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## How sleep quality shapes post-vaccination health: A multi-organ system investigation

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### Abstract

Significant diversity remains regarding the reported adverse events post COVID-19 vaccinations. However, the data on the impact of sleep on COVID-19 vaccination's adverse effects are very limited. This hinders our capacity to deliver truly personalised risk-benefit guidance and optimise vaccination strategies for diverse populations. Therefore, the study aims to explore the impact of sleep duration on the body systems post-COVID-19 vaccinations among healthy adults. This cross-sectional study was conducted between April 1 and June 30, 2022, in the Eastern Province, Saudi Arabia. The survey instrument is composed of two main core components. First, participant characteristics include health data, age, gender, body metrics, and sleeping habits. Second, self-reported body system side effects were assessed using a 32-item questionnaire. A total of 375 participants completed the survey and were included in the study. The majority were Female, obese and young participants. The majority of participants exhibited optimal sleep patterns. Our findings suggest that inadequate sleep may be accompanied by cardiorespiratory side effects such as shortness of breath and chest pain, and neurological side effects such as headache and dizziness after all COVID-19 vaccination doses. Moreover, involvement of gastrointestinal, dermatological, and musculoskeletal systems can follow in irregular temporal patterns after sequential COVID-19 vaccine doses. In conclusion, sleep-deprived individuals, particularly young healthy, may face amplified potential risks post COVID-19 vaccination, particularly after repeated vaccination doses. Understanding these interactions is crucial for developing personalised vaccination approaches that maximise benefits while minimising harm, particularly as booster vaccination.

**Keywords:** COVID-19, Healthy, Hurvey, Side effects, Sleep, Vaccination.

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**Transparency:** The authors confirm that the manuscript is an honest, accurate, and transparent account of the study; that no vital features of the study have been omitted; and that any discrepancies from the study as planned have been explained. This study followed all ethical practices during writing.

**Institutional Review Board Statement:** Ethical oversight was ensured through approval by the Imam Abdulrahman Bin Faisal University Ethics Committee (Protocol IRB-2022-19-147), aligning with institutional standards for human subject research. All participants were electronically consented.

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## 1. Introduction

In late December 2019, investigations recognized the outbreak of Coronavirus Disease 2019 (COVID-19), caused by a novel highly contagious coronavirus later named Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). It began as a few unexplained cases of pneumonia in Wuhan city of China and is believed to have originated in a seafood market [1, 2].

According to World Health Organization (WHO) reports, confirmed cases between December 2019 and March 2020 reached 750,890 and led to 36,405 deaths globally [3].

Saudi Arabia experienced a significant rise in cases with the first incidence reported in early March 2020 [4]. The incidence and prevalence of cases differed depending on the region [5].

COVID-19 vaccinations have helped save millions of lives globally. However, vaccinations are not without potential adverse effects. Previous studies reported three primary categories of aftereffects. Injection site reactions such as pain, redness, induration, and itch. Systemic side effects include symptoms like fever, headache, fatigue, dizziness, muscle pain, abdominal pain, diarrhea, vomiting, nausea, cough, dyspnea, impaired appetite, sore throat, hives, and nasal congestion. Serious vaccination-induced adverse events include thrombotic complications, hospitalization, and deaths [6].

Sleep and circadian rhythm play a role in the immunological homeostasis. Sleep favors the proinflammation state while daytime favors the anti-inflammation state. Therefore, any disturbance in sleep habits and circadian rhythm may disturb immunity and increase susceptibility to viral infection [7]. Sleep affects the adaptive immune system which has a role in the memory formation of viruses and vaccination [7]. Many studies investigate the impact of sleep and circadian rhythm on vaccination success. The sleep duration affects antibody titers after vaccination [7].

Although COVID-19 vaccines are generally well-tolerated overall [8] significant diversity remains regarding the reported adverse events that differ across vaccine platforms (e.g., mRNA vs. viral vector) and dose sequences (e.g., primary series vs. boosters) [9, 10].

