Pilot and Feasibility Studies

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Comparison of 45-min nap versus no-nap during simulated night shift work on endothelial function: a randomized crossover feasibility trial

P. Daniel Patterson[1,2*], Cassie J. Hilditch[3], Sarah E. Martin[1], David G. L. Roach[1], Matthew D. Weaver[4,5], Tiffany S. Okerman[1], David Hostler[6], Leonard S. Weiss[1] and Steven E. Reis[7]

Abstract

Background Night shift workers face increased risk of cardiovascular disease (CVD) compared to non-shift workers. Evidence supports on-shift napping and regular non-invasive monitoring of endothelial function for risk mitigation, yet neither strategy is widely used.

Methods We evaluated the feasibility of non-invasive assessment of peripheral arterial tone (PAT) to assess the effect of napping during simulated night shift work on endothelial function. We used a single-site, randomized crossover trial of simulated night shift work with a 45-min nap condition versus a control, no-nap condition (ClinicalTrials.gov NCT05436951).

Results The primary outcome was the number of participants with ≥ 70% of endothelial function assessments. Secondary outcomes included mean reactive hyperemia index (RHI), BP, and cognitive performance with the brief psychomotor vigilance task (PVT-B). Of the 10 consented, 9 completed both conditions. All participants exceeded feasibility benchmarks. Mean RHI did not differ by nap condition, and the delta from pre- to post measure did not differ (difference in delta = −0.26, 95% *CI* −1.09, 0.58). Hourly PVT-B assessments from 19:00 to 07:00 h did not differ by nap condition. Compared to pre-nap measures, cognitive performance on the PVT-B was poorest at + 0 min post-nap.

Conclusion Our findings can inform larger studies evaluating the effects of night shift work and napping on endothelial function.

Trial registrations ClinicalTrials.gov (NCT05436951, registered on June 23, 2022).

Keywords Night shift work, Napping, Cardiovascular disease, Endothelial function, Sleep

*Correspondence:
P. Daniel Patterson
pdp3@pitt.edu
Full list of author information is available at the end of the article

Key messages regarding feasibility

- What uncertainties existed regarding the feasibility? Primary concerns for this trial were feasibility of measuring endothelial function with a non-invasive peripheral arterial tone (PAT) device under simulated night shift work conditions.
- What are the key findings? A key finding was high compliance and completeness with desired outcome measures, which supports feasibility for night shift work-like conditions.
- What are the implications of the feasibility findings for the design of the main study? We demonstrate feasibility of non-invasive PAT measurement pre- and post-night shift work with high compliance and low attrition. We also provide data regarding the acute impact of night shift work (with and without napping) on endothelial function, which may be used to design future, larger trials both in the laboratory and field settings.

Background

Cardiovascular disease (CVD) is a leading cause of death in the USA and globally [1]. The risk of hypertension, myocardial infarction, ischemic stroke, and CVD-related hospital admission are higher among night shift workers than traditional daylight workers [2–5]. Regular monitoring of preclinical signs of CVD, such as endothelial dysfunction [6], may enable early detection and risk mitigation. In addition, non-invasive assessment of endothelial function may aid researchers with evaluating on-shift interventions, such as napping, which has been shown to restore normal circadian patterns in blood pressure (BP) during night shift work [7, 8]. However, regular monitoring of endothelial dysfunction for night shift workers is not widespread, which may be due to a lack of evidence or uncertainty regarding the full utility of different non-invasive techniques and if they are feasible in occupational settings.

The endothelium layer lining the vascular system has been described as one of the largest organs in the human body [9–12]. The endothelium directly impacts vascular tone, BP, and cardiovascular homeostasis [13]. Arterial stiffness, inflammation of the vasculature, and atherosclerosis are indicators of dysfunction [6, 14]. Dysfunction detected in the macro- or micro-vasculature correlate with dysfunction in coronary arteries and are prognostic of CVD [15]. Given that the endothelium is important to vascular homeostasis [9], dysfunction can be detected preclinically before clinical care is sought for conditions like hypertension [10, 14]. Further, given that dysfunction has been linked to numerous CVD outcomes [6, 16], there is increased interest in incorporating evaluation of endothelial function/dysfunction as a risk mitigation strategy [15, 17].

