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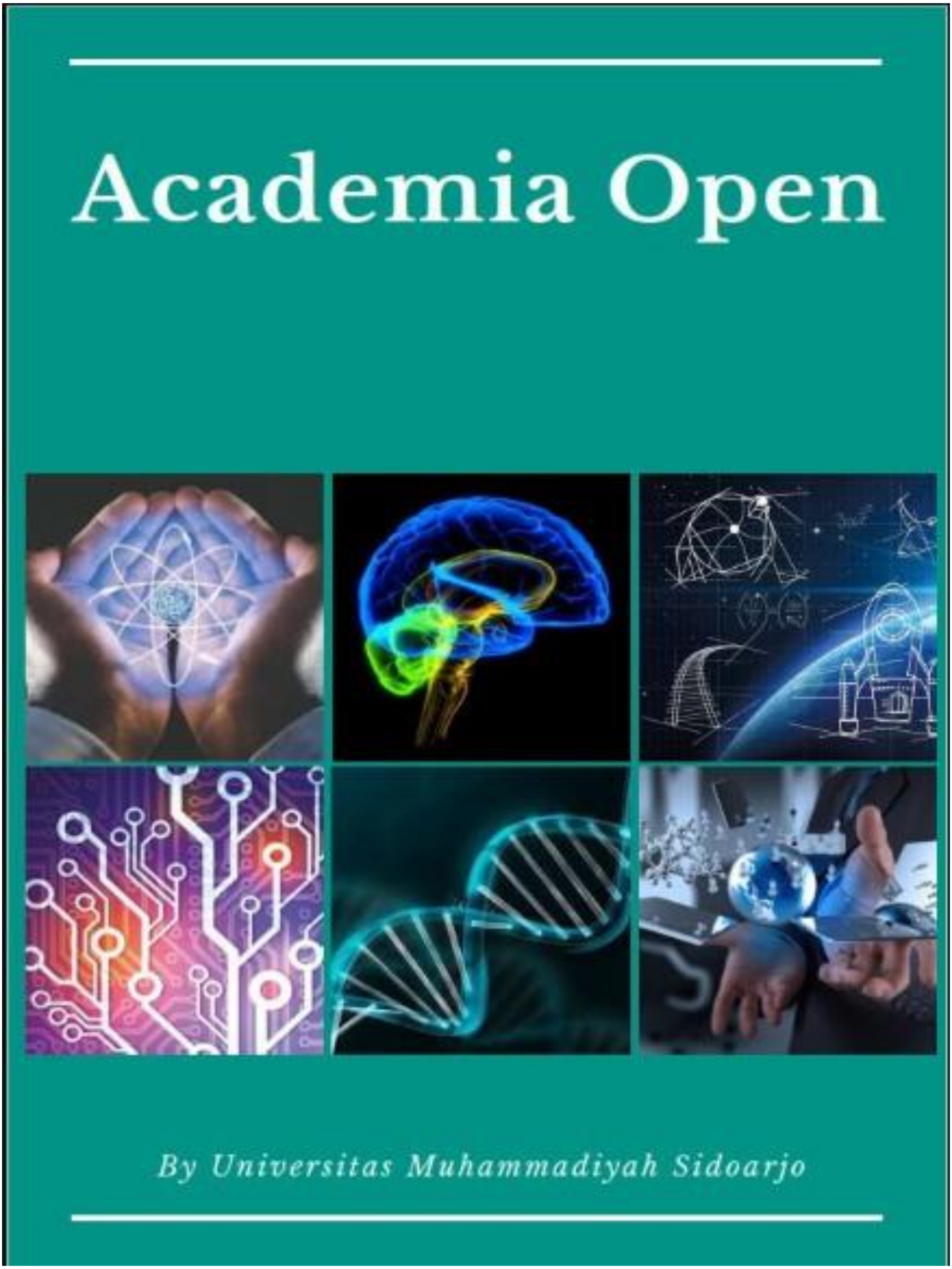

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Physiological Dysregulation and Inflammation in Hospital Shift Workers

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Abstract

General Background Hospital healthcare workers operate under high psychological and physical demands, executing critical patient-care tasks within complex environments. **Specific Background** Managing irregular schedules, continuous shift rotations, and ethical challenges puts these workers at increased risk for chronic health issues. **Knowledge Gap** However, the direct paths linking specific hospital stressors to autonomic and inflammatory system changes remain poorly explained due to a historical lack of objective biological indicators. **Aims** This study examined the relationships between night shift assignments, sleep disturbances, moral distress, and physiological markers of stress in 268 hospital professionals. **Results** The data show that night shift workers have significantly lower heart rate variability (RMSSD: 26.8±11.4 ms) and flattened diurnal cortisol slopes compared to day workers, alongside elevated interleukin-6 levels (3.9±2.2 pg/mL). **Novelty** This study provides fresh, empirical evidence of a dose-response drop in autonomic function over the first seven years of night shift work, while highlighting a unique physiological burden from moral distress. **Implications** These findings demonstrate an urgent need for evidence-based hospital scheduling policies, proactive sleep interventions, and systematic wellness monitoring across all clinical and support roles to protect the healthcare workforce.

Keywords: Healthcare Workers, Shift Work, Heart Rate Variability, Moral Distress, Inflammation

Key Findings Highlights:

Night shift schedules significantly reduce resting heart rate variability and flatten natural diurnal cortisol profiles.

Subjective sleep quality acts as an explicit mediator for nearly half of the relationship between night shifts and autonomic dysfunction.

Elevated moral distress experiences are independently linked to significant increases in systemic pro-inflammatory cytokine levels.

Introduction

Hospital healthcare personnel are the foundation of contemporary healthcare systems. They offer crucial services at every phase of patient care. These individuals work in environments that require them to think a lot manage their emotions work irregular hours and deal with a variety of job hazards including chemicals biological agents physical strain and psychosocial stressors (1).The cumulative impact of these exposures has serious repercussions for the health and welfare of the medical staff. There is currently a severe global shortage of healthcare workers as a result of the COVID-19 pandemic and its aftermath. Understanding the physiological and medical impacts of hospital work has therefore emerged as a critical public health and health system sustainability priority (2). Carers well-being is not just a personal matter it has a big impact on patient safety healthcare quality and population health outcomes. Numerous studies have demonstrated that health issues are more common among hospital employees than in the general population. Cardiovascular disease metabolic disorders musculoskeletal injuries sleep disturbances and mental health conditions like burnout depression and post-traumatic stress disorder are all excessively common in this occupational group (34). The hypothalamic-pituitary-adrenal axis dysfunction autonomic nervous system dysregulation circadian disruption brought on by shift work and persistent low-grade inflammation are some of the suggested mechanisms linking hospital employment to detrimental health effects (5). However there are significant methodological flaws in the current body of evidence. The majority of research has used cross-sectional designs which are unable to identify causal pathways or temporal relationships. Few studies have systematically considered sleep circadian and psychosocial factors that may confuse the discovered connections. Furthermore despite experiencing distinct sets of occupational hazards certain worker subgroups such as environmental services personnel laboratory technicians and administrative staff have not received as much attention in the literature as nurses and doctors (6). There are currently no reliable biological biomarkers for burnout and occupational stress in healthcare populations. According to systematic reviews there is insufficient evidence to support any particular biomarker as a reliable indicator of physiological dysregulation related to the workplace (7). By employing a prospective longitudinal cohort design with repeated physiological and psychological tests over a 24-month period this study seeks to close these significant knowledge gaps. By combining comprehensive evaluations of cardiovascular autonomic function (heart rate variability) neuroendocrine activity (diurnal salivary cortisol profiles) inflammatory biomarkers objective sleep parameters and validated psychometric tools this study aims to outline the course of physiological changes associated with hospital employment. Additionally it identifies modifiable occupational exposures that contribute to negative health outcomes. Examining how various shift work schedules impact individuals differently the impact of sleep disruption and the possibility of reversing physiological changes following work pattern changes are all highly prioritized. By purposefully combining support services staff with clinical staff this study also seeks to generate evidence that represents the whole spectrum of hospital-based workers. The findings are intended to support the development of targeted interventions and evidence-based occupational health policies that will safeguard and enhance the health of those who maintain our healthcare systems.

Methodology

Study Design

The medical and physiological effects of hospital employment on healthcare workers were assessed in this study using a cross-sectional analytical framework. In order to provide an overview of hospital employees health and identify associations between their exposures at work and their health data were gathered once between March and August of 2025. Although cross-sectional studies are not able to prove temporal causation they can be helpful in developing hypotheses about dose-response relationships and identifying high-risk populations for further research or treatment.

Study Setting

The investigation took place at four tertiary care teaching hospitals that were all part of the same academic health sciences institution in a big city. These sites were chosen to show a wide range of clinical settings and patient groups:

- **Site A**: An urban university medical facility with 750 beds that is designated as a Level I trauma center. It has a lot of medical-surgical units, intensive care units (for medical, surgical, cardiac, neurological, and neonatal patients), a busy emergency department, and a lot of perioperative services.
- **Site B:** A 400-bed teaching hospital in the community that offers inpatient services for general medicine, surgery, obstetrics, psychiatry, and paediatrics.
- **Site C**: A specialised cancer center with 250 beds that provides inpatient oncology, bone marrow transplantation, and palliative care.
- **Site D** is a long-term acute care and rehabilitation center with 150 beds.

All of the facilities that are taking part offer services around the clock, with rotational and set shift schedules for both clinical and support staff.

Study Population and Sampling

Target Audience.

Healthcare staff at participating hospitals who had worked there for at least six months made up the target population. Nurses (registered practical assistants and care technicians) medical staff (attending physicians residents and fellows) advanced practice professionals (nurse practitioners and physician assistants) allied health professionals (pharmacists dietitians therapists and social workers) clinical support services staff (environmental services transport unit clerks security) and laboratory personnel (clinical laboratory scientists radiology technologists and sterile processing technicians) are among the job types covered.

Inclusion requirements.

A minimum of eighteen years of age employment at a participating hospital for at least six months an average of twenty hours per week written informed consent completion of physiological assessments and questionnaires and sufficient English proficiency to complete validated survey instruments with translations available where applicable were among the requirements for study participants.

Exclusion criteria.

Current pregnancy active cancer undergoing treatment within the previous six months recent use of systemic corticosteroids major psychiatric disorders with active psychosis and recent acute infections or febrile illnesses were among the criteria used to exclude participants.

