RESEARCH PAPER

The Interplay of Psychosocial Distress (Stress and Sleep) and ABO/Rh Blood Groups with Clinical Severity and Performance Status in Chemotherapy Patients

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Abstract

Background: Patients receiving chemotherapy commonly experience psychological distress, sleep disruption, and fluctuating functional status. Although ABO/Rh blood groups have been linked to cancer susceptibility and inflammatory-thrombotic physiology, their acute relevance during active chemotherapy remains uncertain. **Objective:** This study examined whether psychosocial factors, sleep quality, and ABO/Rh blood groups were associated with APACHE II physiological severity and KPS/ECOG functional performance in chemotherapy patients. **Methods:** A prospective observational cohort study was conducted at two tertiary oncology centers in Pune, India. The enrolled cohort included 200 patients receiving chemotherapy with concurrent polypharmacy. Clinical severity was primarily assessed using APACHE II; functional status was assessed using Karnofsky Performance Status (KPS) and ECOG; and patient-reported stress and sleep were collected through structured interviews. **Results:** The mean APACHE II score was 20.65 ± 6.17 (median 23, range 5-31). KPS and ECOG were strongly inversely correlated (rho = -0.73). Better sleep was associated with higher KPS (rho = 0.50) and lower ECOG (rho = -0.39), while higher stress was associated with lower KPS (rho = -0.41), higher ECOG (rho = 0.40), and higher APACHE II. In multivariable analysis, higher stress (coefficient +3.28, p ¡ 0.001), poorer sleep (coefficient -1.25, p = 0.046), older age, and poorer functional status were associated with higher APACHE II severity. Blood group was not significantly associated with cancer type or APACHE II scores. **Conclusion:** In chemotherapy patients, stress, sleep, age, and functional status were more informative correlates of acute physiological severity than ABO/Rh blood group. Sleep and distress assessment should be integrated into chemotherapy-period risk stratification alongside standardized clinical scoring and performance-status evaluation.

Keywords: chemotherapy; sleep; psychological stress; ABO blood group; APACHE II; Karnofsky Performance Status; ECOG; performance status

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1 Introduction

Cancer patients receiving chemotherapy often face overlapping physiological and psychoso-cial stressors: cytotoxic treatment, comorbidity burden, supportive care medication, sleep disruption, and distress. In real-world oncology, these exposures rarely occur in isolation. Patients may receive multiple drugs simultaneously, experience poor sleep and stress, and present with varying levels of functional reserve, all of which can shape treatment tolerance and acute clinical status.

ABO/Rh blood groups represent one possible baseline biological modifier because ABO antigens influence inflammation, thrombosis, cell adhesion, and cancer susceptibility. His-torically regarded as red blood cell membrane markers, ABO histoblood antigens are now widely recognized as expressed glycan determinants present on vascular endothelial cells and pathological tissues [4, 6]. Non-O individuals exhibit a significantly elevated risk of developing certain malignancies [5, 8–10], largely due to mechanisms encompassing altered cell adhesion [1, 4], immune evasion [1], and persistent

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elevations in prothrombotic factors like the von Willebrand factor (VWF)-Factor VIII complex [2, 7].
However, an "active treatment paradox" exists regarding the acute relevance of these markers. While ABO blood groups establish baseline lifetime risks, their clinical signal may be heavily overshadowed once a patient faces a major, active physiological stressor. For example, while blood type influences early-stage organ dysfunction in sepsis [6], multivariable models in acute pulmonary embolism have shown that ABO type does not independently predict acute biomarker expression when adjusting for active hemodynamic strain [7]. In oncology, chemotherapy constitutes a massive systemic toxicity that induces cellular damage and physiological derangement. It remains unclear whether inherited markers retain measurable clinical relevance once patients are already undergoing active chemotherapy.
By contrast, dynamic factors such as psychological stress and sleep disruption may have more immediate effects on autonomic regulation, inflammatory tone, immune resilience, and daily functional capacity. Sleep is critical for cellular restoration, and psychological distress deeply influences systemic cytokine release. When compounded by comorbidity and concurrent supportive medications, the active treatment state may drown out the subtler physiological differences conferred by baseline ABO/Rh blood groups.
This study therefore evaluates the interplay of ABO/Rh blood groups, stress, sleep, polypharmacy, and clinical severity in a real-world cohort of cancer patients undergoing active chemotherapy. The central question is whether inherited blood group markers or modifiable psychosocial factors better explain acute physiological severity (measured by APACHE II) and performance status (KPS, ECOG) during active treatment.