Direct measurement of endothelial function is an invasive procedure comprising intracoronary infusion of acetylcholine to measure arterial diameter, blood flow, and vascular resistance [18]. Accepted biomarker measures include interleukin-6, C-reactive protein, syndecan-1, and others [19, 20]. Invasive measurements, including sampling for biomarkers, are not feasible for all settings, yet regular assessments of non-invasive indicators (e.g., BP) are likely more feasible in a workplace environment [21]. Non-invasive techniques for assessing endothelial function or dysfunction include flow-mediated dilation (FMD) of the macro-vasculature of the proximal upper extremities (i.e., circulation in brachial artery) and peripheral arterial tone (PAT) of the microvasculature (i.e., capillary circulation in fingers) [17, 22]. These techniques have not been adequately tested with night shift workers [23, 24]. In addition, it is unclear if the acute negative effects of night shift work on endothelial function detected previously with FMD [25–27] are also detectable with a non-invasive PAT device, which some have claimed is easier to use and less sensitive to tester/operator variability than FMD [15].

Napping during night shifts or long duration shifts is one of five recommendations comprising the 2018 Evidence-Based Guideline for Fatigue Risk Management in Emergency Medical Services [28], and napping is also a key countermeasure for the negative effects of shift work described in the 2021 guiding principles for determining shift duration produced by the American Academy of Sleep Medicine and Sleep Research Society [29]. Recent research testing the impact of napping on BP suggest the intervention may also improve endothelial function [7, 8]. Several studies have measured endothelial function with FMD following night shift work and showed decreases in the diameter of the brachial artery when compared to measures taken after a normal night of sleep [25–27]. Investigations of the potential benefits of napping during night shift work on endothelial function are limited [24].

Methods

Study aims

The aim of this crossover randomized trial was to evaluate the feasibility of using PAT during simulated night shift work, perform exploratory analyses of the effect of sleep deprivation on endothelial function, and explore the effect of a short on-shift nap on endothelial function.

Study design and setting

We used a single-site, laboratory-based, single-blinded, crossover randomized trial study design with two

conditions assigned at random. Our trial was preregistered with ClinicalTrials.gov prior to enrollment of the first participant (NCT05436951, registered on June 23, 2022) and approved by the University of Pittsburgh Institutional Review Board.

Participants

We recruited adults 18 years of age or older from the community who self-reported no prior diagnosis of sleep problems (e.g., insomnia), CVD (e.g., hypertension), metabolic disease, adrenal disease, thyroid disease, cancer, kidney disease, or other medical condition that may impact indicators of endothelial function. Participant screening did not include objective assessments of endothelial function or hypertension. Current pregnancy was an exclusion criterion. Participants self-reported prescription and over-the-counter medications, which were reviewed by a physician who determined eligibility based on the potential impact a medication may have on endothelial function. All eligible individuals provided written informed consent and remunerated US $800 for completing the protocol as designed. Enrollment began July 12, 2022, and was closed March 4, 2023. Members of the targeted population and members of the public were not involved in the design, conduct, reporting, or dissemination of this research.

Randomization and blinding

Following baseline assessments, participants were randomized with simple randomization (coin flip) into one of two conditions: nap or no nap. Participants were blinded to napping status until just prior to the time for the nap opportunity to begin (02:00 h). Members of the study team were not blinded.

Intervention

The intervention was a 45-min nap opportunity during a simulated 12-h night shift. Participants were equipped with multiple non-invasive devices for monitoring BP and depth of sleep. Participants entered the designated nap room several minutes prior to 02:00 and instructed to lay supine to limit positional interference of one or more monitoring devices. Staff evaluated monitoring devices prior to exiting the nap room and informed participants they would be awoken by study staff at 45 min into the nap opportunity.