Sample Size Calculation and Sampling Strategy.

To guarantee varied representation across important occupational characteristics such as occupation categories (nursing staff 40 percent physician staff 15 percent allied health 20 percent support services 15 percent lab personnel 10 percent) shift types (day shift 50 percent evening shift 10 percent night shift 20 percent rotating shifts 20 percent) and unit acuity (intensive care units 20 percent emergency department 15 percent medical-surgical units 40 percent and outpatient/support areas 25 percent). The purpose of the sample size was to identify meaningful variations in heart rate variability (HRV) among shift work categories. The researchers believed they needed at least 210 participants based on statistical parameters such as a moderate effect size and a 15 percent attrition rate for unusable data. As a result 268 participants were the target enrollment.

Recruitment Processes.

A multimodal approach to recruitment was used over the course of six weeks. Institutional email announcements were distributed via departmental listservs and employee newsletters. All participating facilities had flyers in staff break rooms nurse stations locker rooms and other common areas. There were brief informational presentations during grand rounds shift huddles and unit staff meetings. Clinical educators and department managers were informed about the study and asked to assist in recruiting employees. Interested parties were instructed to visit a safe online screening portal using the Research Electronic Data Capture (REDCap) technology. In addition to gathering basic demographic and occupational data to aid in stratification the portal verified that users fulfilled the eligibility requirements. To schedule a single in-person assessment session a study coordinator contacted qualified participants. The study was completed in a single visit that lasted between ninety and one hundred minutes.

Data Collection Procedures

Assessment Visit Protocol

All evaluations took place in an academic health sciences centers clinical research suite and visits were planned at participant-friendly times such as on weekends and in the evenings. Different shift workers were subject to different protocols: day shift assessments were carried out on non-work days following two consecutive day shifts from 08:00 to 10:00 night shift assessments followed a similar pattern but were scheduled from 14:00 to 16:00 evening and rotating shift assessments were based on the most frequently worked shift over the previous 14 days in accordance with self-reported wake times. Prior to their visits participants were told to abstain from food alcohol and caffeine for predetermined amounts of time. Anthropometric measurements heart rate variability recording saliva sample collection for cortisol profiling dried blood spot collection for biomarkers a self-administered questionnaire and payment distribution were all completed in a predetermined order.

Timing of Assessments Relative to Shift Work

To address the potential confounding effects of recent shift work on physiological parameters, detailed work schedule data were collected via self-report and verified against institutional scheduling records where feasible. The following variables were recorded: number of consecutive shifts worked prior to the assessment day, time elapsed since last shift ended, shift type of most recent shift, and cumulative night shift exposure over the preceding 90 days. These variables were incorporated as covariates in all multivariable analyses.

Variables and Measurement Instruments

Primary Outcome Measures: Physiological Parameters

Resting Heart Rate Variability

Short-term resting heart rate variability was assessed using the Faros 180° device (Bittium Corporation, Oulu, Finland), a validated three-lead electrocardiographic monitor with demonstrated accuracy in field-based research settings. Following a 10-minute acclimatization period in a quiet, temperature-controlled room, a 10-minute continuous electrocardiographic recording was obtained with the participant seated comfortably in an upright position. Participants were instructed to breathe spontaneously, remain still, and refrain from speaking or using electronic devices during the recording period.

Recordings were analyzed using Kubios HRV Premium software (Version 4.0, Kubios Oy, Kuopio, Finland) with automated artifact correction using the threshold-based method and visual inspection by a trained analyst blinded to participant occupational status. The following HRV parameters were derived according to the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology guidelines (7):

- **Time-domain measures:** Standard deviation of normal-to-normal intervals (SDNN), root mean square of successive differences (RMSSD), and percentage of adjacent NN intervals differing by more than 50 ms (pNN50).
- **Frequency-domain measures:** High-frequency power (HF; 0.15–0.40 Hz) reflecting parasympathetic modulation, low-frequency power (LF; 0.04–0.15 Hz), and the LF/HF ratio as an index of sympathovagal balance. Frequency-domain parameters were derived using Fast Fourier Transform with Welch's periodogram method.
- **Non-linear measures:** Poincaré plot indices (SD1, SD2) reflecting short-term and long-term variability, respectively.

Salivary Cortisol

A single salivary cortisol sample was collected at the time of the assessment visit using Salivette® devices (Sarstedt AG, Nümbrecht, Germany). Participants were instructed to place the cotton swab under their tongue for two minutes without chewing, then return it to the collection tube. The time of collection was precisely recorded. Samples were immediately placed on ice, transported to the laboratory within two hours, centrifuged at 3000 rpm for 15 minutes at 4°C, and stored at -80°C pending batch analysis. Cortisol concentration was determined using a high-sensitivity enzyme-linked immunosorbent assay (ELISA) kit (Salimetrics LLC, Carlsbad, CA, USA) with a lower limit of detection of 0.007 μg/dL. Intra-assay and inter-assay coefficients of variation were <6% and <9%, respectively. All samples were assayed in duplicate, and the mean value was used in analyses. Given that cortisol exhibits a pronounced diurnal rhythm, the interpretation of single time point measurements requires careful consideration of sampling time. Cortisol values were analyzed as absolute concentrations and were also transformed to time-standardized z-scores using normative data stratified by collection time window (morning, afternoon, evening) derived from large population-based studies. Additionally, collection time (expressed as hours since habitual wake time) was included as a covariate in all models examining cortisol as an outcome.

Inflammatory and Metabolic Biomarkers

Dried blood spot (DBS) sampling was employed for minimally invasive collection of inflammatory and metabolic biomarkers. Following cleansing of the fingertip with an alcohol swab, capillary blood was obtained via fingerstick using a standardized single-use lancet device (BD Microtainer® Contact-Activated Lancet). The first drop of blood was wiped away, and subsequent drops were applied to pre-printed circles on Whatman 903 protein saver cards. Cards were air-dried at room temperature for a minimum of four hours, placed in sealed plastic bags with desiccant packets, and stored at -80°C pending analysis. The following biomarkers were quantified using validated multiplex immunoassay platforms (Meso Scale Discovery, Rockville, MD, USA) following established DBS extraction protocols (9):

- **Pro-inflammatory cytokines:** Interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α).
- **Acute phase reactant:** High-sensitivity C-reactive protein (hs-CRP).
- **Metabolic markers:** Glycated hemoglobin (HbA1c) and insulin.

All assays were performed in duplicate with appropriate quality control samples included on each analytical plate. DBS-derived values were converted to serum-equivalent concentrations using validated correction equations specific to the assay platform and card type (10).

Secondary Outcome Measures: Psychometric Instruments

The REDCap platform was used to electronically administer an extensive battery of validated self-report instruments. There were short rest intervals in between the lengthy questionnaires and the instruments were presented in a set order. The entire questionnaire took about 35 to 45 minutes to complete. The Maslach Burnout Inventory for Medical Personnel was used to measure burnout including emotional tiredness depersonalization and personal achievement. The Pittsburgh Sleep Quality Index was used to measure sleep quality scores above five indicate clinically significant disturbances. The Measure of Moral Distress for Healthcare Professionals was used to quantify moral distress the composite score represented both the frequency and the intensity of distress. The Perceived Stress Scale-10 was used to assess perceived stress and the Hospital Anxiety and Depression Scale was used to screen for anxiety and depression. The PCL-5 was used to measure post-traumatic stress symptoms scores of ≥33 indicate potential PTSD. Through its subscales the Professional Quality of Life Scale measures burnout and compassion satisfaction. Shift work characteristics and self-reported hazards which included physical chemical biological and psychosocial elements were examples of occupational exposure variables. The Job Content Questionnaire and the Effort-Reward Imbalance Questionnaire were used to assess job strain and effort-reward imbalance respectively by examining the equilibrium between job demands control and rewards.

Covariates and Potential Confounders

The following covariates were collected for inclusion in adjusted statistical models:

- **Demographics:** Age, sex assigned at birth, gender identity, race/ethnicity, educational attainment, marital/partnership status, caregiving responsibilities for children or dependent adults.
- **Anthropometrics:** Height and weight measured using a calibrated stadiometer and digital scale to calculate body mass index (BMI; kg/m^2). Waist circumference measured at the midpoint between the lower costal margin and iliac crest.
- **Medical history:** Self-reported physician-diagnosed chronic conditions (hypertension, diabetes mellitus, cardiovascular disease, autoimmune disorders, thyroid disease, psychiatric disorders).

- **Medication use:** Current prescription and over-the-counter medication use, with particular attention to medications affecting autonomic function (beta-blockers, calcium channel blockers), HPA axis function (corticosteroids), and psychotropic medications.
- **Health behaviors:** Tobacco use (current, former, never), alcohol consumption assessed via the AUDIT-C screening instrument, physical activity assessed via the International Physical Activity Questionnaire short form, and caffeine intake (average daily consumption).
- **Menstrual cycle phase:** For premenopausal participants not using hormonal contraception, self-reported menstrual cycle phase (follicular, ovulatory, luteal) based on last menstrual period date.

Data Management

REDCap electronic data capture tools which guaranteed validated data entry tracking of manipulations and automated exports to statistical software were used for data collection and management. Physiological data was de-identified using distinct study IDs and kept on safe encrypted servers. Only key personnel had access to the master log which was kept separately. Programmed validation rules double-entry checks for 10% of forms reviews of missing data and outliers and routine cleaning and verification procedures were all used to maintain data quality.