However, the data on the impact of sleep on COVID-19 vaccination's adverse effects are very limited. This hinders our capacity to deliver truly personalised risk-benefit guidance and optimise vaccination strategies for diverse populations. Therefore, the study aims to explore the impact of sleep duration on the body systems post-COVID-19 vaccinations among healthy adults.

## 2. Materials and Methods

This cross-sectional study was conducted between April 1 and June 30, 2022, in the Eastern Province Saudi Arabia's. To ensure broad representation, recruitment utilized convenience sampling alongside targeted social media outreach.

The inclusion criteria for this study were healthy adults who had received all three doses of a COVID-19 vaccination (Pfizer) and electronically consented to join the study. Individuals with active COVID-19 infections or unvaccinated status were excluded to maintain focus on post-vaccination experiences.

The survey instrument composed two main core components. First, participant characteristics health data, age, gender, body metrics, and sleeping habits. Second, self-reported body systems side effects were assessed using a 32-item questionnaire adapted from validated instruments employed in prior research represent body systems, with responses gauged on an 11-point severity scale [11, 12].

To guarantee linguistic accuracy, the questionnaire underwent a rigorous forward-and-backward translation process, adhering to established methodological practices for cross-cultural studies [13].

The required sample size was calculated as 384 using the OpenEpi online sample size calculator, based on a 95% confidence level, 5% margin of error, and an estimated population of 1,090,268 [14].

Ethical oversight was ensured through approval by the Imam Abdulrahman Bin Faisal University Ethics Committee (Protocol IRB-2022-19-147), aligning with institutional standards for human subject research. All participants were electronically consented.

### **3. Data Analysis**

Data management and initial descriptive statistics (mean  $\pm$  standard deviation) summarizing participant characteristics were conducted using Microsoft Excel and IBM SPSS Statistics (Version 26). Addressing our core research questions on sleep and vaccination effects, we categorized sleep duration into three levels: insufficient ( $<5$  hours), intermediate (5 to  $<7$  hours), and sufficient ( $\geq 7$  hours). We then used multivariate analysis of variance (MANOVA) in SPSS to evaluate the overall association between these sleep groups and combined effects across body systems following each COVID-19 vaccine dose. The model also included list confounders (age, sex, and BMI). Where MANOVA indicated significant differences, we performed follow-up Tukey's Honestly Significant Difference (HSD) tests to identify which specific sleep duration groups differed from each other. Results were considered statistically significant at  $p < 0.05$ .

### **4. Results**

#### *4.1. Demographic Data*

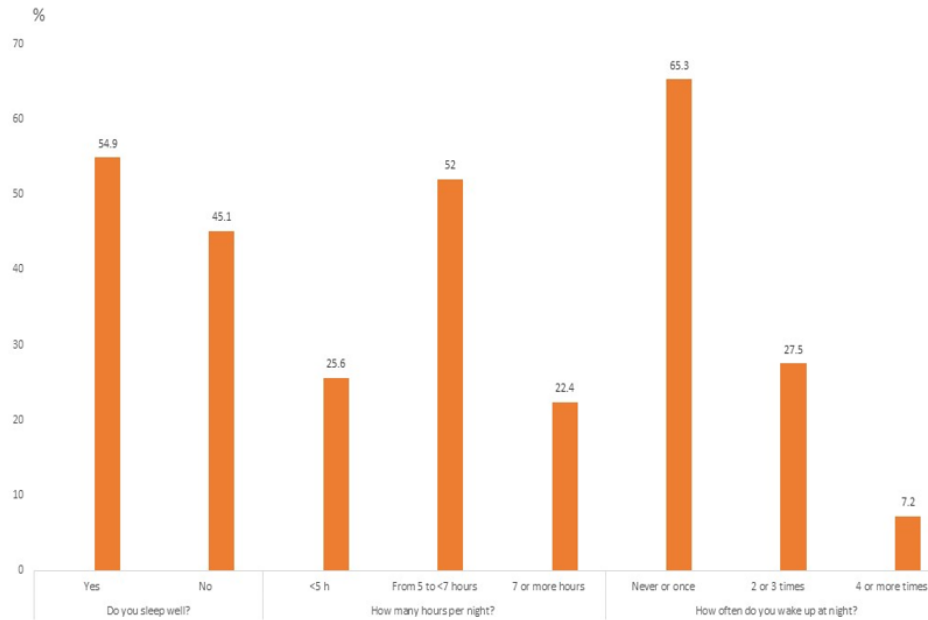
Table 1 shows the demographic data of the study participants. A total of 375 participants were completed the survey and included in the study. The majority were Female, obese and young participants.