Protocol

All consented participants completed two separate 48-h conditions with the first 36 h of each condition completed at home and the final 12 h (a simulated night shift) completed in the laboratory. One condition involved a 45-min nap opportunity scheduled to begin at 02:00 h during the 12-h simulated night shift. The second condition enforced continuous wakefulness (no nap). Condition order was randomized, and participants completed a minimum of 1-week washout between the two conditions. Sleep and activity were not monitored during washout periods, and participants did not receive instruction on limiting or structuring sleep or activity. Prior to arriving to the lab to begin a 48-h condition, all participants were instructed to abstain from caffeine, food, alcohol, and medications (under the supervision of the study team physician) at least 6 h prior to arrival. The baseline assessment began at 07:00 h at the start of the 48-h condition with participants completing a baseline survey and then the first non-invasive assessment of endothelial function with the EndoPAT® device (EndoPAT, ZOLL® Itamar Medical, Atlanta, GA, USA). The EndoPAT assessment produces two scores, the reactive hyperemia index (RHI) and natural log (lnRHI). These scores are derived over an approximate 20-min assessment of PAT (with setup time included). The assessment requires participants to be seated comfortably with both forearms at heart level and supported on foam wedges and hands (fingers) hanging over the outside edge. Device-specific probes are placed on both index fingers and connected to the EndoPAT device tower with tubing. The assessment begins with participants seated quietly, not moving, and maintaining wakefulness with finger probes inflated. Following a 1-min equipment (air-leak) check, participants sit quietly for 5 min (the pre-occlusion phase) after which time a BP cuff on the right arm is inflated to 200 mmHg and held constant at 200 mmHg for 5 min (the occlusion phase). After the occlusion phase, the BP cuff is deflated, and the participant sits still for five more minutes (the post-occlusion phase). The ratio of the post- to-pre-occlusion phase in the occluded arm relative to the non-occluded arm is believed to reflect nitric oxide bioavailability [30] and is correlated with coronary artery vasodilation and brachial-derived FMD [31, 32].

Following PAT test, we programmed the Oscar 2 ABPM device (SunTech Medical, Inc., Morrisville, NC, USA) to measure BP hourly, including during sleep. Participants completed a brief 3-min psychomotor vigilance task (PVT-B) [33–35] and received a paper-based sleep diary and the wGT3X-BT wrist-worn actigraph (ActiGraph, Pensacola, FL, USA) for purposes of measuring sleep/wake. Following the in-lab baseline assessment, participants returned home, maintained wakefulness until approximately 22:00 h at which time participants were instructed to sleep until no later than 07:00 h, and return to the laboratory between 07:00 and 08:00 h. In this laboratory session, participants completed scheduled measurements with the PVT-B and exchanged the non-invasive equipment (i.e., ABPM device) to permit

continued monitoring. Participants then returned home and maintained wakefulness prior to returning to the laboratory at 18:30 h, at which time participants prepared for the 12-h in-lab simulated night shift from 19:00 to 07:00 h. During the simulated night shift, participants were observed continuously by study staff, completed hourly PVT-B measurements and hourly ABPM measures, and maintained wakefulness by watching television, reading, and using a personal computer. Light meals were provided at the beginning of the simulated night shift and at midnight. For conditions that involved the 45-min nap at 02:00 h, the Zmachine® Synergy device (General Sleep, Cleveland, OH, USA) was applied for purposes of measuring sleep depth during the nap opportunity. The Zmachine® Synergy is a non-invasive portable electroencephalogram sleep staging device that measures total sleep, sleep efficiency, and depth of sleep. Findings from previous research confirm the device provides valid assessments of sleep staging [36–38]. Post-nap PVT-Bs were assessed at +0, +10, +20, and +30 min after waking before returning to hourly measures. Participants fasted (no food) for 4 h prior to the second PAT measurement, which occurred at the end of the 12-h simulated night shift (beginning immediately after the 07:00 h measure). Participants returned home following the final PAT assessment.

Feasibility outcomes

Since feasibility was the focus of this study, our primary outcomes of interest were as follows: [1] the number of participants with at least 70% of required endothelial function assessments with the EndoPAT device and [2] the number of participants with at least 70% of required ambulatory BP assessments. Failure to reach these benchmarks may indicate poor or limited feasibility in future studies with larger sample sizes.

Secondary outcomes and measures

Participants completed a standardized baseline survey comprised of reliable and valid sleep and fatigue questionnaires (i.e., Pittsburgh Sleep Quality Index (PSQI), Chadler Fatigue Questionnaire (CFQ), Epworth Sleepiness Scale (ESS)). Secondary outcomes were as follows: [1] mean BP while awake during the simulated night shift; [2] mean RHI and the lnRHI, as measured by PAT at baseline; and [3] mean RHI and mean lnRHI after simulated night shift. The RHI summary measure is a ratio with normal/healthy values > 1.67 for RHI and > 0.51 for lnRHI and abnormal values ≤ 1.67 for RHI and ≤ 0.51 for lnRHI [31, 39, 40].