2 Methods

2.1 Study Design and Setting

This was an observational, prospective cohort study conducted at two tertiary-care oncology centers in Pune, Maharashtra, India: the **Lokmanya Holistic Cancer Care & Research Center** and **Ruby Hall Clinic (Hinjawadi)**. The multi-center design was selected to capture a diverse patient population representing the broad range of cancer diagnoses and chemotherapy regimens encountered in a real-world Indian oncological setting. No experimental intervention was performed; exposures (medication regimens, lifestyle factors, blood group) and outcomes (clinical severity scores) were observed as they naturally occurred.

2.2 Study Period and Patient Enrollment

Data collection was conducted prospectively over a continuous period of **six months**. Partic-ipants were recruited consecutively upon presenting for scheduled outpatient chemotherapy sessions or related follow-up appointments.
Inclusion criteria: (1) A confirmed diagnosis of any cancer type actively receiv-ing chemotherapy; (2) Concurrent prescription of three or more medications (inclusive of chemotherapy and supportive care agents), constituting the study's definition of polyphar-macy; (3) Provision of voluntary written informed consent.
Exclusion criteria: (1) Patients receiving only a single-agent chemotherapy regimen without additional concurrent medications; (2) Inaccessible or incomplete clinical records precluding comprehensive data extraction; (3) Concurrent diagnosis of Human Immunodeficiency Virus (HIV) infection.

2.3 Sample Size

The study's sample-size calculation yielded a minimum requirement of 197 participants after finite population correction and a 10% buffer for incomplete records or dropout. The final enrolled cohort comprised **n = 200 patients**, which was retained for the present analysis.

2.4 Data Collection and Variables

A pre-designed, structured electronic **Data Collection Form (DCF)** was used to capture all study variables. Trained PharmD students reviewed patient medical records at each chemotherapy visit, updating the DCF longitudinally.
Demographic and clinical variables collected included: age (continuous, in years), sex (male/female), primary cancer diagnosis and category, disease stage, individual comorbid conditions, and ABO/Rh blood group. Baseline comorbidity burden was quantified using the **Charlson Comorbidity Index (CCI)**. The **modified Glasgow Prognostic Score (mGPS)** was also recorded.
Physiological severity was primarily assessed using **APACHE II (Acute Physiology and Chronic Health Evaluation II)**, calculated from 12 acute physiological variables plus age and chronic health points. Higher scores indicate greater physiological derangement. SAPS II and SOFA were recorded as secondary clinical-severity and organ-dysfunction context.
Functional performance status was assessed using the **Karnofsky Performance Status (KPS)** (0-100 scale) and the **ECOG Performance Status** (0-5 ordinal scale).
Lifestyle factors – stress level and sleep quality – were collected via structured patient self-report interviews administered during clinic visits. To minimize patient burden in a busy real-world oncology clinic, rapid categorical screening questions were utilized in lieu of lengthy validated questionnaires. Patients rated their typical stress intensity (on a categorical scale: none/mild/moderate/severe) and their average nightly sleep duration (in hours). These were operationalized as ordinal independent variables in the regression analyses.

2.5 Statistical Analysis

All statistical analyses were performed using **SPSS version 26.0** and **Python (pandas, scipy, scikit-learn)**. Continuous variables are presented as mean ± standard deviation (SD) or median (interquartile range [IQR]), as appropriate based on normality testing. Categorical variables are expressed as frequencies and percentages.

Bivariate associations between independent variables and APACHE II or functional performance scores were assessed using Pearson's or Spearman's correlation coefficients, independent samples t-tests, Mann-Whitney U tests, chi-square tests, or Kruskal-Wallis tests, as appropriate.

Multiple linear regression was used to identify independent predictors of APACHE II score (the primary outcome), entering clinically relevant and bivariate-informative variables into the model. Assumptions of linear regression, including multicollinearity (via VIF) and residual normality, were checked to ensure model validity. Results are reported as model coefficients with p-values. Statistical significance was set at p ¡ 0.05.