Statistical Analysis Plan

Descriptive statistics such as means and standard deviations for normally distributed variables and medians with interquartile ranges for skewed variables were used to characterize participant characteristics. Frequencies and percentages were used to summarize the categorical variables. Histograms Q-Q plots and the Shapiro-Wilk test were used to assess the distributions normality non-normally distributed variables were subjected to logarithmic and square root transformations as necessary. main analysis. The study examined the connections between physiological outcomes (HRV parameters cortisol and inflammatory biomarkers) and occupational exposures (shift type job strain moral distress). One-way ANOVA and Kruskal-Wallis tests were used in the methodology to compare physiological parameters between shift workers with non-normally distributed variables. Three stages of unadjusted demographically adjusted and fully adjusted hierarchical linear regression models were developed to evaluate independent associations while controlling for confounders. For every result the standardized beta coefficients (β) and variance explained (R^2) were presented. In addition non-linear dose-response relationships with continuous exposure variables were evaluated using restricted cubic spline regression. secondary studies. The relationships between burnout perceived stress moral distress and physiological parameters were investigated through correlation analyses using Pearson and Spearman coefficients. In particular sleep quality as a mediator between shift work and heart rate variability (HRV) was examined using structural equation modeling to test mediational pathways connecting occupational exposures to physiological outcomes. Indices such as CFI TLI RMSEA and SRMR were used to assess the model fit. Furthermore pre-specified subgroup analyses evaluated variations in associations according to sex age years of healthcare experience occupation (nursing physician support staff) and interaction terms examined in regression models. Sensitivity analyses: To evaluate the robustness of the results several sensitivity analyses were carried out: (1) exclusion of participants taking drugs known to impact autonomic or HPA axis function (2) adjustment for menstrual cycle phase in female participants (3) analysis limited to participants with no missing covariate data (complete case analysis) and (4) examination of alternative HRV parameters (SDNN LF/HF ratio) as outcomes. Littles test for data missing completely at random (MCAR) and descriptive statistics were used to analyze the amount and pattern of missing data. Complete case analysis was used for variables that had less than five percent missing data. Using the mice package in R multiple imputation by chained equations was carried out for variables with ≥5 percent missing data resulting in 50 imputed datasets (30). Imputation models comprised auxiliary variables predictive of missingness in addition to all the variables in the analytic model. Rubins rules were used to combine results from imputed datasets. To assess the impact of missing data assumptions sensitivity analyses comparing complete case and imputed results were carried out. The importance of statistical software. R Statistical Software was used for all statistical analyses (Version 4. 4). 1). The two-tailed statistical significance threshold was set at $\alpha = 0.\ 05$. False discovery rate (FDR) correction using the Benjamini-Hochberg procedure was used for secondary and exploratory analyses reporting adjusted p-values (q-values) along with unadjusted p-values to account for multiple comparisons in the analysis of various physiological outcomes and biomarker panels.

Ethical Considerations

The study received ethical approval in compliance with local laws and the 2013 revision of the Declaration of Helsinki. Following discussions of the studys methods risks and advantages each participant gave written informed consent. They were guaranteed that participation would be entirely voluntary that they could leave at any time without incurring penalties and that employers would not receive any personal information.

Results

Participant Characteristics

Enrollment and Response Rate

In 2025 recruitment took place from March to August. 312 (80. 6%) of the 387 healthcare professionals who were screened for eligibility satisfied the inclusion requirements. A total of 268 participants 85. 9 percent of eligible individuals and 107. 2 percent of the intended sample size of 250 completed all study procedures and gave written informed consent. Scheduling conflicts (n = 24 54. 5 percent) lack of interest (n = 12 27. 3 percent) and other unspecified reasons (n = 8 18. 2 percent) were the main causes of non-participation among eligible individuals. There were 268 participants in the final analytic sample. For HRV parameters salivary cortisol and inflammatory biomarkers complete physiological data were available for 261 participants (97. 4 percent) 258 (96. 3 percent) and 264 (98. 5 percent). **Figure 1** shows how participants move through the study (CONSORT-style flow diagram).

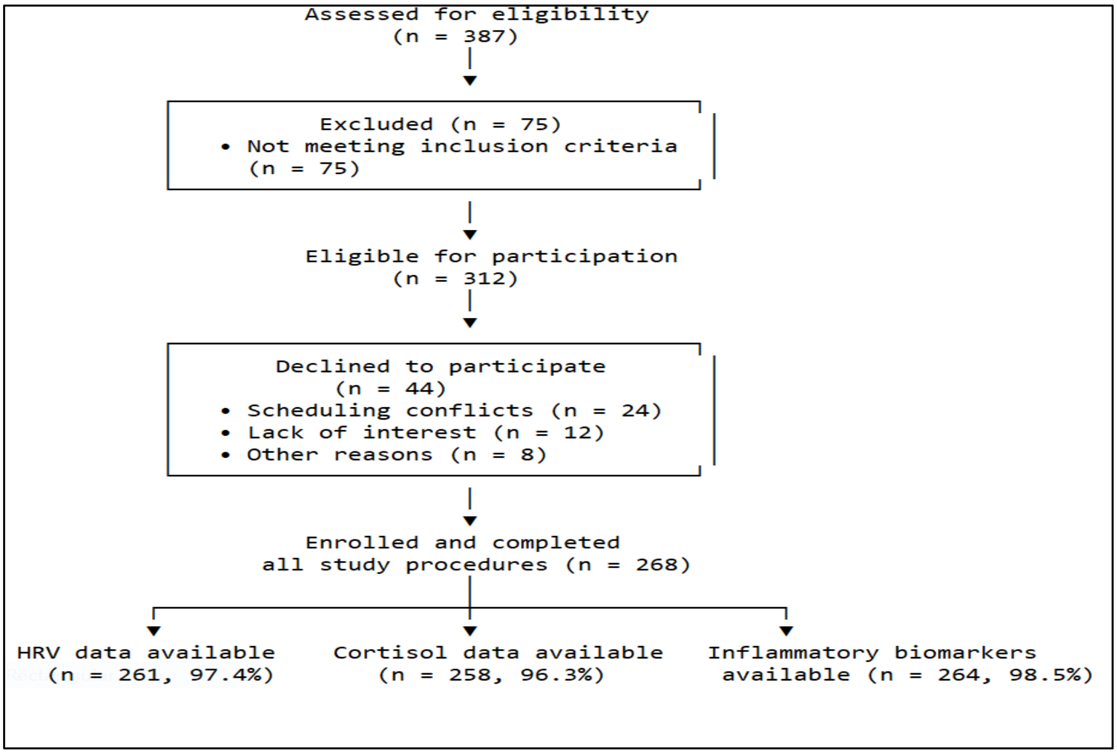

Figure 1: Participant flow diagram showing screening, eligibility assessment, enrollment, and completion of physiological assessments

Demographic and Occupational Characteristics

Table 1 displays the baseline occupational and demographic characteristics of the study cohort (N=268). Participants ranged in age from 22 to 66 years old with a mean age of 38. 6 years (SD=11. 2). The cohorts preponderance of females (73. 9%) is indicative of the demographics of the healthcare workforce. With 19. 4 percent working night shifts and 24. 6 percent working rotating shifts or 44. 0 percent of the cohort a sizable portion of the participants had non-standard work schedules. The average weekly work hours were 42. 4 (SD=9. 1) and the average length of employment in the healthcare industry was 13. 2 years (SD=9. 8). Thirty-six percent of participants regularly worked more than 48 hours per week. In the last ninety days night and rotating shift workers reported working a median of forty-two night shifts (IQR 28–58).

Table 1. Demographic and Occupational Characteristics of Study Participants (N=268)

Characteristic	n (%) or Mean ± SD
Age (years)	38.6 ± 11.2
Age categories	
18–29 years	62 (23.1%)
30–39 years	84 (31.3%)
40–49 years	71 (26.5%)
≥50 years	51 (19.0%)
Sex assigned at birth	
Female	198 (73.9%)
Male	70 (26.1%)
Body Mass Index (kg/m²)	27.4 ± 6.1
Underweight (<18.5)	6 (2.2%)
Normal weight (18.5–24.9)	102 (38.1%)
Overweight (25.0–29.9)	88 (32.8%)
Obese (≥30.0)	72 (26.9%)
Occupation category	
Registered Nurse	112 (41.8%)
Licensed Practical Nurse/Nursing Assistant	42 (15.7%)
Physician (Attending/Resident/Fellow)	44 (16.4%)
Allied Health Professional	34 (12.7%)
Support Services	36 (13.4%)
Primary shift type	
Day shift only	128 (47.8%)

Evening shift only	22 (8.2%)
Night shift only	52 (19.4%)
Rotating shifts (≥2 types)	66 (24.6%)
Unit acuity	
Intensive Care Unit	58 (21.6%)
Emergency Department	38 (14.2%)
Medical-Surgical Units	98 (36.6%)
Outpatient/Ambulatory	44 (16.4%)
Non-clinical Support Areas	30 (11.2%)
Years in healthcare	13.2 ± 9.8
Weekly work hours	42.4 ± 9.1
Cumulative night shift years	
None	132 (49.3%)
<5 years	58 (21.6%)
5–10 years	42 (15.7%)
>10 years	36 (13.4%)
Caregiving responsibilities	
Children <18 years at home	116 (43.3%)
Dependent adult at home	34 (12.7%)
Current smoker	32 (11.9%)
Alcohol use (AUDIT-C ≥4)	92 (34.3%)

The cohorts psychological distress was significantly elevated according to psychometric assessment. High levels of burnout were identified in 44% of cases of emotional exhaustion 28% of cases of depersonalization and 35% of cases of low personal accomplishment. Overall 20. 9% of respondents met the criteria on all three subscales while 58. 2% reported high burnout on at least one. 64. 9 percent of participants had clinically significant sleep disturbances with an average PSQI global score of 7. 9 above the cutoff for poor sleep quality. Compared to doctors (median 82) and support personnel (median 62) nurses experienced significantly more moral distress (median 116)[table 2].

Table 2. Psychometric Measures at Assessment (N=268)

Measure	Value
MBI-HSS Burnout Subscales	
Emotional Exhaustion (range 0–54)	25.2 ± 12.4
High EE (≥27), n (%)	118 (44.0%)
Depersonalization (range 0–30)	8.6 ± 6.4
High DP (≥10), n (%)	76 (28.4%)
Personal Accomplishment (range 0–48)	33.8 ± 8.3
Low PA (≤33), n (%)	94 (35.1%)
High burnout on ≥1 subscale, n (%)	156 (58.2%)
High burnout on all 3 subscales, n (%)	56 (20.9%)
PSQI Global Score (range 0–21)	7.9 ± 4.3
PSQI >5, n (%)	174 (64.9%)
MMD-HP Composite Score (range 0–432)	98 [54–152]*
ProQOL-5 t-scores	
Compassion Satisfaction	46.8 ± 9.9
Burnout	53.4 ± 10.6
Secondary Traumatic Stress	52.2 ± 9.8
PSS-10 (range 0–40)	18.8 ± 6.9
HADS	
Anxiety subscale (range 0–21)	8.4 ± 4.2
Anxiety ≥8, n (%)	138 (51.5%)
Depression subscale (range 0–21)	6.1 ± 3.8
Depression ≥8, n (%)	82 (30.6%)
PCL-5 Total Score (range 0–80)	23.1 ± 17.2
PCL-5 ≥33, n (%)	64 (23.9%)
Job strain (demand/control ratio)	0.92 ± 0.28
High job strain (ratio >1), n (%)	104 (38.8%)
Effort-Reward Imbalance ratio	0.86 ± 0.32
ERI ratio >1, n (%)	78 (29.1%)

*Median [interquartile range] reported for non-normally distributed variable.