We also report on the following: [1] the mean BP during nap opportunities (sleep-related BP); [2] mean sleep-related dip in BP during nap conditions (determined by taking the mean wake BP minus the mean sleep BP divided by the mean wake BP multiplied by 100) [41]; [3] the difference in RHI from baseline to post-simulated night shift, stratified by nap condition; [4] the mean minutes of sleep during the pre-laboratory at-home period, as well as the mean minutes of sleep during the 45-min in-lab nap opportunity, with the latter stratified by sleep stage (light, deep, or rapid eye movement sleep); and [5] hourly assessments of cognitive performance as measured by the brief 3-min version of the psychomotor vigilance test (the PVT-B) and change (the delta) in PVT-B performance from pre- to post-nap opportunity at +0, +10, +20, and +30 min. The PVT-B is widely used for cognitive performance assessment, is reliable, and a valid assessment in response to sleep loss in occupational settings [33–35]. Four measures produced from the 3-min PVT-B include reaction time (RT in milliseconds (ms)), lapses (RT > 355 ms), false starts (reactions before stimulus or $RT < 100$ ms), and speed (1000/RT) [33].

Sample size

We did not perform a sample size calculation on any specific outcome given our focus on feasibility. We sought to enroll 10 total participants given (1) our previous research revealed a limited number of studies that tested the EndoPAT device in relation to shift work exposure [24], (2) the financial resources available for this investigation were limited, and (3) our belief that our experience with 10 participants would likely reveal important lessons learned that could guide our design for future, larger trials.

Data analysis

We did not propose any hypotheses to test given the overarching goal of this trial was feasibility and to inform a larger future trial. The proposed goal enrollment was 10 participants, based on assessments of feasibility and availability of resources. As prescribed [42], a power calculation was not performed. Analyses began with descriptive statistics, including determining means and corresponding standard deviations (SD) and frequencies with corresponding percentages. For primary outcomes of feasibility, we calculated frequencies and percentages. We calculated means with corresponding SD for multiple secondary outcome measures (e.g., BP dipping, PVT-B outcomes, and sleep measures) immediately before, during, and immediately after the 45-min nap opportunity. We used a paired *t*-test to estimate potential differences in RHI and lnRHI scores at baseline and following the simulated night shift. We chose to use paired *t*-tests after evaluating data distribution and assumptions of normality, which included examining plots of the data, the Shapiro–Wilk test, Kolmogorov–Smirnov test, the

Cramer-von Mises test, and the Anderson–Darling test. We used mixed-effects linear models with a random subject effect to estimate for differences by nap condition in the change (delta) in RHI scores from baseline- to post-simulated night shift. We also used mixed-effects linear models with a random subject effect to estimate for differences by nap condition at hourly PVT-B assessments determine if the change in PVT-B measures from pre-nap to post-nap (delta) assessed at +0, +10, +20, and +30 min was different from 0. All linear mixed-effects models included the Kenward-Roger approximation to adjust for small sample sizes and bias in variance estimates. Where appropriate, we used generalized estimating equations with log link to address a Poisson or negative binomial distribution. To address concerns of small sample sizes and overdispersion, we used the deviance scale (DSCALE) and Pearson scale (PSCALE) options in model statements to adjust standard errors. We report estimated least square and differences in least square means and corresponding 95% confidence intervals (CI). The statistical software program SAS V9 (Cary, NC, USA) was used for all statistical analyses.

Results

Of the 18 screened, 10 individuals consented to participate (Fig. 1). One participant was withdrawn from the study by investigators during the first couple hours of starting the protocol after the participant reported a previously undisclosed prescription medication that investigators believed would impact their BP and possibly the RHI score. In total, 9 participants completed the study as designed. Half of participants were female (55.6%), and most reported white race (77.8%) and self-described as not Hispanic or Latino (88.9%). Half were not shift workers (55.6%), and most worked part-time (66.7%). Mean age was 22.4 years (*SD* 1.8; Table 1). Mean PSQI sleep quality score was 4.7 (*SD* 2.1) and 33.3% classified as having poor sleep quality (score > 5). None of the participants was classified as having severe daytime sleepiness based on the ESS, but 22.2% were classified as having severe work-related fatigue with the CFQ.

