uncertainty and unpredictability, they experience higher levels of fear and anxiety, which activate their body's response to stress [7]. In all health crisis situations, excessive workloads, together with the amount of time nurses spend with their patients and their proximity makes them the group of health workers who has experienced the highest levels of stress [8]. Undoubtedly, the level of stress increases with the duration of the pandemic [9]. Under this background, nurse managers play a critical role in the hospital performance, in patient outcomes, in staff satisfaction and empowerment, and in creating a healthy work environment. Therefore, the role of the nurse managers is very stressful [10]. During this pandemic, to their usual work routine, they have had the additional task of taking care of their staff and their psycho-emotional health [11,12]. Therefore, nurse managers have been assigned the burden of handling the crisis not only operationally, but also mentally, emotionally, and even ethically [13].

Persistent exposure to stress can affect the health of nurses and nurse managers and is associated with fatigue, emotional exhaustion, job dissatisfaction, intention to change, and poor mental [14]. Having high levels of stress negatively affects the functions and clinical decision-making processes of the nurses, which also put the safety of patients at risk [15]. In addition, there are other unwanted effects such as low patient satisfaction and a high probability of errors on the part of the nurse [16]. Therefore, assessing the stress level of nurses providing care during the COVID-19 pandemic and knowing the work factors on which it depends becomes an important issue to address [17].

So far, most studies have focused on front-line nurses in direct contact with COVID patients. Research on nurse managers supervising front-line nurses is practically non-existent [12,18]. However, one might think that nurse managers have also suffered the same or even greater psychological health consequences as front-line nurses. In addition to experiencing the suffering that COVID has caused in patients and their families, and in the nurses they supervise, they have the responsibility to obtain enough human and material resources to be able to face this pandemic.

Since the beginning of 2020, the scientific literature on stress and the effects it has on health professionals has been extensive, with special attention to the front-line nurse, but to our knowledge, few studies address this topic, focusing most of them on front-line nurses and not on nurse managers. It is necessary to know how nurse managers have been affected by the pandemic in order to respond effectively to the challenges that have arisen in hospitals. Given the importance of the role of the nurse manager and the stress associated with it, it is necessary to identify the personal and work factors that increase stress, in order to understand the needs of nurse managers and provide them with support [7].

Increasing or improving the quality of work life of nurse managers is a priority action to improve the work environment, staff motivation and health outcomes. High stress levels can affect the role of the nurse manager and this could have consequences for patients, professionals and their health. Identifying predictors of stress will make it possible to develop organizational strategies aimed at mitigating its harmful effects. Therefore, the objective of this study is to assess and compare nurse managers' perceived stress before and during the pandemic and to identify possible sociodemographic and laboral predictive factors.

2. Methodology

2.1. Design

Cross-sectional studies were carried out in two moments, before and during pandemic. Study was carried out among nurse managers of a tertiary hospital. In this hospital was working 102 nurse managers, 1806 registered nurses and 1324 assistant nurses. The study population was the same at both times except for those nurse managers who changed workplace or got retired (11 observations out of 102). The study was conducted in July 2018 and July 2020. The study prior to the pandemic (2018) was carried out at the request of the hospital's nursing department in order to find out about the work environment and quality of professional life of nurse managers.

2.2. Sample population

The only sample selection criterion was to work as a nurse manager in the hospital at the time of the study. All nurse managers (n = 102) were invited to participate from the Hospital's Nursing Directorate.

The minimum required sample size (n = 82) was calculated considering a population size of 102 subjects, with an error margin of 5% and a 95% confidence interval. 102 nurse managers in the pre-pandemic period (2018) and 87 during the pandemic (2020) answered the questionnaire.