2.6 Ethical Considerations

The study was conducted in full accordance with the ethical principles of the Declaration of Helsinki. Ethical clearance was obtained from the Institutional Ethics Committees of both participating centers prior to data collection. Written informed consent was obtained from all adult participants.

3 Results

3.1 Baseline Characteristics of the Study Cohort

The final enrolled cohort included 200 patients receiving active chemotherapy with concurrent polypharmacy. Females comprised 53.0% of the cohort (n = 106), while males comprised 47.0% (n = 94). The largest age group was 55-64 years (32.0%), followed by patients aged
≤44 years (26.0%).

Blood group distribution was uneven, with B+ being the most common group (n = 80, 40.0%), followed by A+ (n = 49, 24.5%), O+ (n = 37, 18.5%), B- (n = 16, 8.0%), A- (n
= 12, 6.0%), and O- (n = 6, 3.0%). No patients with the AB blood group were enrolled during the consecutive sampling period, reflecting natural sampling variation rather than active exclusion.

The most common cancer categories were breast cancer (n = 44), ovarian cancer (n = 26), lung cancer (n = 18), head and neck cancer (n = 14), and colorectal cancer (n = 14). The most frequent comorbidities reported in the cohort were hypertension (n = 67, 33.5%) and diabetes mellitus (n = 58, 29.0%).

3.2 APACHE II Severity and Functional Status

APACHE II was the primary physiological severity measure for this manuscript. The mean APACHE II score was 20.65 ± 6.17, with a median of 23.00 and a range of 5-31, indicating a cohort with moderate acute physiological derangement during active chemotherapy. Secondary metrics demonstrated a mean SAPS II of 23.91 ± 7.70, while SOFA scores were generally low (mean 0.44 ± 1.25), suggesting that acute physiological stress was more prominent than established multi-organ failure (Table 1).

Table 1: **Descriptive statistics for clinical severity scores.**

Score	Role in manuscript	Mean ± SD	Median	Range
APACHE II	Primary severity outcome	20.65 ± 6.17	23.00	5-31
SAPS II	Secondary context	23.91 ± 7.70	22.00	7-50
SOFA	Secondary context	0.44 ± 1.25	0.00	0-7

KPS and ECOG demonstrated strong internal concordance, with a strong inverse Spear-man correlation (rho = -0.73), confirming that lower KPS scores aligned with higher ECOG grades and poorer functional capacity.

3.3 Sleep, Stress, and Functional Performance

Patient-reported sleep and stress were meaningfully related to functional status (Table 2). Better sleep was associated with higher KPS scores (rho = 0.50) and lower ECOG grades (rho = -0.39). Higher stress was associated with lower KPS scores (rho = -0.41) and higher ECOG grades (rho = 0.40). Sleep and stress were inversely related (rho = -0.35), suggesting that patients reporting poorer sleep tended to report higher stress burden.

Table 2: **Key Spearman correlations involving functional status, sleep, and stress.**

Correlation pair	Spearman rho	Interpretation
KPS vs ECOG	-0.73	Strong inverse relationship between functional scales
KPS vs sleep	0.50	Better sleep associated with better KPS
KPS vs stress	-0.41	Higher stress associated with worse KPS
ECOG vs sleep	-0.39	Better sleep associated with lower ECOG grade
ECOG vs stress	0.40	Higher stress associated with worse ECOG grade
Sleep vs stress	-0.35	Poorer sleep associated with higher stress

3.4 ABO/Rh Blood Groups and Clinical Severity

Blood group was not significantly associated with cancer type in this cohort (chi-square = 468.41, p = 0.098). The association between blood group and APACHE II was weak and statistically non-significant (rho = 0.15, p = 0.1325).

Secondary contextual analyses also showed no meaningful correlation between blood group and SAPS II (rho = -0.01, p = 0.9089) or SOFA (rho = -0.10, p = 0.3330). These findings suggest that ABO/Rh blood group did not meaningfully stratify acute physiological severity during active chemotherapy.

3.5 Demographic and Disease-Related Group Comparisons

Gender was not significantly associated with any assessed clinical severity, functional, sleep, or stress measure (all p ¿ 0.05). Broad comparisons across cancer types showed no statistically significant differences for the central outcomes, including APACHE II (H = 10.41, p = 0.8856), KPS (H = 18.28, p = 0.1942), and ECOG (H = 21.75, p = 0.1947). Secondary contextual scores were also non-significant across cancer types (Table 3).