**Table 1.**

Participant characteristics.

Characteristics	% or Mean± standard deviation
Males/Females (%)	44/56
Body mass index (Mean± standard deviation)	23.7±5.6
Age (Mean± standard deviation)	22.0±8.9

As illustrated in Figure 1 the majority of participants exhibited optimal sleep patterns, characterized by 5-7 hours of sleep duration and  $\leq 1$  nightly awakening.

**Figure 1.**

Sleeping habits and quality of the participants.

#### 4.2. Impact of Sleeping Hours on Body Systems Post-COVID-19 Vaccinations

The results of the impact of sleeping duration on the body systems reported after the three doses of COVID-19 vaccinations were categorized into the following groups: cardiorespiratory, gastrointestinal, dermatological/musculoskeletal, and neurological (Table 2).

**Table 2.**  
Impact of sleeping hours on body systems post COVID-19 Vaccinations.

Systems	1 <sup>st</sup> dose			2 <sup>nd</sup> dose			3 <sup>rd</sup> dose		
	<5 hr vs 5 to <7 hr MD (95% CI)	<5 hr vs ≥7 hr MD (95% CI)	5 to <7 hr vs ≥7 hr MD (95% CI)	<5 hr vs 5 to <7 hr MD (95% CI)	<5 hr vs ≥7 hr MD (95% CI)	5 to <7 hr vs ≥7 hr MD (95% CI)	<5 hr vs 5 to <7 hr MD (95% CI)	<5 hr vs ≥7 hr MD (95% CI)	5 to <7 hr vs ≥7 hr MD (95% CI)
Cardiorespiratory									
Shortness of breath	0.40 (-0.21 to 1.01)	0.77* (0.03 to 1.50)	0.37 (-0.28 to 1.01)	0.84* (0.18 to 1.49)	0.71 (-0.07 to 1.5)	-0.12 (-0.81 to 0.56)	0.83* (0.2 to 1.46)	1.01* (0.25 to 1.77)	0.18 (-0.49 to 0.84)
Hoarse voice	0.38 (0.00 to 0.76)	0.34 (-0.12 to 0.80)	-0.04 (-0.45 to 0.36)	0.19 (-0.17 to 0.56)	0.26 (-0.18 to 0.7)	0.7 (-0.32 to 0.45)	0.44* (0.05 to 0.84)	0.43 (-0.04 to 0.9)	-0.01 (-0.42 to 0.4)
Chest pain	0.68* (0.06 to 1.30)	0.88 (0.14 to 1.63)	0.2 (-0.45 to 0.86)	0.76* (0.14 to 1.37)	0.75* (0.01 to 1.48)	-0.01 (-0.66 to 0.63)	0.82* (0.18 to 1.45)	1.2* (0.45 to 1.96)	0.39 (-0.28 to 1.05)
Sore throat	0.59* (0.01 to 1.16)	0.37 (-0.31 to 1.05)	-0.22 (-0.81 to 0.38)	0.29 (-0.14 to 0.73)	0.26 (-0.26 to 0.79)	-0.03 (-0.49 to 0.43)	0.60* (0.08 to 1.12)	0.76* (0.14 to 1.38)	0.16 (-0.38 to 0.70)
Sneezing	0.40 (-0.18 to 0.97)	0.19 (-0.49 to 0.88)	-0.20 (-0.80 to 0.40)	0.07 (0.52 to 0.65)	0.15 (-0.55 to 0.85)	0.09 (-0.53 to 0.70)	0.52* (0.01 to 1.04)	0.35 (-0.27 to 0.97)	-0.18 (-0.72 to 0.37)