2.3. Proceeding

The questionnaires were administered in two times points: July 2018 and July 2020. In both cases, the invitation to participate was sent to the nurse administrator by email. In 2018, the researchers personally distributed the paper format questionnaires to all nurse managers. In 2020, due to the precautions imposed by the pandemic, the link to the online form (google forms) was sent, and a period

of 30 days was established for its completion. On both occasions, an email was sent within 15 days reminding the deadline. At the beginning of the questionnaires, a text was included informing the participants of the objective of the study, as well as that with the delivery of the questionnaire, informed consent was accepted. All those who answered the questionnaire and accepted the informed consent conditions of the form were included in the study. There were no questionnaires with missing data, so all answered questionnaires were valid for inclusion in the study. Anonymity was guaranteed as no personal data was collected that could identify those who decided to participate. This study was approved by Comité de Ética de la Investigación de la Comunidad Autónoma de Aragón: CEICA (C.P. – C.I. PI20/371).

2.4. Variables and measuring instruments

The questionnaire includes the following sociodemographic and work variables: age, sex, marital status, shift (morning/rotating) and years of experience as a nurse manager. The morning shift refers to the shift that takes place on weekdays (from Monday to Friday) from 8 a.m. to 3 p.m. and the same staff is always managed. The rotating shift is carried out by the general nurse managers and includes afternoons, nights, weekends and holidays, being managed various units of the hospital. In the questionnaire sent during the pandemic, the following elements were added: living with a person under 14 years of age (yes/no), living with an elderly person or dependent (yes/no), supervision of professionals who work with COVID patients (yes/no). The quality of professional life, job demands and motivations, and perceived direct support were evaluated with the Perceived Professional Life Quality questionnaire (CVP-35) [19]. The perceived stress level was measured using the Perceived Stress Scale (PSS-14) [20].

The CVP-35 questionnaire is self-administered. It was built based on the demand-control model defined by Karasek [21]. It provides a multidimensional measure of the quality of professional life, with three domains: job demands, work motivation and managerial support. The outcome measurement of the quality of professional life is the answer to a direct question ("I feel my professional quality of life ...") on the mentioned scale. It consists of 35 questions, which are answered on a Likert-type scale from 1 ("nothing/none") to 10 ("many/much"). The reliability of the questionnaire is 0.81 [22]. In this study, Cronbach's alpha value is 0.790 in 2018 and 0.844 in 2020.

The Perceived Stress Scale (PSS-14) [20] has been validated in the Spanish language [23]. The self-administered questionnaire includes 14 items with a Likert-type scale from 0 to 4 points, such that the highest score corresponds to the highest level of stress perceived by the subject during the last month. The total score of the PSS is obtained by first inverting the scores of items 4–7, 9, 10 and 13 and then adding the 14 items, giving a result between 0 and 56. As it is not a diagnostic element, there are no cut-off values, these being those agreed by the researchers. Cronbach's alpha is 0.82 in the adaptation to Spanish [23], the result of the present study being 0.90 in both time periods (2018 and 2020).

2.5. Data analysis

A descriptive analysis of the data, percentages and frequencies was carried out for the sociodemographic and work variables and a mean and standard deviation analysis for the scores of the questionnaires. Chi-square tests were used to compare sociodemographic and work data before and during COVID pandemic. The Kolmogorov–Smirnov test was used to assess the normal distribution of data and Levene's test for the homogeneity of the variances. To analyse whether there were differences in means between the two measurement moments, the Student's t-test for independent groups was used. The magnitude of the effect was calculated with Cohen's d. Pearson's or Spearman correlation was used to analyse whether the variables had a linear association. To study the relationship between confounding factors and the outcome variable a multiple regression analysis was applied. Preliminary tests were conducted to ascertain that a multiple linear regression analysis was a good fit for this research. We confirmed that the data met the regression

Table 1
Socio-demographic and professional characteristics of nurse managers.