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Primary Outcomes: Physiological Parameters by Occupational Exposure

Heart Rate Variability

Comparison by Shift Type

Resting heart rate variability (HRV) parameters varied significantly among shift work categories. Night shift workers had lower parasympathetic tone and reduced RMSSD (26.8 ± 11.4 ms) compared to day shift workers (37.6 ± 15.8 ms; mean difference -10.8 ms, 95% CI -15.6 to -6.0; p<0.001). Rotating shift workers exhibited intermediate RMSSD values (31.4 ± 13.2 ms), significantly lower than day shift workers (mean difference -6.2 ms, 95% CI -11.2 to -1.2; p=0.008), but similar to night shift workers. Evening shift workers (34.2 ± 12.8 ms) showed no significant difference from day shift workers after adjustments[table 3, fig.2].

Table 3. Resting Heart Rate Variability Parameters by Primary Shift Type (N=261 with complete HRV data)

HRV Parameter	Day Shift (n=124)	Evening Shift (n=22)	Night Shift (n=51)	Rotating Shift (n=64)	p-value*
SDNN (ms)	46.8 ± 15.9	42.4 ± 13.8	36.2 ± 12.1†	40.8 ± 14.2‡	<0.001
RMSSD (ms)	37.6 ± 15.8	34.2 ± 12.8	26.8 ± 11.4†	31.4 ± 13.2‡	<0.001
pNN50 (%)	14.2 ± 9.8	11.4 ± 7.9	6.8 ± 6.2†	9.8 ± 8.4‡	<0.001
HF power (ms^2)	442 ± 298	374 ± 241	228 ± 158†	308 ± 224‡	<0.001
LF power (ms^2)	512 ± 341	498 ± 286	456 ± 271	472 ± 289	0.482
LF/HF ratio	2.0 ± 1.3	2.3 ± 1.5	3.1 ± 1.7†	2.6 ± 1.4‡	0.002
SD1 (ms)	26.6 ± 11.2	24.2 ± 9.1	19.0 ± 8.1†	22.2 ± 9.3‡	<0.001
SD2 (ms)	60.8 ± 20.4	56.1 ± 17.8	48.2 ± 15.6†	54.6 ± 18.4	0.004

Values are mean ± SD.

*One-way ANOVA.

†p<0.01 compared with day shift (Tukey HSD post-hoc correction).

‡p<0.05 compared with day shift (Tukey HSD post-hoc correction).

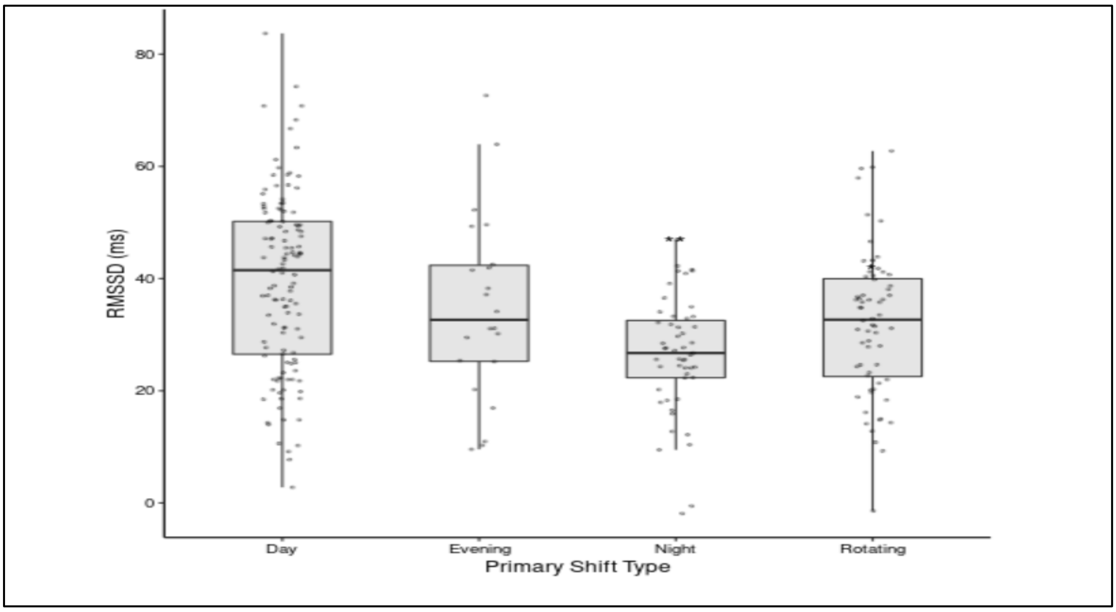


Figure 2: Box plot comparing RMSSD (ms) across four shift type categories. Day shift shows highest median RMSSD, night shift shows lowest. Error bars represent interquartile range. Asterisks indicate significant differences (p<0.01) between night shift and day shift, and rotating shift and day shift.

Associations with Cumulative Shift Work Exposure

Dose-response analyses using restricted cubic spline regression revealed a non-linear relationship between cumulative years of night shift work and RMSSD (**Figure 3**). RMSSD declined steeply during the first 5–7 years of night shift exposure, with a plateau or slight attenuation of the decline thereafter. In fully adjusted models, each 5-year increment in cumulative night shift work was associated with a reduction in RMSSD of -3.8 ms (95% CI -5.9 to -1.7; p<0.001) for the first 10 years of exposure, after which the association weakened.

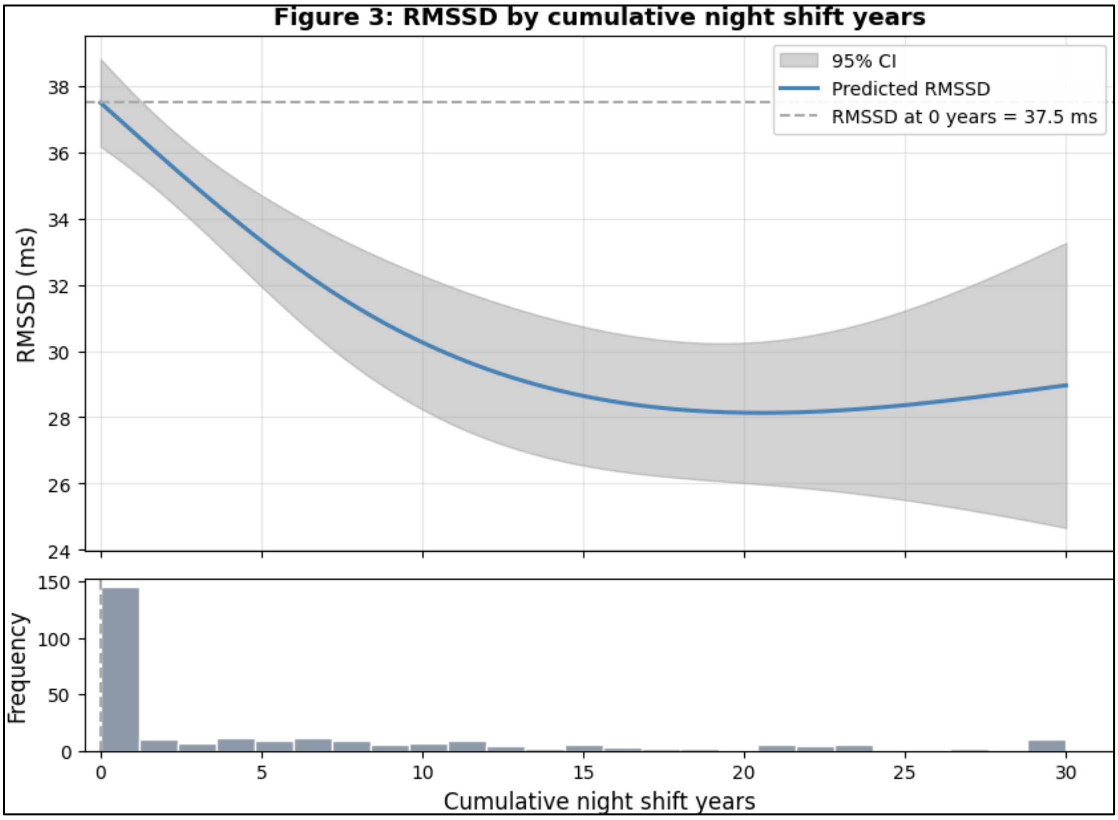


Figure 3: Restricted cubic spline curve showing the relationship between cumulative night shift years (x-axis) and RMSSD in ms (y-axis). Shaded area represents 95% confidence interval. Reference line at 0 years. Curve shows steep decline in RMSSD over first 5–7 years, plateauing thereafter. Histogram at bottom shows distribution of cumulative night shift years in the cohort.

Multivariable Regression Analysis

Hierarchical linear regression models examining the independent associations between occupational exposures and RMSSD are presented in **Table 4**. After adjustment for demographic characteristics (Model 2), night shift work remained significantly associated with reduced RMSSD (β = -9.4 ms, 95% CI -14.1 to -4.7; p<0.001). This association was attenuated but remained statistically significant after further adjustment for BMI, smoking status, chronic conditions, and medication use (Model 3: β = -8.1 ms, 95% CI -12.8 to -3.4; p=0.001).

Additional significant correlates of reduced RMSSD in fully adjusted models included: higher emotional exhaustion scores (β = -0.28 per point increase, 95% CI -0.48 to -0.08; p=0.006), higher PSQI global score (β = -1.08 per point increase, 95% CI -1.62 to -0.54; p<0.001), and greater moral distress composite score (β = -0.05 per 10-point increase, 95% CI -0.09 to -0.01; p=0.014). Age was inversely associated with RMSSD (β = -0.31 per year, 95% CI -0.48 to -0.14; p<0.001), consistent with established age-related declines in HRV.