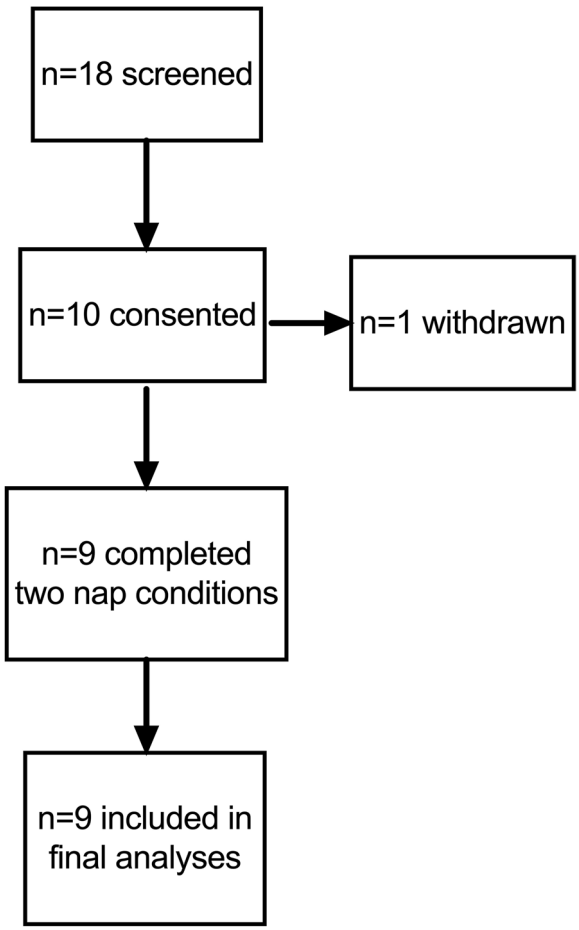

Fig. 1 Participant flow diagram

Feasibility outcomes

Nine participants completed all required baseline and post-simulated night shift PAT assessments for the 2 nap conditions. All nine participants exceeded the 70% benchmark for ambulatory BP assessments while on protocol. The proportion of complete hourly ABPM assessments by participants during the no-nap condition was 97.4% (95% *CI* 94.2, 100). The proportion of complete hourly ABPM assessments by participants during the 45-min nap condition was 96.8% (95% *CI* 94.3, 99.2). All but 1 participant recorded all 3 scheduled ABPM measures taken every 15 min during the 45-min nap opportunity. This missing measurement was due to device failure (air leak).

Secondary outcomes

Mean wake BP during the simulated night shift with a nap (SBP/DBP 135/78, SBP 95% *CI* 126.2, 143.5, DBP 95% *CI* 72.9, 83.2) did not differ from the mean wake BP during the simulated night shift without a nap (SBP/DBP 133/76, SBP 95% *CI* 124.1, 141.4, DBP 95% *CI* 70.6, 81.2). The differences in SBP and DBP between these conditions were small (SBP difference estimate = 2.1 95% *CI* − 10.1, 14.4; DBP difference estimate = 2.3 95% *CI* − 5.1, 9.6). Mean BP during the 45-min nap opportunity was SBP/DBP 118/60 (SBP 95% *CI* 108.7, 127.4, DBP 95% *CI* 55.3, 69.7). The mean sleep-related dip in SBP was 12.1% (95% *CI* 3.8, 20.3), whereas the mean dip in DBP was 19.4% (95% *CI* 8.8, 30.1). Figure 2a and b shows the mean RHI and mean lnRHI at baseline and immediately after the simulated night shift. Mean RHI and mean lnRHI did not differ by nap condition at baseline or post-night shift.