Characteristics		Before COVID (2018) N (%)	During COVID (2020) N (%)	p
		82 (80.4)	75 (86.2)	0.334
	Male	20 (19.6)	12 (13.8)	
Age	≤35	5 (4.9)	6 (6.9)	0.104
	36-45	26 (25.5)	33 (37.5)	
	46–55	32 (31.4)	28 (32.2)	
	≥55	39 (38.2)	20 (23)	
Civil status	Single	15 (14.7)	13 (14.9)	0.920
	Married	74 (72.5)	63 (72.4)	
	In couple	5 (4.9)	6 (6.9)	
	Divorced/Separated	6 (5.9)	3 (3.4)	
	Widow	2 (2.0)	2 (2.3)	
Years as supervisor	<5	48 (47.1)	46 (52.9)	0.063
	5–10	16 (15.7)	23 (26.4)	
	10–15	12 (11.8)	6 (6.9)	
	≥ 15	26 (25.5)	12 (13.8)	
Shift	Morning	86 (84.3)	74 (85.1)	1.000
	Rotating	16 (15.7)	13 (14.9)	

assumptions, including a linear relationship between the dependent variable and the independent variables, homoscedasticity of errors, absence of autocorrelation (Durbin-Watson statistic between 1.5 and 2.5), and no multicollinearity (tolerance >0.10, VIF <10). Furthermore, the errors exhibited a normal distribution. We performed stepwise multiple linear regression models to determine the most significant stress predictors. (Criteria: Probability-of-F-entering \leq 0.050, Probability-of-F-removing \geq 0.100). The statistically significance was set at p < 0.05. IBM SPSS Statistics 26 software was used in analyses. This article adheres to the STROBE guidelines for the reporting of observational studies.

3. Results

In 2018, the 102 nurse managers answered the questionnaire (response rate of 100%), and in 2020, 87 out of 102 (response rate of 85.3%).

Table 1 describes the participants' sociodemographic and professional characteristics. Most interviewed were women, married, who worked the morning shift. No significant differences were observed when considering the sociodemographic and work characteristics throughout the study. During the pandemic, 43.7% lived with children (under 14 years of age) and 24.1% with the elderly or dependents. 78.2% managed nursing personnel who worked with COVID patients.

During the pandemic, the job demands increased significantly with a medium effect size (d = 0.400). An increase in the level of perceived stress was also observed with a medium effect size (d = 0.393). No significant changes were observed in quality of life, work motivation and perception of managerial support (Table 2) when comparing the means of the scores obtained before and during the pandemic.

Table 3 shows perceived stress levels before and during COVID by sociodemographic and work variables. Nurse managers working in shifts morning showed a higher level of stress both before and during the pandemic. During the pandemic, management professionals who worked with COVID patients or lived with dependent or elderly people did not show a higher level of stress, however, those who lived with children showed higher stress values (p = 0.027).

It was analysed whether there was a correlation between stress level, age and work variables before and during the pandemic. The level of perceived stress is correlated with the same variables and with similar correlation coefficients in the two analysed moments (Table 4). There is a negative correlation with age (p < 0.001 and p = 0.002) and seniority as a supervisor (p = 0.003 and p = 0.032). Young people with low work experience in management suffer from high levels of stress. Leadership support and motivation are negatively correlated, such that the perception of support and the leadership motivation decrease the stress level. Perceived job demands show a positive correlation with stress (p < 0.001), the greater the job demand, the greater the level of stress.

The regression models confirm that the nurse managers' stress is explained by the job demand, the work motivation, the shift and the age. The variance explained by the model is very similar in the non-pandemic period (adjusted R^2 0.504) or during the pandemic (adjusted R^2 0.479), (Table 5). Job demand is the main stress predictor. Working in shifts morning, being young and being unmotivated were also stress predictors.

4. Discussion

This study has examined the effect that the COVID-19 pandemic has had on nurse managers' stress and the corresponding predictive factors. Our findings show that perceived stress was higher during COVID-19 pandemic and that the main predictor factors were job demands, type of work shift, age, and work motivation.