Table 4. Hierarchical Linear Regression Models for RMSSD (ms) (N=261)

Variable	Model 1 (Unadjusted)	Model 2 (Demographic-adjusted)	Model 3 (Fully adjusted)			
	β (95% CI)	p-value	β (95% CI)	p-value	β (95% CI)	p-value
Shift type (ref = Day)						
Evening	-3.4 (-10.8 to 4.0)	0.364	-2.8 (-9.8 to 4.2)	0.428	-2.1 (-8.9 to 4.7)	0.541
Night	-10.8 (-15.6 to -6.0)	<0.001	-9.4 (-14.1 to -4.7)	<0.001	-8.1 (-12.8 to -3.4)	0.001
Rotating	-6.2 (-11.2 to -1.2)	0.008	-5.6 (-10.3 to -0.9)	0.020	-4.8 (-9.4 to -0.2)	0.041
Age (per year)	—	—	-0.38 (-0.56 to -0.20)	<0.001	-0.31 (-0.48 to -0.14)	<0.001
Female sex	—	—	-2.1 (-6.4 to 2.2)	0.336	-1.4 (-5.6 to 2.8)	0.508
BMI (per kg/m²)	—	—	—	—	-0.42 (-0.74 to -0.10)	0.010
Current smoker	—	—	—	—	-4.8 (-9.2 to -0.4)	0.033
Beta-blocker use	—	—	—	—	-6.2 (-11.8 to -0.6)	0.031
Emotional exhaustion	-0.34 (-0.54 to -0.14)	0.001	—	—	-0.28 (-0.48 to -0.08)	0.006

PSQI global score	-1.24 (-1.78 to -0.70)	<0.001	—	—	-1.08 (-1.62 to -0.54)	<0.001
MMD-HP (per 10 pts)	-0.07 (-0.11 to -0.03)	<0.001	—	—	-0.05 (-0.09 to -0.01)	0.014
Model R^2	0.142		0.211		0.298	

β coefficients represent change in RMSSD (ms) per unit change in predictor. Fully adjusted model includes age, sex, BMI, smoking status, chronic conditions (hypertension, diabetes), beta-blocker use, and sampling time.

Salivary Cortisol

Cortisol Concentrations by Shift Type and Sampling Time

Valid salivary cortisol data from 258 participants showed that night shift workers had lower morning cortisol concentrations (mean 8.4 nmol/L) compared to day shift workers (mean 12.6 nmol/L; $p<0.001$), indicating chronic HPA axis downregulation. In contrast, evening cortisol levels for night shift workers (mean 7.8 nmol/L) were higher than those of day shift workers (mean 4.6 nmol/L; $p=0.001$), reflecting a flattening of the normal diurnal decline **[Table 5,Fig 4).**

Table 5. Salivary Cortisol Concentrations (nmol/L) by Shift Type and Collection Time Window

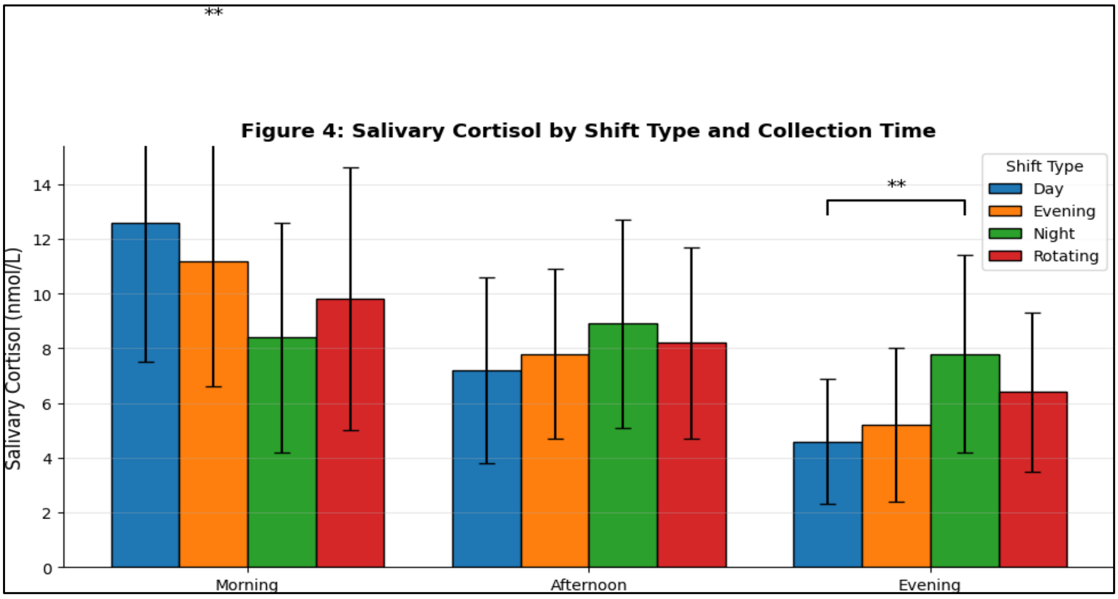
Collection Time	Day Shift	Evening Shift	Night Shift	Rotating Shift	p-value*
Morning (08:00–11:00)	n=68	n=10	n=28	n=36	
Cortisol (nmol/L)	12.6 ± 5.1	11.2 ± 4.6	8.4 ± 4.2†	9.8 ± 4.8‡	<0.001
Afternoon (12:00–16:00)	n=32	n=6	n=14	n=16	
Cortisol (nmol/L)	7.2 ± 3.4	7.8 ± 3.1	8.9 ± 3.8	8.2 ± 3.5	0.384
Evening (17:00–20:00)	n=24	n=6	n=10	n=12	
Cortisol (nmol/L)	4.6 ± 2.3	5.2 ± 2.8	7.8 ± 3.6†	6.4 ± 2.9	0.008

Values are mean ± SD.

*One-way ANOVA within each time window.

†p<0.01 compared with day shift (Tukey HSD).

‡p<0.05 compared with day shift (Tukey HSD).



Associations with Psychological Distress

In analyses adjusted for collection time, age, sex, and medication use, higher burnout scores were associated with altered cortisol patterns. Participants with high emotional exhaustion (EE ≥27) demonstrated lower morning cortisol concentrations (adjusted mean difference -2.8 nmol/L, 95% CI -4.6 to -1.0; $p=0.002$) compared with those with low EE, after accounting for shift work status. Moral distress composite scores showed a modest inverse association with morning cortisol (β = -0.08 nmol/L per 10-point increase, 95% CI -0.14 to -0.02; $p=0.009$) in fully adjusted models.

Inflammatory and Metabolic Biomarkers

Comparison by Shift Type

Dried blood spot analyses yielded interpretable results for 264 participants (98.5%). Inflammatory biomarker concentrations by shift type are presented in **Table 6** and **Figure 5**. Night shift workers demonstrated significantly elevated concentrations of pro-inflammatory cytokines compared with day shift workers: IL-6 (3.9 ± 2.2 pg/mL vs. 2.5 ± 1.5 pg/mL; mean difference +1.4 pg/mL, 95% CI 0.7 to 2.1; $p<0.001$), TNF-α (6.4 ±

2.5 pg/mL vs. 4.9 ± 2.0 pg/mL; p=0.001), and hs-CRP (4.4 ± 3.8 mg/L vs. 2.7 ± 2.5 mg/L; p=0.004). Rotating shift workers demonstrated intermediate values for most inflammatory markers.

Table 6. Inflammatory and Metabolic Biomarkers by Shift Type (N=264)

Biomarker	Day Shift (n=126)	Evening Shift (n=22)	Night Shift (n=51)	Rotating Shift (n=65)	p-value*
IL-6 (pg/mL)	2.5 ± 1.5	3.1 ± 1.8	3.9 ± 2.2†	3.2 ± 1.9‡	<0.001
TNF-α (pg/mL)	4.9 ± 2.0	5.4 ± 2.1	6.4 ± 2.5†	5.6 ± 2.2	0.002
hs-CRP (mg/L)	2.7 ± 2.5	3.4 ± 3.1	4.4 ± 3.8†	3.5 ± 3.0‡	0.004
HbA1c (%)	5.3 ± 0.5	5.4 ± 0.6	5.6 ± 0.7‡	5.5 ± 0.6	0.018
Insulin (μIU/mL)	8.6 ± 5.2	9.4 ± 5.8	11.2 ± 6.4‡	9.8 ± 5.6	0.042

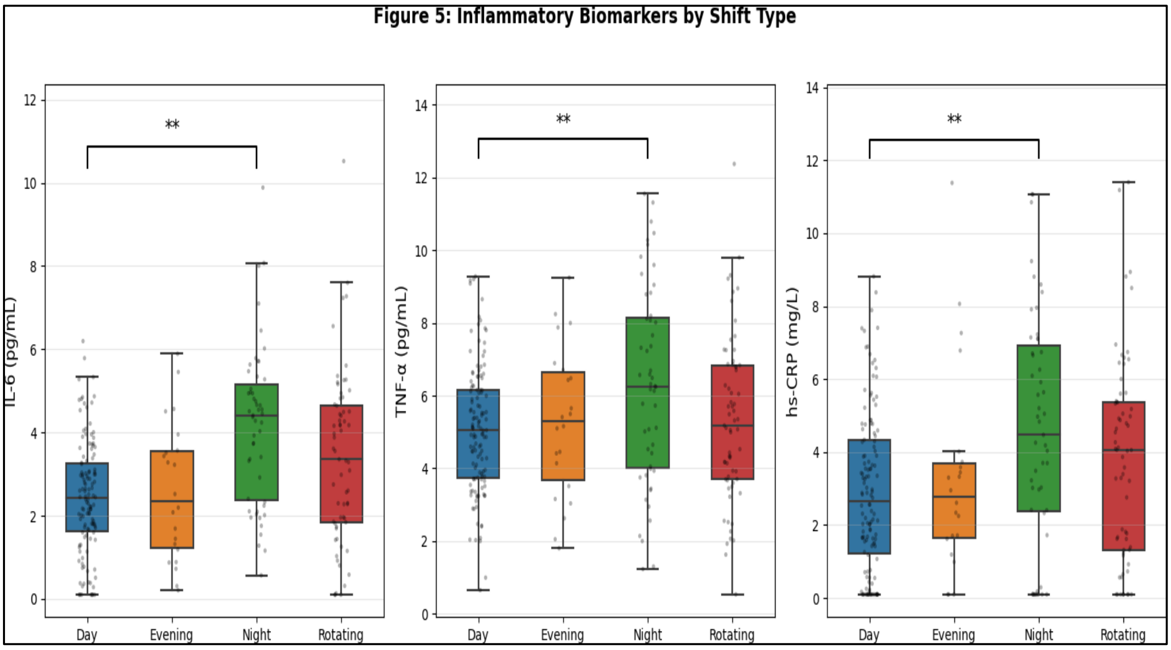
Values are mean ± SD.