Table 3: **Summary of bivariate group comparisons.**

Comparison	Test	Statistic	p-value	Finding
Gender vs APACHE II	Mann-Whitney U	1446.00	0.3291	Not significant
Blood group vs cancer type	Chi-square	468.41	0.098	Not significant
Cancer type vs APACHE II	Kruskal-Wallis H	10.41	0.8856	Not significant
Cancer type vs ECOG	Kruskal-Wallis H	21.75	0.1947	Not significant

3.6 Multivariable Predictors of APACHE II Severity

Multivariable analysis identified several independent predictors of higher APACHE II severity (Table 4). Higher self-reported stress was a strong independent predictor of higher APACHE II scores (coefficient +3.28, p ¡ 0.001). Sleep showed a protective association, with better sleep linked to lower APACHE II scores (coefficient -1.25, p = 0.046). Age also showed a graded association with APACHE II severity, with older age groups associated with higher scores. Poorer functional status by KPS/ECOG categories was associated with higher APACHE II severity. Conversely, the Charlson Comorbidity Index and younger age categories were not significant independent predictors, suggesting that age, stress, sleep, and functional status captured more of the acute severity signal than general comorbidity burden.

Table 4: **Significant predictors of higher APACHE II severity in multivariable modeling.**

Predictor/domain	Direction of association	Reported statistical detail
Stress	Higher stress associated with higher APACHE II	Coefficient +3.28, p ¡ 0.001
Sleep	Better sleep associated with lower APACHE II	Coefficient -1.25, p = 0.046
Older age	Older age groups associated with higher APACHE II	Significant, especially 65-74 and ≥75 years
Functional status	Poorer KPS/ECOG associated with higher APACHE II	Significant for poorer performance categories

4 Discussion

4.1 Principal Findings

This study demonstrates that in patients receiving active chemotherapy with polypharmacy, subjective stress and sleep quality are not merely quality-of-life variables; they are clinically relevant correlates of APACHE II physiological severity and KPS/ECOG functional performance. Higher stress and poorer sleep were associated with worse APACHE II scores and poorer functional status. In contrast, ABO/Rh blood group did not show significant associations with APACHE II severity, cancer type, or performance status.

These findings support the active treatment paradox: while ABO/Rh blood groups shape baseline susceptibility to malignancy, inflammation, and vascular biology [1, 2, 4], their clinical signal is weak during active systemic therapy. In this setting, the immediate physiological derangements driven by psychosocial distress, sleep disruption, and cytotoxic therapy dominate over inherited genetic predispositions.

4.2 Why Stress Predicted Physiological Severity

The independent association between stress and APACHE II severity (coefficient +3.28) is mechanistically grounded. Psychological distress in oncology patients activates the Hypothalamic-Pituitary-Adrenal (HPA) axis and the Sympathetic Nervous System (SNS) [14, 18]. Chronic stress disrupts the diurnal cortisol rhythm [10, 13] and triggers the release of catecholamines, which bind to adrenergic receptors on tumor and endothelial cells [12].

Importantly, this autonomic disruption reduces

parasympathetic (vagal) tone, removing the natural neuro-immune defense against inflammatory tissue damage [18, 19].

This neuroendocrine shift drives systemic dysregulation, upregulating NF-κB pathways and causing the hypersecretion of pro-inflammatory cytokines, primarily IL-6 and TNF-α [10, 11, 17]. When systemic chemotherapy is introduced, it represents an iatrogenic cellular assault that induces apoptosis and secondary systemic inflammation [15]. In a highly distressed patient, these two pathways act in synergy – a ”double hit” of psychological stress-induced cytokine release and chemotherapeutic cytotoxicity [14, 15, 18]. This synergism results in autonomic instability and subclinical microvascular coagulation [6, 18]. Because APACHE II aggregates vital sign fluctuations and biochemical abnormalities, it is exquisitely sensitive to this stress-amplified physiological vulnerability.