Table 1 Participant demographics

Variable	Total $n = 9$ Frequency (%) Mean (SD)
Sex	
Female	5 (55.6%)
Mean age	22.44 (1.8)
Mean BMI (kg/m^2)	23.49 (1.7)
Race	
Asian	1 (11.1%)
Black or African American	1 (11.1%)
White	7 (77. 8%)
Ethnicity	
Hispanic or Latino	1 (11.1%)
Not Hispanic or Latino	8 (88.9%)
Certification/license	
EMT	3 (33.3%)
Paramedic	1 (11.1%)
Not a shift worker	5 (55.6%)
Where do most work as EMS clinician	
Ground-based EMS	4 (44.4%)
Not a shift worker	5 (55.6%)
Work multiple jobs (yes)	5 (55.6%)
Mean years of experience in EMS	2.5 (1.7)
Employment status	
Full time	2 (22.2%)
Part-time	6 (66.7%)
Volunteer	1 (11.1%)
Type of shift most commonly worked	
12 h	1 (11.1%)
8 h	2 (22.2%)
Other	1 (11.1%)
Not a shift worker	5 (55.6%)
Health status	
Excellent	1 (11.1%)
Good	8 (88.9%)
Drink caffeine (yes)	6 (66.7%)
Drink alcohol (yes)	7 (77.8%)
Smoke tobacco products (no)	9 (100%)
Mean sleep quality (PSQI)	4.7 (2.1)
% with poor sleep (*PSQI* > 5)	3 (33.3%)
Mean daytime sleepiness (ESS)	3.9 (2.0)
% with excessive sleepiness (*ESS* > 9)	0 (0%)
Mean fatigue (CFQ)	2.44 (1.6)
% with severe fatigued (*CFQ* > 4)	2 (22.2%)

Footnotes: *BMI* refers to body mass index. *EMT* refers to emergency medical technician. *EMS* refers to emergency medical services. *PSQI* refers to Pittsburgh Sleep Quality Index. *ESS* refers to Epworth Sleepiness Scale. *CFQ* refes to Chalder Fatigue Questionnaire

Figure 2a illustrates the RHI scores at baseline and post-night shift. The mean baseline RHI scores did not differ between conditions (0.25, 95% *CI* − 0.39, 0.89). The mean post-night shift RHI scores did not differ between conditions (− 0.003, 95% *CI* − 0.63, 0.62). Figure 2b shows mean lnRHI scores at baseline and mean post-night shift lnRHI scores. These scores did not differ by condition at baseline (0.14, 95% *CI* − 0.15, 0.43) and did not differ by condition post-night shift (− 0.03, 95% *CI* − 0.30, 0.23). The mean difference (delta) in the change in RHI from baseline to post-night shift was 0.10 (95% *CI* − 0.47, 0.68) for the no-nap condition and − 0.15 (95% *CI* − 0.76, 0.45) for the nap condition (Fig. 2a). The estimated mean difference in RHI from baseline to post-night shift when comparing the nap vs. the no-nap conditions was not significant − 0.26 (95% *CI* − 1.10, 0.58). The mean difference (delta) in the change in lnRHI from baseline to post-night shift was 0.08 (95% *CI* − 0.17, 0.34) for the no-nap and − 0.09 (95% *CI* − 0.61, 0.37) for the nap condition (Fig. 2b). The estimated mean difference between these measures was − 0.17 (95% *CI* − 0.54, 0.19).

Mean total minutes of sleep during the pre-laboratory at-home night (the first 24 h on protocol) did not differ by nap condition (no nap 441.2 min, 95% *CI* 393.0, 489.5 vs. 45-min nap 460.7 min, 95% *CI* 419.2, 502.2). In addition, there was no difference in mean sleep efficiency during at-home sleep by condition (no nap 89.7%, 95% *CI* 85.9, 93.5 vs. 45-min nap 90.8%, 95% *CI* 87.2, 94.4). During the 45-min nap opportunity, mean total minutes of sleep were 27.4 (95% *CI* 24.0, 30.9), mean sleep efficiency was 60.3% (95% *CI* 52.0, 68.6), mean minutes of light sleep were 18.3 (95% *CI* 13.4, 23.3), mean minutes of deep sleep were 8.7 (95% *CI* 3.6, 13.8), and mean minutes of REM sleep were 0.4 (95% *CI* − 0.2, 1.0). Figure 3 illustrates the proportion of participants in the different stages (depths) of sleep stratified into 30-s intervals over the 45-min nap opportunity.

Hourly PVT-B assessments from 19:00 to 07:00 h did not differ by nap condition (Fig. 4a, b, c, d; all 95% CIs cross 0). When compared to pre-nap measures, cognitive performance was poorer post-nap at + 0 min for PVT-B RT and PVT-B speed and at + 0, + 10, and + 30 min for PVT-B lapses (Fig. 5a, b, c).