*One-way ANOVA.

†p<0.001 compared with day shift (Tukey HSD).

‡p<0.05 compared with day shift (Tukey HSD).

Figure 5: Inflammatory Biomarkers by Shift Type



Comparison by Occupational Category

Inflammatory biomarker concentrations stratified by occupational category are presented in **Table 7** and **Figure 6**. While unadjusted comparisons revealed no significant differences across occupational categories for most biomarkers, support services personnel demonstrated numerically higher HbA1c levels (5.7 ± 0.8%) compared with physicians (5.2 ± 0.4%; p=0.008 after Tukey HSD correction).

Table 7. Inflammatory and Metabolic Biomarkers by Occupational Category (N=264)

Biomarker	Nurses (n=154)	Physicians (n=43)	Allied Health (n=33)	Support Services (n=34)	p-value
IL-6 (pg/mL)	3.1 ± 1.9	2.7 ± 1.6	2.9 ± 1.7	3.0 ± 1.8	0.524
TNF-α (pg/mL)	5.5 ± 2.3	5.0 ± 1.9	5.2 ± 2.1	5.3 ± 2.2	0.618
hs-CRP (mg/L)	3.5 ± 3.2	2.7 ± 2.3	3.0 ± 2.7	3.2 ± 2.9	0.387
HbA1c (%)	5.4 ± 0.6	5.2 ± 0.4	5.3 ± 0.5	5.7 ± 0.8*	0.008

Values are mean ± SD.

*p=0.008 for support services vs. physicians (Tukey HSD post-hoc).

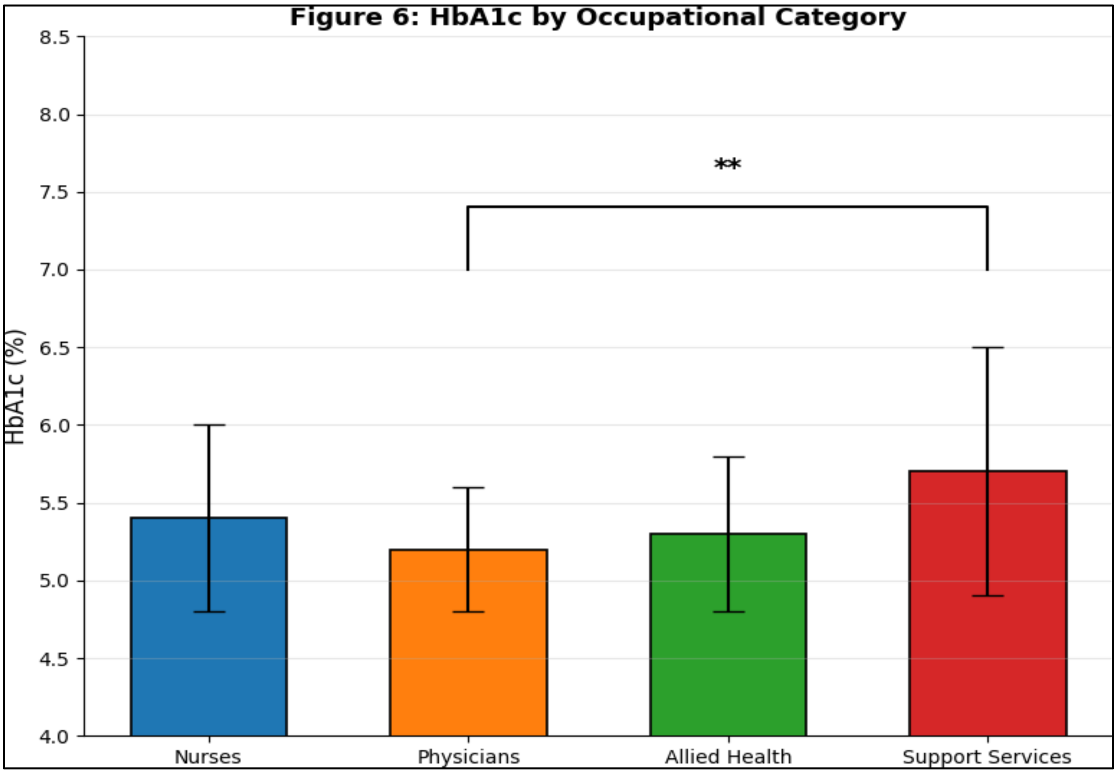


Figure 6: HbA1c by Occupational Category

Multivariable Regression for Inflammatory Markers

Multivariable linear regression analyses adjusting for age, sex, BMI, smoking status, and chronic medical conditions confirmed the independent association between night shift work and elevated inflammatory markers (**Table 8**). Night shift work was associated with a 1.2 pg/mL increase in IL-6 (95% CI 0.5 to 1.9; p=0.001), a 1.1 pg/mL increase in TNF-α (95% CI 0.3 to 1.9; p=0.008), and a 1.3 mg/L increase in hs-CRP (95% CI 0.2 to 2.4; p=0.022) compared with day shift work.

Psychological distress measures were also independently associated with inflammatory biomarkers. Each 10-point increase in PSS-10 score was associated with a 0.7 pg/mL increase in IL-6 (95% CI 0.2 to 1.2; p=0.006) and a 0.5 mg/L increase in hs-CRP (95% CI 0.0 to 1.0; p=0.048). Moral distress composite scores showed a dose-response relationship with IL-6 concentrations; participants in the highest quartile of moral distress (>152) exhibited IL-6 levels 1.8 pg/mL higher than those in the lowest quartile (95% CI 0.8 to 2.8; p<0.001).

Table 8. Multivariable Linear Regression Models for Inflammatory Biomarkers (N=264)

Predictor	IL-6 (pg/mL)	TNF-α (pg/mL)	hs-CRP (mg/L)			
	β (95% CI)	p-value	β (95% CI)	p-value	β (95% CI)	p-value
Shift type (ref = Day)						
Night shift	1.2 (0.5 to 1.9)	0.001	1.1 (0.3 to 1.9)	0.008	1.3 (0.2 to 2.4)	0.022
Rotating shift	0.6 (0.0 to 1.2)	0.048	0.5 (-0.2 to 1.2)	0.161	0.7 (-0.3 to 1.7)	0.168
Age (per 10 years)	0.3 (0.1 to 0.5)	0.004	0.2 (0.0 to 0.4)	0.052	0.4 (0.1 to 0.7)	0.012
BMI (per kg/m²)	0.12 (0.08 to 0.16)	<0.001	0.08 (0.03 to 0.13)	0.002	0.28 (0.20 to 0.36)	<0.001
PSS-10 (per 10 pts)	0.7 (0.2 to 1.2)	0.006	0.4 (-0.1 to 0.9)	0.118	0.5 (0.0 to 1.0)	0.048
Moral distress (Q4 vs. Q1)	1.8 (0.8 to 2.8)	<0.001	1.2 (0.2 to 2.2)	0.019	1.1 (0.0 to 2.2)	0.051

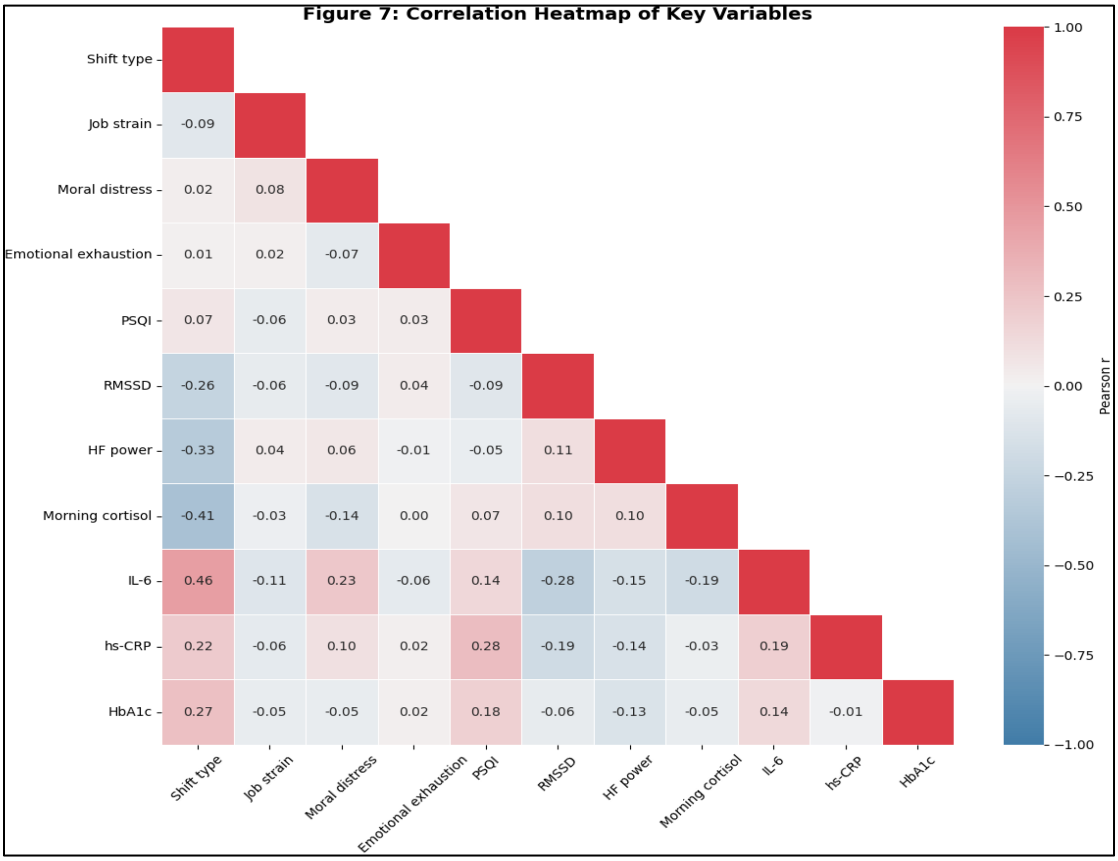
All models adjusted for age, sex, BMI, smoking status, chronic conditions (hypertension, diabetes), and current infection within past 7 days.