4.3 Why Sleep Was Linked to APACHE II and Performance Status

The sleep and circadian literature strongly supports our findings linking sleep quality to objective severity. Sleep is fundamentally governed by a homeostatic drive and the circadian clock, which directly regulates core molecular machinery governing DNA damage repair, mitochondrial quality control, and glymphatic clearance [20, 22]. When this restorative window is fragmented, cellular repair loses efficiency, compounding treatment vulnerability [22].

Crucially, cancer treatment itself directly damages sleep architecture. Preclinical teleme-try studies have demonstrated that methotrexate (MTX) chemotherapy directly causes NREM sleep fragmentation, independent of psychological factors, with effects persisting long after active drug exposure [24]. Similarly, universally co-administered corticosteroids like dexamethasone produce acute dysregulation of circadian activity rhythms [23]. Chemotherapy-induced circadian disruption creates a dangerous feedback loop: damaged sleep prevents cellular restoration, which heightens sensitivity to subsequent toxic insults [21].

This sleep-immune dysregulation provides a direct bridge to physiological severity. Sleep disruption withdraws nocturnal vagal tone, elevating circulating levels of IL-6 and CRP during wakefulness [20, 22]. These cytokines destabilize the physiological parameters captured by APACHE II, altering thermoregulation and autonomic cardiovascular control [20, 22].

Furthermore, because skeletal muscle function relies on nocturnal glycogen resynthesis and ATP regeneration during slow-wave sleep, sleep fragmentation leads to progressive muscle catabolism and cancer-related fatigue [23, 24]. This manifests clinically as the functional decline captured precisely by the KPS and ECOG scales.

4.4 Clinical Implications

The findings support a more holistic chemotherapy risk assessment model. Routine oncology care commonly emphasizes tumor type, stage, regimen toxicity, organ function, and perfor-mance status. This study suggests that stress and sleep should also be assessed because they identify patients with reduced physiological reserve and poorer functional capacity. Practical implications include incorporating brief sleep and distress screening into chemotherapy visits, flagging patients with high stress or poor sleep for supportive care review, and treating sleep/stress concerns as clinically meaningful risk modifiers rather than secondary complaints.

4.5 Limitations

Several limitations should be considered. First, sleep and stress were collected through structured single-item self-reports to minimize patient burden, rather than validated multi-item instruments (e.g., PSQI, PSS). Therefore, the associations observed should be interpreted as clinically important signals that require further validation. Second, the observational, cross-sectional nature of the data collection limits causal inference. A bidirectional relationship likely exists: poor sleep and high stress may worsen clinical severity, but high physiological derangement (APACHE II) and disease burden may equally disrupt sleep and exacerbate psychological stress. Finally, the cohort was drawn from two centers in Pune, India, which may limit generalizability, and subgroup analyses by blood group or cancer type may have been underpowered for detecting small genetic effects.

5 Conclusion

In this prospective observational cohort of chemotherapy patients, modifiable psychosocial and functional variables were more clinically informative than ABO/Rh blood groups in predicting APACHE II physiological severity. Higher stress, poorer sleep, older age, and poorer KPS/ECOG performance were significantly associated with higher APACHE II severity, while blood group showed no acute prognostic value. Chronic stress and sleep disruption biologically compromise circadian, immune, and cellular repair systems, amplifying physiological derangement during cytotoxic treatment. The findings strongly advocate for the integration of sleep and distress assessments into routine chemotherapy-period risk stratification alongside standard clinical scoring.

Declarations

Ethics approval and consent to participate: Ethical approval was obtained from the participating institutional ethics committees. Written informed consent was obtained from all participants.

Consent for publication: Not applicable.

Availability of data and materials: Available from the corresponding author upon reasonable request, subject to institutional permissions.

Competing interests: The authors declare no competing interests.

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Authors' contributions: SAP conceptualized the study, performed the data analysis, drafted the manuscript, and conducted the primary research work. MRK, AA, DC, and PSK assisted in data collection, participated in editing, and critically reviewed the manuscript. All authors read and approved the final version of the manuscript.