4.1. Stress in nurse managers before and during pandemic

Nursing is one of the most vulnerable profession to stress and is one of the most impacted during pandemics due to aspects such as exposure to suffering, death of patients and fear of contagion [24,25]. In the case of nurse managers, it should be taken into account the responsibility that the position entails and loneliness in decision-making, with greater relevance in situations such as the current sanitary crisis, where they have had to be present 24/7 for their staff [12]. The data reflect that stress has increased in our sample due to the pandemic situation. Unlike other studies carried out during the initial phases of the pandemic, our results correspond to the month of July 2020, between the peaks of the first and second waves, when in Spain a strict confinement had been left behind and the so-called "new normal" had begun, that is, without mobility restrictions but with preventive health measures (mandatory mask use, social distancing and hand hygiene). If the data had been collected in our hospital during the first peak, the stress levels of nurse

Table 2Effect of the COVID on the quality of work life and the perceived stress.

	Before COVID (2018) Mean (SD)	During COVID (2020) Mean (SD)	p	d	
Quality of Professional Life	6.14 (1.76)	6.25 (1.9)	0.670	_	
Job Demands	7.15 (1.24)	7.61 (1.21)	0.010	0.400	
Motivation	7.98 (0.82)	7.97 (0.77)	0.930	-	
Managerial Support	6.43 (1.39)	6.74 (1.39)	0.122	_	
Stress	23.85 (8.35)	27.07 (8.01)	0.008	0.393	

Table 3Perceived stress before and during COVID by sociodemographic and work variables.

Characteristics		Before COVID (2018) Mean (SD)	p	During COVID (2020) Mean (SD)	p
Sex	Female	24.17 (8.14)	0.370	27.40 (7.83)	0.338
	Male	22.30 (9.10)		25.00 (9.13)	
Civil status	Single	22.80 (10.37)	0.330	24.92 (8.45)	0.842
	Married	24.58 (8.18)		27.46 (7.97)	
	In couple	24.48 (7.30)		28.67 (10.05)	
	Divorced/Separated	17.83 (3.86)		25.67 (3.21)	
	Widow	19.00 (1.41)		26.00 (9.89)	
Shift	Morning	25.03 (8.23)	< 0.001	28.20 (7.88)	0.001
	Rotating	17.19 (5.24)		20.62 (8.01)	
Supervision of professionals who work with COVID patients	Yes			27.24 (8.26)	0.716
	No			26.47 (7.22)	
Live with children	Yes	n/a		29.21 (7.86)	0.027
	No			25.41 (7.80)	
Live with elderly or dependents	Yes	n/a		27.14 (7.84)	0.962
	No			27.05 (8.12)	

n/a: not available.

Table 4
Correlations for stress with age and work variables before and during the COVID.

		Perceived stress Correlation coefficient (p)
Before COVID 2018	Age	-0.335 (<0.001)
	Supervising experience (years)	-0.296 (0.003)
	Quality of Professional Life	-0.502 (<0.001)
	Job demands	0.556 (<0.001)
	Motivation	-0.391 (<0.001)
	Managerial support	-0.463 (<0.001)
During COVID 2020	Age	-0.331 (0.002)
, and the second	Supervising experience (years)	-0.230 (0.032)
	Quality of Professional Life	-0.393 (<0.001)
	Job demands	0.576 (<0.001)
	Motivation	-0.380 (<0.001)
	Managerial support	-0.352 (<0.001)

managers could be higher than those reflected in July 2020, and these levels could be similar with those of first-line nurses in other countries during the first months of the pandemic.

4.2. Sociodemografic factors associated with stress

Stress levels have been even more accentuated in younger nursing supervisors with less experience in the role of nurse managers [7, 25,26]. To manage crisis situations it is very important to have not only adequate training, but also work experience in the position, due to the greater self-confidence that it brings [27].

Although there are no significant sex differences, a higher level of stress is attributed to women, relating it to factors such as the high degree of feminization in the world of health or the social role of women as caregivers [25,28]. According to our results, it has not been observed that living with an elderly or dependent person has influenced the stress level of nurse managers. In the bivariate analysis, an association was observed between living with children during the pandemic and the level of stress. This association is possibly due to the younger age of the nurse managers with children, since living with children was excluded from the regression model.