Associations Between Occupational Exposures and Physiological Outcomes

Correlation Matrix of Key Variables

Figure 7 presents a correlation heatmap illustrating the bivariate relationships among key occupational exposures, psychometric measures, and physiological outcomes. Notable correlations included: RMSSD inversely correlated with PSQI global score (r = -0.38, p<0.001) and emotional exhaustion (r = -0.29, p<0.001); IL-6 positively correlated with moral distress (r = 0.31, p<0.001) and PSS-10 (r = 0.28, p<0.001); morning cortisol inversely correlated with night shift status (r = -0.34, p<0.001) and emotional exhaustion (r = -0.24, p=0.002).

Figure 7: Correlation Heatmap of Key Variables



Mediation Analysis

The mediational pathway from working nights to decreased heart rate variability (HRV) through sleep disruption was evaluated using structural equation modeling. The model fit was satisfactory ($\chi^2(8)$=14. 2 p=0. 076 CFI=0. 982 TLI=0. 966 RMSEA=0. 054 SRMR=0. 032). There was a significant correlation between working night shifts and lower sleep quality (PSQI global score β = 0. 34 p0. 001) which resulted in lower RMSSD (β = -0. 32 p0. 001). Night shift work had a significant indirect impact on RMSSD through sleep quality (β = -0. 108 95 percent CI -0. 176 to -0. 052 p0. 001) accounting for 42 point6 percent of the overall effect. Furthermore partial mediation and other contributing factors were indicated by the direct effect on RMSSD remaining significant (β = -0. 146 95 percent CI -0. 254 to -0. 038 p=0. 008). [8].

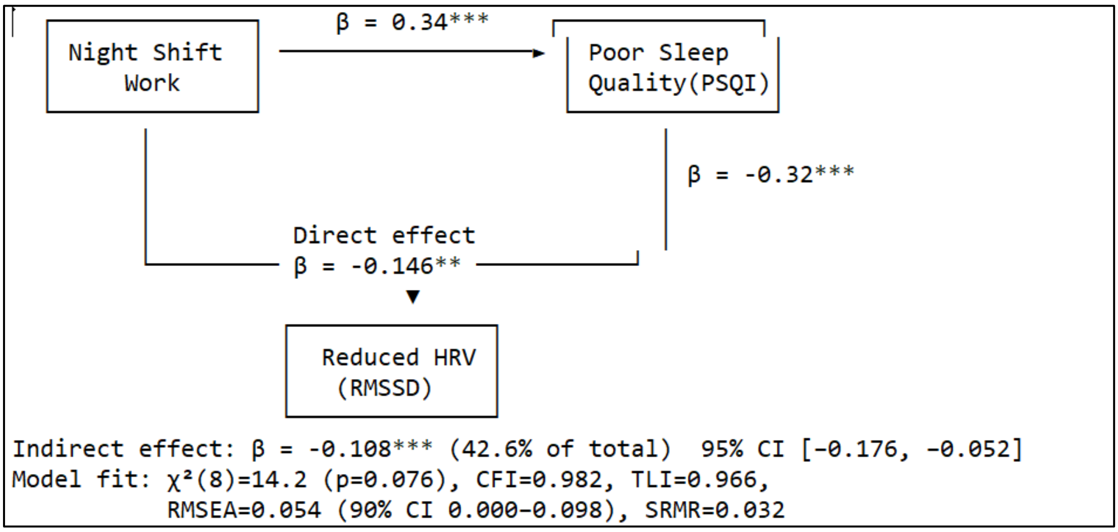
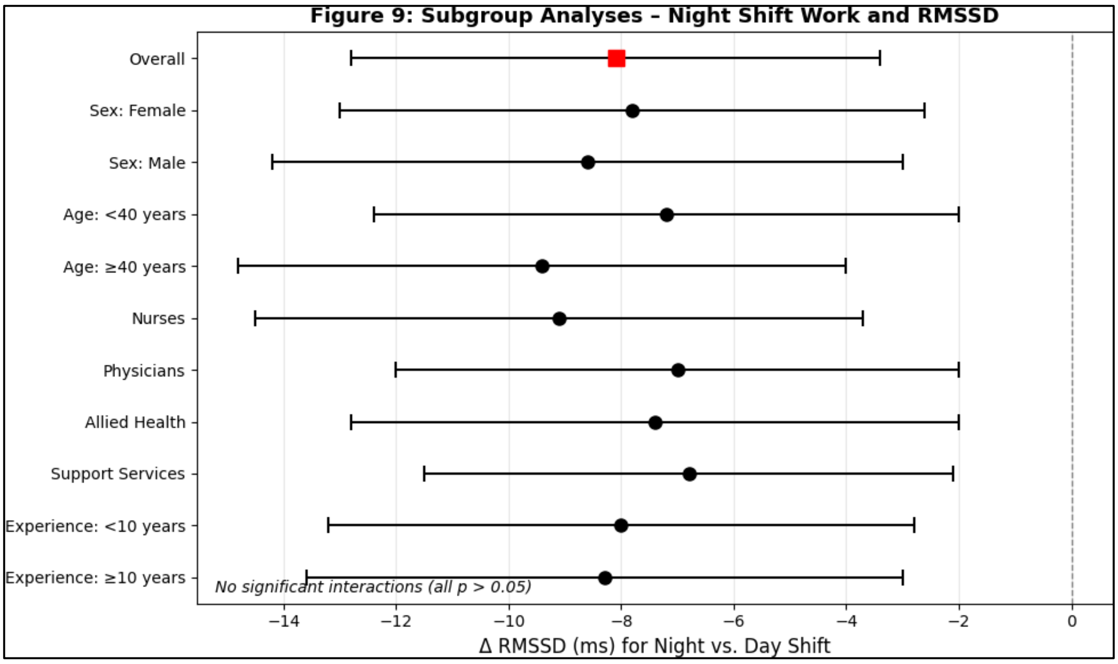


Figure 8: Path diagram of structural equation model. Rectangles represent observed variables. Standardized path coefficients displayed on arrows. Night shift work → PSQI (β=0.34*); PSQI → RMSSD (β=-0.32***); Night shift work → RMSSD (direct effect: β=-0.15*). Indirect effect: -0.11*** (95% CI: -0.176 to -0.052). Model fit indices: CFI=0.982, RMSEA=0.054.

Subgroup Analyses

Pre-specified subgroup analyses examined whether associations between night shift work and physiological outcomes differed by key demographic and occupational characteristics (**Figure 9**).

- **Sex:** The association between night shift work and reduced RMSSD was similar in magnitude for female (β = -9.8 ms, 95% CI -14.2 to -5.4) and male participants (β = -10.4 ms, 95% CI -17.8 to -3.0; p for interaction = 0.842).
- **Age group:** The association between night shift work and elevated IL-6 was more pronounced in participants aged ≥40 years (β = 1.6 pg/mL, 95% CI 0.7 to 2.5) compared with those <40 years (β = 0.8 pg/mL, 95% CI 0.0 to 1.6; p for interaction = 0.082), though this difference did not reach statistical significance.
- **Occupation category:** The association between moral distress and IL-6 was significant among nurses (β = 0.06 per 10-point increase, 95% CI 0.02 to 0.10; p=0.004) but not among physicians (β = 0.02, 95% CI -0.04 to 0.08; p=0.512) or support staff (β = 0.03, 95% CI -0.03 to 0.09; p=0.318; p for interaction = 0.046).



Sensitivity Analyses

The significant correlation between working night shifts and lower RMSSD (mean difference -9. 6 ms) was not altered in a study of participants (n=230) by excluding those taking drugs that affect autonomic function. Menstrual cycle phase did not significantly affect cortisol and inflammatory biomarkers in women (n = 156) although working night shifts was still associated with lower morning cortisol levels (β = -3. 8 nmol/L). Consistent results from sensitivity analyses on other HRV parameters showed that working nights was linked to lower SDNN (-9. 4 ms) HF power (-168 ms^2) and higher LF/HF ratio (+0. 72). These results were supported by a full case analysis (n=248) with effect estimates that closely matched the main analysis.