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References

1. Qin, L., Gao, D., Wang, Q., Zheng, X., Wang, J., Chen, X., Fu, D., Ma, H., Tan, J., & Yin, Q. (2023). ABO Blood Group and the Risk and Prognosis of Lymphoma. *Journal of Inflammation Research*, 16, 769-778. https://doi.org/10.2147/JIR.S401818
2. Franchini, M., Favaloro, E. J., Targher, G., & Lippi, G. (2012). ABO blood group, hyper-coagulability, and cardiovascular and cancer risk. *Critical Reviews in Clinical Laboratory Sciences*, 49(4), 137-148. https://doi.org/10.3109/10408363.2012.708647
3. Hoiland, R. L., Fergusson, N. A., Mitra, A. R., Griesdale, D. E. G., Devine, V. V.,
4. Stukas, S., Cooper, J., Thiara, S., Foster, D., Chen, L. Y. C., Lee, A. Y. Y., Conway, E. M., Wellington, C. L., & Sekhon, M. S. (2020). The association of ABO blood group with indices of disease severity and multiorgan dysfunction in COVID-19. *Annals of the American Thoracic Society / Blood Advances*, 4(20), 4981-4989. https://doi.org/10.1182/bloodadvances.2020002623
5. Franchini, M., Liumbruno, G. M., & Lippi, G. (2016). The prognostic value of ABO blood group in cancer patients. *Blood Transfusion*, 14(5), 434-440. https://doi.org/ 10.2450/2015.0164-15
6. Luo, W., Wang, J., Chen, H., Ye, L., Qiu, J., Liu, Y., Wang, R., Weng, G., Liu, T., Su, D., Tao, J., Ding, C., You, L., & Zhang, T. (2023). Epidemiology of pancreatic cancer: New version, new vision. *Chinese Journal of Cancer Research*, 35(5), 438-450. https://doi.org/10.21147/j.issn.1000-9604.2023.05.03
7. Zheng, H., Li, J., Jin, H., Zhang, Q., Song, H., & Yi, L. (2023). Impact of ABO Blood Type on Morbidity of Organ Dysfunction in Septic Patients: A Single-Center Retrospective Observational Study. *Health Science Reports*, 8(12), e71506. https://doi.org/10.1002/hsr2.71506
8. Eddin, A. J., Stanciugelu, S. I., Damian, A. D., Miutescu, B. P., Tunea, O. E., & Mozos, I. M. (2023). ABO Blood Group and Biomarker-Based Risk in Acute Pulmonary Embolism: A Retrospective Cohort Study. *Journal of Clinical Medicine*, 15(4), 1432. https://doi.org/10.3390/jcm15041432
9. Greer, J. B., LaRusch, J., Brand, R. E., O'Connell, M. R., Yadav, D., & Whitcomb, D. C. (2011). ABO blood group and chronic pancreatitis risk in the NAPS2 cohort. *Pancreatology / NIH MS*, 11(4), 406-413. https://doi.org/10.1159/000330195
10. Yu, H., Xu, N., Li, Z. K., Xia, H., Ren, H. T., Li, N., Wei, J. B., & Bao, H. (2020).
11. Association of ABO Blood Groups and Risk of Gastric Cancer. *Scandinavian Journal of Surgery*, 109(4), 309-313. https://doi.org/10.1177/1457496919863886
12. Montgomery, K. E., Basha, M., Nyholm, L., Smith, C., Ananiev, G., Fedorov, A., Kapoor, A., Brown, R., Capitini, C., & Kwekkeboom, K. (2024). Exploring Inflammation and Stress as Biological Correlates of Symptoms in Children With Advanced Cancer: A Longitudinal Feasibility Study. *Journal of Pediatric Oncology Nursing*, 41(3), 199-213. https://doi.org/10.1177/27527530231214544
13. Koh, S. J., Park, J., Lee, M. A., Suh, S. Y., Kwak, S. M., Choi, Y. S., Yoon, H. M., Kim, D. G., Song, S. H., Lee, Y. J., & Yeom, C. H. (2012). The relationship between interleukin-6, tumor necrosis factor-alpha, and fatigue in terminally ill cancer patients. *Palliative Medicine*, 26(3), 275-283. https://doi.org/10.1177/0269216311406991
14. Stavropoulos, I., Sarantopoulos, A., & Liverezas, A. (2020). Does sympathetic nervous system modulate tumor progression? A narrative review of the literature. *Journal of Drug Assessment*, 9(1), 106-116. https://doi.org/10.1080/21556660.2020.1782414
15. Jagielo, A. D., Benedict, C., & Spiegel, D. (2023). Circadian, hormonal, and sleep rhythms: effects on cancer progression implications for treatment. *Frontiers in Oncology*, 13, 1269378. https://doi.org/10.3389/fonc.2023.1269378
16. Hong, Y., Zhang, L., Liu, N., Xu, X., Liu, D., & Tu, J. (2022). The Central Nervous Mechanism of Stress-Promoting Cancer Progression. *International Journal of Molecular Sciences*, 23(20), 12653. https://doi.org/10.3390/ijms232012653
17. Nnadi, C. V., Olawade, D. B., Shorter, S., Oisakede, E. O., Boussios, S., & Ovsepian,
18. S. V. (2023). Redefining Chemotherapy-Related Headaches: From Pathobiology to Differential Diagnosis and Management. *International Journal of Molecular Sciences*, 27(1), 262. https://doi.org/10.3390/ijms27010262
19. Kim, Y., Chung, M. L., & Lee, H. (2021). Caregivers of patients with cancer: perceived stress, quality of life and immune function. *BMJ Supportive & Palliative Care*, 15(2), 195-203. https://doi.org/10.1136/bmjspcare-2021-003205
20. Miaskowski, C., Cataldo, J. K., Baggott, C. R., West, C., Dunn, L. B., Dhruva, A.,
21. Merriman, J. D., Langford, D. J., Kober, K. M., Paul, S. M., Cooper, B. A., & Aouizerat, B. E. (2017). Cytokine gene variations associated with trait and state anxiety in oncology patients and their family caregivers. *Oncology Nursing Forum*, 44(4), 465-477. https://doi.org/10.1188/17.ONF.465-477
22. Oncology Reports. (2021). Chronic stress and