Irregular heartbeat	0.41 (-0.29 to 1.1)	0.73 (-0.11 to 1.56)	0.32 (-0.41 to 1.05)	0.51 (-0.10 to 1.12)	0.37 (-0.37 to 1.11)	-0.14 (-0.79 to 0.5)	0.58 (-0.10 to 1.27)	0.88* (0.05 to 1.70)	0.29 (-0.43 to 1.02)
Gastrointestinal									
Diarrhea	0.27 (-0.15 to 0.69)	0.25 (-0.25 to 0.75)	-0.02 (-0.46 to 0.42)	0.44* (0.03 to 0.85)	0.27 (-0.22 to 0.77)	-0.16 (-0.59 to 0.27)	0.46 (-0.02 to 0.94)	0.27 (-0.31 to 0.84)	-0.19 (-0.70 to 0.31)
Skipped meals	0.67 (-0.08 to 1.42)	1.15* (0.25 to 2.05)	0.48 (-0.31 to 1.26)	0.43 (-0.24 to 1.09)	0.76 (-0.03 to 1.56)	0.34 (-0.36 to 1.03)	0.72* (0.06 to 1.38)	1.34* (0.56 to 2.13)	0.62 (-0.07 to 1.31)
Dermatological & musculoskeletal									
Unusual muscle pains	0.16 (-0.89 to 1.22)	0.92 (-0.32 to 2.17)	0.76 (-0.33 to 1.85)	-0.06 (-1.04 to 0.91)	0.79 (-0.37 to 1.95)	0.86 (-0.15 to 1.87)	0.49 (-0.47 to 1.45)	1.29* (0.15 to 2.42)	0.79 (-0.20 to 1.79)
Rash	0.19 (-0.15 to 0.54)	0.36 (-0.5 to 0.77)	0.17 (-0.19 to 0.53)	0.35* (0.04 to 0.66)	0.25 (-0.13 to 0.62)	-0.10 (-0.42 to 0.22)	0.27 (-0.09 to 0.62)	0.40 (-0.03 to 0.83)	0.13 (-0.24 to 0.51)
Sensation of skin burning	0.28 (-0.11 to	0.40 (-0.08 to 0.87)	0.11 (-0.30 to 0.53)	0.38* (0.02 to 0.74)	0.20 (-0.23 to 0.64)	-0.18 (-0.55 -0.20)	0.13 (-0.28 to 0.55)	0.19 (-0.30 to	0.06 (-0.37 to

	0.68)							0.69)	0.49)
Neurological									
Delirium or reported confusion	0.31 (-0.09 to 0.70)	0.41 (-0.07 to 0.88)	0.10 (-0.32 to 0.52)	0.24 (-0.11 to 0.58)	0.14 (-0.27 to 0.55)	-0.10 (-0.46 to 0.26)	0.54* (0.16 to 0.92)	0.56* (0.11 to 1.02)	0.02 (-0.37 to 0.42)
Headache	1.14* (0.19 to 2.09)	1.60* (0.47 to 2.72)	0.46 (-0.53 to 1.44)	1.04* (0.19 to 1.89)	1.51* (0.50 to 2.53)	0.48 (-0.41 to 1.36)	1.39* (0.49 to 2.29)	1.39* (0.32 to 2.46)	0.00 (-0.94 to 0.94)
Dizziness/ lightheadedness	0.80 (-0.05 to 1.65)	1.09* (0.07 to 2.10)	0.29 (-0.60 to 1.17)	0.85* (0.05 to 1.65)	0.99* (0.04 to 1.95)	0.14 (-0.70 to 0.98)	0.87* (0.03 to 1.71)	1.09* (0.09 to 2.10)	0.22 (-0.65 to 1.10)
Low mood	0.53 (-0.29 to 1.36)	0.77 (-0.22 to 1.76)	0.24 (-0.63 to 1.10)	0.77* (0.01 to 1.53)	0.74 (-0.17 to 1.65)	-0.03 (-0.83 to 0.77)	0.70 (-0.07 to 1.47)	0.74 (-0.18 to 1.65)	0.04 (-0.77 to 0.84)
Tinnitus	0.43* (0.05 to 0.81)	0.46* (0.01 to 0.92)	0.03 (-0.36 to 0.43)	0.28 (-0.12 to 0.68)	0.14 (-0.34 to 0.62)	0.14 (-0.56 to 0.29)	0.13 (-0.26 to 0.52)	0.26 (-0.20 to 0.73)	0.13 (-0.27 to 0.54)