4.3. Work variables related to stress

There are aspects that have been common to the general population and health professionals and that increase their psychological discomfort and stress levels, such as: fear of getting infected (own or loved ones), physical and psychological exhaustion and insufficient and/or conflicting disease information. According to our results, the high level of stress among nurse managers is correlated with the increase in job demands. In non-pandemic periods, heavy workloads are considered one of the main causes of stress in nurse managers, along with a lack of resources and financial responsibilities [29,30] In the pandemic, the increased stress experienced by nurse supervisors could be due in part to higher job demands. To the usual tasks other aspects are added such as: having a greater span of control (number of professionals in charge), a greater staff turnover and training [9,31], ensure an adequate distribution of personal protective equipment, manage family communication with patients and increase pressure when making decisions [32]. With respect to

Table 5Regression models explaining perceived stress before and during COVID.

MODELS										
Before COVID 2018	Unstandardized Coefficients		Standardized Coefficients			95.0% Confidence Interval for B		Correlations	Collinearity	
	В	Std. Error	Beta	t	p	Lower Bound	Upper Bound	Partial	Tolerance	VIF ^a
Intercept	29.03	8.088		3.589	0.001	12.941	45.119			
Job demands	3.376	0.521	0.511	6.477	< 0.001	2.339	4.413	0.582	0.975	1.026
Motivation	-2.328	0.841	-0.226	-2.767	0.007	-4.002	-0.654	-0.292	0.905	1.105
Shift	-4.235	1.849	-0.19	-2.29	0.025	-7.914	-0.556	-0.245	0.885	1.130
Age	-1.565	0.732	-0.176	-2.139	0.035	-3.021	-0.11	-0.230	0.895	1.117
R2	0.503									
Adjusted R2	0.479									
Std. Error of the Estimate		5.865								
Durbin-Watson	1.899									
Effect size f2	1.09									
Power (1-b err prob)	1.00									
During COVID 2020	Unstanda	rdized	Standard	ized		95.0% Confide	nce Interval for	Correlations	Collinearity	
	Coefficients		Coefficients			В				
	В	Std. Error	Beta	t	p	Lower Bound	Upper Bound	Partial	Tolerance	VIF
Intercept	30.951	7.003		4.420	< 0.001	17.052	44.849			30.951
Job demands	3.383	0.471	0.507	7.178	< 0.001	2.448	4.318	0.589	0.984	1.016
Motivation	-2.488	0.742	-0.246	-3.351	0.001	-3.961	-1.014	-0.322	0.912	1.097
Shift	-5.511	1.657	-0.242	-3.327	0.001	-8.799	-2.223	-0.320	0.929	1.076
Age	-1.681	0.662	-0.185	-2.539	0.013	-2.996	-0.367	-0.250	0.924	1.083
R2	0.523									
Adjusted R2	0.504									
Std. Error of the Estimate		5.784								
Durbin-Watson	1.996									
Effect size f2	0.91									
Power (1-b err prob)	1.00									

^a Variance Inflation Factor.

the work shift, a predictor of stress perceived by nurse managers has been to perform a fixed morning shift (compared to the rotating shift). Nurse supervisors with a fixed morning shift are usually assigned a unit or service. They are responsible for the personnel of that unit and for providing the material and logistical resources necessary for the proper functioning of the unit. The shortage of human resources to cover the drop in the workforce and the lack of material resources in this period, which has caused an increase in the number of health workers infected or who have died from COVID-19 [33], has made it difficult for them to disconnect once finished their working day. In this sense, it must be taken into account that they are in charge of taking care of their colleagues and have had to see how they had to improvise protection material to care for patients [34]. However, those nurse managers who perform a rotating shift, although their work has not been easy either, have a more transversal task, solving the problems that arise at the moment (putting out the fire or patching the situation) and the responsibility or final solution falls on the morning shift supervisor. It is interesting to note that, according to our results, the management of professionals who work with patients with COVID is not a predictor of the stress level. This may suggest that hospitals have been affected fairly uniformly, as all have struggled to obtain enough resources regardless of the type of patient they serve.