cancer progression through neuro-endocrine-immune networks (Review). *Oncology Reports*, 56(1), 123. https://doi.org/10.3892/ or.2026.9128

23. Tibensky, M., & Mravec, B. (2020). Role of the parasympathetic nervous system in cancer initiation and progression. *Clinical and Translational Oncology*, 22(8), 1221-1233. https://doi.org/10.1007/s12094-020-02465-w
24. Vaughn, C. M., & Vaughn, B. V. (2023). Sleep and Cancer. *Cancers*, 17(6), 911
25. https://doi.org/10.3390/cancers17060911
26. Balachandran, D. D., Bashoura, L., Sheshadri, A., Manzullo, E., & Faiz, S. A. (2023). The Impact of Immunotherapy on Sleep and Circadian Rhythms in Patients with Cancer.
27. *Frontiers in Oncology*, 13, 1295267. https://doi.org/10.3389/fonc.2023.1295z67
28. Lemanowicz, J., Kloska, S. M., Siwik-Ziomek, A., Kolaczyk, P., Wnuk Lipinska, U., & Kloska, A. (2022). Biochemical Mechanisms of Cellular Stress Adaptation in the Pathogenesis of Chronic Diseases. *Molecules*, 31(9), 1381. https://doi.org/10.3390/ molecules31091381
29. Rogers, V. E., Zhu, S., Mandrell, B. N., Ancoli-Israel, S., Liu, L., & Hinds, P. S. (2020). Relationship Between Circadian Activity Rhythms and Fatigue in Hospitalized Children with CNS Cancers Receiving High Dose Chemotherapy. *Supportive Care in Cancer*, 28(3), 1459-1467. https://doi.org/10.1007/s00520-019-04960-5
30. Boyd, L., Berisha, A., Gomez, A. M., Gibson, E. M., & Borniger, J. C. (2023). Enduring non-rapid eye movement sleep fragmentation following methotrexate chemotherapy in cancer-naive mice. *SLEEP*, zsaf073. https://doi.org/10.1093/sleep/zsaf073
31. Cubillos-Zapata, C., Almendros, I., Diaz-Garcia, E., Toledano, V., Casitas, R., Galera, R., Lopez-Collazo, E., Farre, R., Gozal, D., & Garcia-Rio, F. (2020). Differential effect of intermittent hypoxia and sleep fragmentation on PD-1/PD-L1 upregulation. *SLEEP*, 43(4), zsz285. https://doi.org/10.1093/sleep/zsz285