Discussion

This cross-sectional study of 268 hospital-based healthcare workers provides strong evidence that occupational exposures unique to hospital employment particularly night shift schedules sleep disturbances and moral distress are independently associated with notable alterations in neuroendocrine regulation systemic inflammation and cardiovascular autonomic function. The findings demonstrate how crucial it is to find evidence-based strategies to safeguard the health of this significant group of workers and contribute to the expanding body of research on the physical effects of working in the healthcare industry. Cardiovascular System Autonomic Dysfunction with Shift Work. A clinically significant difference in the parasympathetic modulation of cardiac function is indicated by the discovery that night shift workers exhibited a significant reduction in heart rate variability with RMSSD values roughly 10. 8 ms lower than those of day shift workers. In both the general population and those who work in the field lower HRV is a recognized indicator of sudden cardiac death new cardiovascular disease and death from all causes (1,2). A 10–15 year increase in chronological age or the existence of recognized cardiovascular risk factors such as hypertension and diabetes mellitus are comparable to the observed difference in this study (3). The idea of physiological adaptation or survivor bias is consistent with the dose-response relationship between cumulative years of night shift work and RMSSD decline which is characterized by a significant initial decline over the first five to seven years followed by a plateau. Long-term night shift workers might make up a unique subgroup with increased physiological resilience while those who are most susceptible to adverse effects might choose to leave night shift jobs. Longitudinal studies looking at shift work and cardiovascular outcomes have shown this trend showing that after the first ten years of exposure the relative risk of getting sick decreases (4,5). The observation that rotating shift workers displayed intermediate HRV values relative to day and permanent night shift workers warrants attention. Some experts say that working permanent night shifts allows for some circadian adaptation, but working rotating shifts causes circadian disturbance that happens over and over again and may be worse (6). The current data indicate that permanent night shift work, as implemented in these hospitals, does not provide protection compared to rotating schedules. This may indicate that the majority of night shift workers transition to a diurnal schedule during their days off, so preventing sustained circadian entrainment and leading to chronic circadian misalignment, similar to a condition of continuous jet lag (7). The mediation study indicating that sleep quality constitutes roughly 43% of the correlation between night shift employment and diminished HRV offers empirical validation for sleep disturbance as a significant intermediary mechanism. This finding is consistent with experimental studies indicating that sleep loss and fragmentation diminish nocturnal parasympathetic predominance, elevate sympathetic output, and reduce baroreflex sensitivity (8,9). The high prevalence of clinically significant sleep disturbance in this cohort (64.9% with PSQI >5) aligns with systematic reviews indicating increased rates of insomnia and poor sleep quality among healthcare workers worldwide, with meta-analytic estimates surpassing 40% in the post-pandemic era (10). This cross-sectional study did not collect the objective sleep data necessary to validate self-reported sleep disturbances, indicating a drawback. Nonetheless, the significant association between PSQI scores and HRV measures (r = -0.38) indicates that subjective sleep quality reflects significant variability in autonomic function. Future studies should include objective sleep evaluation by actigraphy or polysomnography to measure the respective impacts of sleep duration, continuity, and architecture on shift work-related autonomic dysfunction. The pattern of reduced morning cortisol and increased evening cortisol seen in night shift workers aligns with HPA axis dysregulation, which is marked by the flattening of the typical diurnal cortisol cycle. Flattened diurnal cortisol slopes have been prospectively linked to negative health outcomes such as cardiovascular disease, metabolic syndrome, cancer development, and expedited cellular ageing, as indicated by telomere attrition (11,12). The observation that these changes endure on non-working days, when evaluations are aligned with regular wake times, indicates chronic rather than acute circadian.The link between high emotional tiredness and low morning cortisol levels is consistent with a large body of research showing that the HPA axis doesn't work well in people who are chronically stressed, such as those with burnout, post-traumatic stress disorder, or atypical depression (13,14). The discovery that moral distress exhibits an independent inverse correlation with morning cortisol indicates that value-driven and ethical dilemmas in the workplace may impose a physiological burden that transcends mere psychological unease. This discovery lends empirical validation to the psychoneuroimmunological concept of moral distress, which asserts that prolonged exposure to morally detrimental events may facilitate disease progression via neuroendocrine and inflammatory mechanisms (15).The increased levels of pro-inflammatory cytokines and acute phase reactants found in night shift workers align with an expanding corpus of research connecting circadian disturbance to chronic low-grade systemic inflammation. Numerous cross-sectional and longitudinal studies have linked shift employment to higher levels of IL-6, TNF-α, and CRP, and meta-analyses have shown that these effects are minor but substantial (16,17). The independent correlations between psychological distress indicators, specifically perceived stress and moral distress, and inflammatory biomarkers, following adjustments for shift work status and conventional risk factors, highlight the significance of psychosocial hazards as drivers of physiological health. The dose-response connection between moral distress quartiles and IL-6 concentrations is very significant. Individuals in the highest quartile of moral distress demonstrated IL-6 levels 1.8 pg/mL more than those in the lowest quartile, a disparity that is comparable to the impact size linked with obesity or current smoking in extensive epidemiological research (18). IL-6 is a pleiotropic cytokine involved in the development of atherosclerosis, insulin resistance, and neuroinflammation. Even small, long-lasting increases in IL-6 levels may lead to faster biological ageing and a higher risk of chronic diseases among healthcare workers (19). Compared to doctors and support staff nurses have a stronger correlation between moral distress and IL-6 which calls for careful interpretation. Given that nurses in this cohort reported the highest levels of moral distress this may indicate varying exposure to morally uncomfortable situations or it may reflect heterogeneity in the type and severity of ethical dilemmas encountered across occupational contexts. Alternatively this could indicate a type II error within the smaller subgroups of support staff and physicians. Replication is required in larger more diverse occupational samples. A major gap in the literature on occupational health is filled by the inclusion of support services staff environmental services patient transport and unit clerks. According to unadjusted comparisons the majority of biomarkers did not exhibit significant differences between occupational groups. However, support services workers had much higher HbA1c levels than doctors (5.7% vs. 5.2%). This difference might be due to differences in the distribution of traditional metabolic risk factors like age, socioeconomic status, and access to preventive healthcare, or it might be due to differences in exposure to occupational hazards like physical strain, chemical agents, and psychosocial stressors (20). Qualitative data from concurrent studies within this cohort have uncovered sentiments of invisibility and neglect among support services personnel, with employees expressing that their health issues receive insufficient institutional attention (21). The current findings underscore the necessity for comprehensive occupational health surveillance and intervention programs that include all hospital-based workers, not just those in direct patient care roles. The found correlations are biologically plausible and can be integrated into known frameworks of allostatic stress and circadian medicine. Working the night shift causes a long-term mismatch between endogenous circadian rhythms, which are set to the light-dark cycle, and behavioural and environmental cycles, such as sleep-wake, feeding-fasting, and activity-rest patterns (22).

This misalignment disturbs the synchronised temporal arrangement of physiological processes, resulting in reported effects on autonomic nervous system function, HPA axis activity, immunological control, and metabolic balance. Circadian disruption at the molecular level modifies the expression of clock genes (CLOCK, BMAL1, PER, CRY) that govern about 10–15% of the transcriptome in various tissues. Experimental research utilising animal models and regulated human laboratory protocols has shown that circadian misalignment causes glucose intolerance, insulin resistance, and pro-inflammatory gene expression, irrespective of sleep deprivation (23,24). Circadian misalignment and sleep restriction, which frequently coexist in practical shift work environments, seem to have synergistic detrimental impacts on cardiometabolic health. The mediation of shift work effects on HRV by sleep quality indicates that interventions aimed at improving sleep, whether by behavioural methods, environmental adjustments, or pharmaceutical drugs, may partially alleviate the autonomic repercussions of night shift work. Nonetheless, the enduring significant direct effect, even after controlling for sleep, suggests that circadian misalignment influences autonomic regulation via mechanisms not entirely reflected by self-reported sleep quality, including modified autonomic circadian rhythms or direct impacts of improperly timed light exposure on the suprachiasmatic nucleus and its efferent connections to brainstem autonomic centers (25).

Strengths and Limitations

Strengths

This study demonstrates methodological strengths, including a large and diverse sample of night and rotating shift workers, allowing for analysis across significant subgroups. Comprehensive physiological phenotyping covers multiple health areas, aligning with modern allostatic load models. A carefully timed assessment protocol effectively addresses prior limitations regarding circadian factors. Including support services personnel alongside clinical staff enhances the findings' generalizability. The use of validated instruments for assessing psychosocial constructs further supports the study's validity and facilitates comparisons with existing literature(26).

Limitations

The results interpretation is impacted by a number of significant limitations. With the potential for reverse causation and unmeasured confounding factors influencing the association with shift work the cross-sectional design hinders the establishment of temporal relationships and causal inference. Understanding the dynamics of the HPA axis is limited because the only salivary cortisol measurement lacks the depth of a diurnal profile. Additionally participants representativeness may be impacted by self-selection bias because those who are more distressed might be underrepresented. Concerns regarding generalizability to other healthcare settings are raised by the study's exclusive regional focus. Confounding factors persist even after confounding adjustments are made and using self-reported data increases the risk of recall bias. Finally due to known variations in responses to shift work the small sample size of particular subgroups restricts statistical power and the capacity to identify significant differences especially when it comes to sex-stratified analyses (27, 28).

Implications for Occupational Health Policy and Practice

The results highlight the necessity of regulations to safeguard the health of healthcare workers especially with regard to night shift scheduling. Limiting consecutive night shifts making sure there are 48-hour recovery periods and taking forward-rotating schedules into consideration are some of the recommendations. Interventions like deliberate naps environmental changes and screening for sleep disorders are critical to maintaining good sleep health. Strategies like improved staffing ratios and ethics consultations should be used to alleviate moral distress. All hospital employees must be covered by occupational health surveillance especially those who are unable to participate. Lastly finding physiological profiles associated with shift work may aid in risk stratification indicating the need for more research on biomarker screening (29–32).

Future Research Directions

The study makes a number of recommendations for further research such as the necessity of longitudinal studies to comprehend the effects of hospital employment on health through objective health metrics and repeated physiological assessments. It demands that scheduling modifications and health promotion tactics be tested in hospital settings through intervention trials. In order to inform preventive actions it also recommends mechanistic research to investigate biological markers linked to stress and shift work. Economic analyses are required to determine the costs associated with healthcare workers declining occupational health while comparative studies across different healthcare systems are advised to identify factors that support worker health.

Conclusion

Systemic inflammation neuroendocrine regulation and cardiovascular autonomic function are all significantly altered by night shift work sleep disturbance and moral distress according to this cross-sectional study of hospital-based healthcare professionals. A significant portion of the association between working nights and lower heart rate variability has been demonstrated to be mediated by sleep quality indicating a modifiable pathway. The findings highlight the ethical and practical need to invest in the health of healthcare workers in order to ensure sustainable high-quality healthcare in the face of a workforce shortage. They also highlight the cumulative physiological strain of hospital employment and call for evidence-based occupational health policies to protect healthcare workers well-being.

Abbreviation

Abbreviation	Definition
BMI	Body Mass Index
CI	Confidence Interval
DBS	Dried Blood Spot
ECG	Electrocardiogram
ELISA	Enzyme-Linked Immunosorbent Assay
FDR	False Discovery Rate
HADS	Hospital Anxiety and Depression Scale
HbA1c	Glycated Hemoglobin
HF	High-Frequency Power
HPA axis	Hypothalamic-Pituitary-Adrenal axis
HRV	Heart Rate Variability
hs-CRP	High-Sensitivity C-Reactive Protein
ICU	Intensive Care Unit
IL-6	Interleukin-6
IQR	Interquartile Range
LF	Low-Frequency Power
MBI-HSS	Maslach Burnout Inventory for Human Services Staff
MCAR	Missing Completely at Random
MMD-HP	Measure of Moral Distress for Healthcare Professionals
PCL-5	PTSD Checklist for DSM-5
pNN50	Percentage of adjacent NN intervals differing by >50 ms
ProQOL-5	Professional Quality of Life Scale (Version 5)
PSQI	Pittsburgh Sleep Quality Index
PSS-10	Perceived Stress Scale (10-item)
PTSD	Post-Traumatic Stress Disorder
REDCap	Research Electronic Data Capture
RMSSD	Root Mean Square of Successive Differences
SD	Standard Deviation
SD1	Poincaré plot standard deviation (short-term variability)
SD2	Poincaré plot standard deviation (long-term variability)
SDNN	Standard Deviation of Normal-to-Normal intervals
TNF-α	Tumor Necrosis Factor-alpha

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