Following the first dose of the COVID-19 Vaccination, cardiovascular manifestations generally did not differ significantly among the sleep duration groups, with one notable exception. Shortness of breath was reported at a significantly higher frequency among individuals sleeping less than 5 hours compared to those sleeping 7 hours or more ( $p < 0.05$ ). Furthermore, participants in the  $<5$ -hour sleep group experienced more frequent chest pain and sore throat than those in the 5 to  $<7$  hours group ( $p < 0.05$ ).

After administration of the second vaccination dose, a subset of participants reported shortness of breath, which was significantly more prevalent among those sleeping less than 5 hours compared to those sleeping 5 to  $<7$  hours ( $p < 0.05$ ). Additionally, chest pain was observed at a significantly higher rate in the  $<5$  hours sleep group than in both the 5 to  $<7$  hours and  $\geq 7$  hours groups ( $p < 0.05$ ).

Following the third vaccination dose, the association between reduced sleep duration and cardiovascular involvement became even more pronounced. Shortness of breath was significantly more common in participants sleeping less than 5 hours compared to both the 5 to  $<7$  hour and  $\geq 7$  hours sleep groups ( $p < 0.05$ ). A similar pattern was observed for chest pain and sore throat. Notably, symptoms such as hoarse voice and sneezing were also significantly elevated in individuals sleeping less than 5 hours relative to those sleeping 5 to  $<7$  hours ( $p < 0.05$ ).

Gastrointestinal effects following COVID-19 vaccination were also examined in relation to sleep duration. Diarrhoea was reported at a significantly higher rate among participants who slept less than 5 hours compared to those who slept between 5 to  $<7$  hours ( $p < 0.05$ ). After receipt of the third Vaccination dose, the proportion of individuals who reported skipping meals was notably greater in the group with less than 5 hours of sleep compared to both the 5 to  $<7$  hours and  $\geq 7$ -hours sleep groups ( $p < 0.05$ ).

Participants sleeping fewer than 5 hours exhibited distinct dermatological responses. After the second vaccination dose, the  $<5$  hours sleep group reported significantly higher rates of rash ( $p < 0.05$ ) and burning skin sensations ( $p < 0.05$ ) relative to the 5 to  $<7$  hours cohort. Individuals who slept fewer than 5 hours reported a significantly ( $p < 0.05$ ) higher prevalence of unusual muscle pains compared to those who slept between 5 to  $<7$  hours post third dose.

Following the third dose of the COVID-19 vaccination, neurological involvement specifically, delirium or reported confusion, headache, and dizziness or lightheadedness, became significantly ( $p < 0.05$ ) more pronounced among participants who slept fewer than 5 hours compared to those in other sleep duration (5 to  $<7$  and  $\geq 7$  hours) groups. Interestingly, across all vaccine doses, individuals sleeping less than 5 hours consistently reported headaches and dizziness/lightheadedness significantly more often than those other sleep duration groups ( $p < 0.05$ ).

## 5. Discussion

Our findings suggest that inadequate sleep may be accompanied by cardiorespiratory side effects such as shortness of breath and chest pain and neurological side effects such as headache and dizziness after all COVID-19 vaccination doses.