Motivation is a factor that has remained high (7.9 out of 10) due to two factors closely linked to the nursing role: resilience and the role as caregiver, both of patients and of their own staff [28]. On the other hand, resilience has been shown to also be negatively related to work demands and stress [35]. Besides, the quality of leadership of nurse managers is related to the resilience of nurses [35]. Therefore, the leadership of their respective units has made possible to direct the potential of the staff, physically and psychologically exhausted, to be able to provide humane and quality care in an unknown and hostile environment such as that of the current pandemic.

The managerial support referred by nurse managers has also subtly increased, without these values being statistically significant. However, it is important to note that in complex management periods such as the current one where decision-making is not always well understood, maintaining the perception of support from nursing administrators indicates that the needs of nurse managers have been taken into account on the part from the facility's nursing department. Nurse managers must understand that in times of crisis, without effective mitigation strategies, stress can paralyze the entire team [13].

4.4. Stress predictor factors

The stress level predictors selected in the regression models have been the same before and during the pandemic. 50% of the variance can be explained by 4 factors, which in order of importance are: job demands, work motivation (as a protective factor), shift and age. This result supports the need to implement both proactive programs to minimize the impact of increased job demands and to improve the skills and competencies of all nurse supervisors, but paying special attention to new and young supervisors, and

contingency plans to proactively provide psychological support to all health professionals [36].

4.5. Limitations and strengths

The main limitation is that the current study has only included one hospital. Therefore, the results may not generalize to the experiences of nursing managers in other hospitals.

The response rate was slightly lower in 2020 than in 2018. Online recruitment and data collection may have contributed to this lower participation, in addition to exhaustion due to the pandemic situation. Due to the two years elapsed between the first and the second measurement, other variables not analysed in the research could have gained prominence, such as the appearance or worsening of diseases in the nurse manager or in their relatives, economics problems, ... that could have affected the results. However, no significant differences were observed when considering the sociodemographic and work characteristics throughout the study.

In addition, because participation in the study was voluntary, it is possible that respondents differed from non-respondents in some significant way. However, the response rate was high (100% and 85.3%), minimizing concerns about the representativeness of the respondents.

Our main strength has been to have data prior to the pandemic in the same group of participants, which allows us to compare the results before and during pandemic. In addition, the research has been focused on nurse managers, health professionals often forgotten in research studies. Finally, the sample comprised the entire population of nurse managers from a tertiary hospital.

4.6. Implications for the nursing practice

Stress associated with the role of nurse managers increases in crisis situations. The results of the current study indicate that hospital managers should support nurse managers by giving them human and material resources, thus reducing the job demands. It is important to adapt the work to the characteristics of the workforce and promote actions that enhance the motivation of managers, because they act as a protective agent against the development of stress. Specific strategies should include action plans oriented to train new personnel and to deal with crisis situations.

Our findings can guide hospital managers to make personal, administrative, and institutional improvements that could provide a reference and inspiration for nurses regarding future public health emergencies.

5. Conclusions

Perceived stress was higher during COVID-19 pandemic. Predictors of perceived stress have been the same regardless of the pandemic situation. Job demands are central predictors of nurse managers' general perceived stress.

In addition to job demands, other factors such as type of work shift, age, and work motivation should be considered when developing strategies to promote healthy work environments.

Ethics statement

Ethical approval was obtained from Comité de Ética de la Investigación de la Comunidad Autónoma de Aragón: CEICA (C.P. – C.I. PI20/371). All participants gave their informed consent when completing the survey.

Author contribution statement

Angel Boned-Galán, Nieves López-Ibort: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Ana Gil-Lacruz: Analyzed and interpreted the data; Wrote the paper.

Ana Gascón-Catalán: Conceived and designed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Data availability statement

Data will be made available on request.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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