The intersection of sleep deprivation and repeated COVID-19 vaccination presents a complex pathophysiological scenario that may significantly amplify cardiovascular and neurological risks through multiple interconnected mechanisms.

While the cardiovascular complications of COVID-19 vaccines have been well-documented, with myocarditis emerging as the most prevalent adverse event occurring in approximately 1.62% of vaccinated individuals, the potential synergistic effects of concurrent sleep deprivation remain underexplored yet clinically significant [15].

Recent large-scale analyses have confirmed that the risk of myocarditis increases with sequential doses, with incidence rate ratios of 1.52, 1.57, and 1.72 for first, second, and booster doses of BNT162b2, respectively [16].

Sleep deprivation creates a pro-inflammatory state that may predispose individuals to enhanced vaccine-related cardiovascular complications through several molecular pathways. Acute sleep loss triggers immediate increases in circulating pro-inflammatory cytokines, including interleukin-1 $\beta$  (IL-1 $\beta$ ), interleukin-6 (IL-6), interleukin-17A (IL-17A), tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), and C-reactive protein (CRP) [17].

These inflammatory mediators create a milieu that may amplify the immune response to vaccination, potentially increasing the likelihood and severity of myocarditis and other cardiovascular complications [17].

The disruption of circadian rhythms through sleep deprivation fundamentally alters the body's molecular clock, leading to cellular stress responses including changes the biological phenotypes of DNA, RNA and apoptosis [18].

This cellular stress environment may compromise cardiac function and increase susceptibility to vaccine-induced inflammatory responses. The temporal relationship between sleep loss and cytokine production is particularly relevant, as pro-inflammatory cytokines naturally peak during early nocturnal sleep but shift toward anti-inflammatory dominance during REM sleep [17].

Sleep deprivation fundamentally disrupts neuroinflammatory regulation, creating conditions that may predispose individuals to enhanced neurological complications following vaccination. The molecular clock disruption caused by insufficient sleep affects not only peripheral inflammatory responses but also central nervous system function, potentially increasing susceptibility to vaccine-related neurological adverse events.

The elevation of inflammatory markers observed in sleep-deprived individuals, particularly the increases in IL-1 $\beta$ , IL-6, and TNF- $\alpha$ , directly impacts neurological function through multiple mechanisms [17].

These cytokines can cross the blood-brain barrier and activate microglial cells, the brain's resident immune cells, potentially leading to neuroinflammation that may be further amplified by vaccination-induced immune responses. The timing and magnitude of this neuroinflammatory response may be particularly relevant for individuals receiving repeated vaccination doses while experiencing chronic sleep deprivation [17].

Our analysis also suggests that multi-system involvement particularly gastrointestinal, dermatological, and musculoskeletal reactions can follow in irregular temporal patterns after sequential COVID-19 vaccine doses. Notably,

sleeping fewer than 5 hours nightly emerged as a common factor among individuals reporting these complex presentations. The escalation of dermatological and musculoskeletal manifestations across vaccination doses underscores the compounding impact of insufficient sleep on post-vaccination symptomology. The absence of significant differences after early doses contrasts sharply with the pronounced effects post-third dose, implying that chronic sleep restriction may progressively impair the body's capacity to modulate inflammatory pathways during sequential immune challenges. Furthermore, the diversity likely arises from interindividual variability in immune responses, and genetic predispositions [19, 20].

## 6. Conclusion

The present study suggests that sleep-deprived individuals, particularly young healthy, may face amplified cardiovascular and potentially neurological risks post COVID-19 vaccination particularly after repeated vaccination doses. Understanding the interplay between sleep and vaccine response is crucial for developing personalised vaccination strategies. This knowledge optimises benefits, minimises risks, and improves patient care by promoting good sleep habits around vaccination time, especially as booster programs evolve.

Despite its contributions, the study has several limitations. Self-administered questionnaires introduce subjectivity potentially limiting generalizability.

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