Discussion

Previous research has examined the impact of night shift work on endothelial function [24–27]. However, to the best of our knowledge, no study has tested the impact of a nap during simulated night shift work on non-invasive indicators of endothelial function using PAT [24]. In this crossover randomized trial, we provide evidence of feasibility with the proportion of required measures of endothelial function and ambulatory BP exceeding

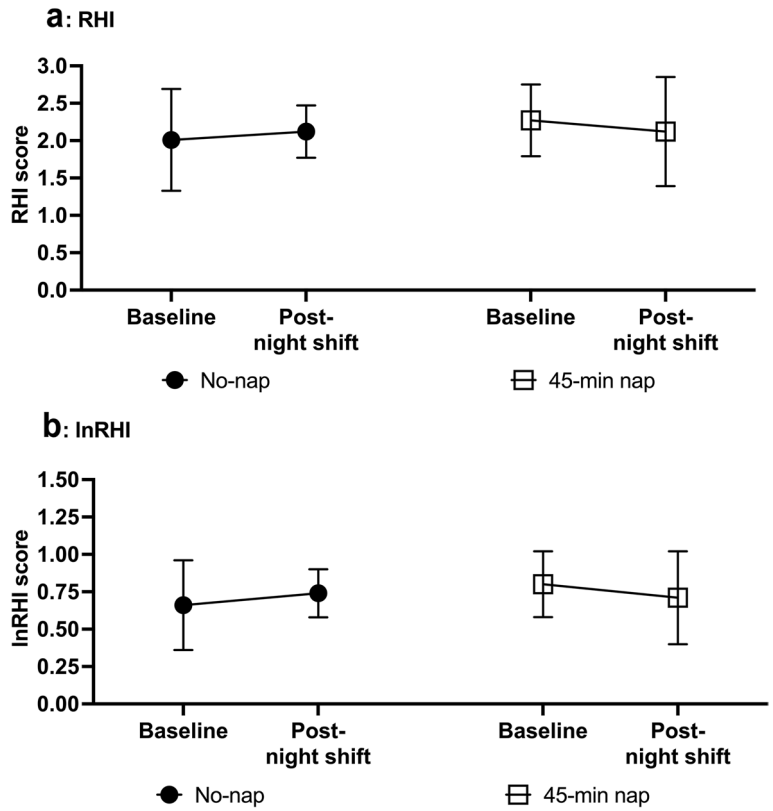

Fig. 2 Change in RHI and lnRHI scores from baseline to post-night shift by nap condition

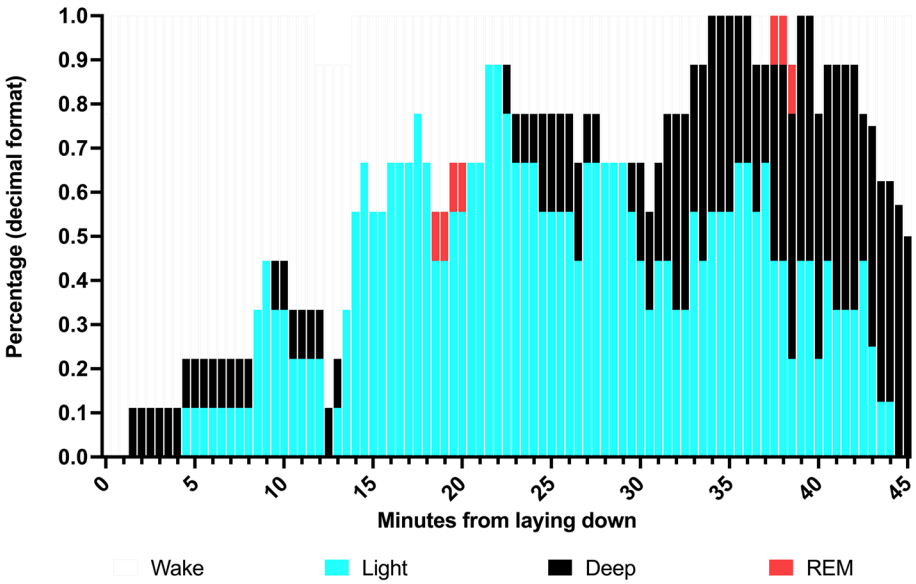

Fig. 3 Proportion of participants in light, deep, rapid eye movement sleep or wake stratified into 30-s time intervals (epochs) during the 45-min nap opportunity

pre-defined benchmarks. Feasibility is further demonstrated with low attrition. In addition, we report on patterns of BP and other secondary measures of interest (e.g., cognitive performance) that may be used for planning, sample size estimates, and effect size projections

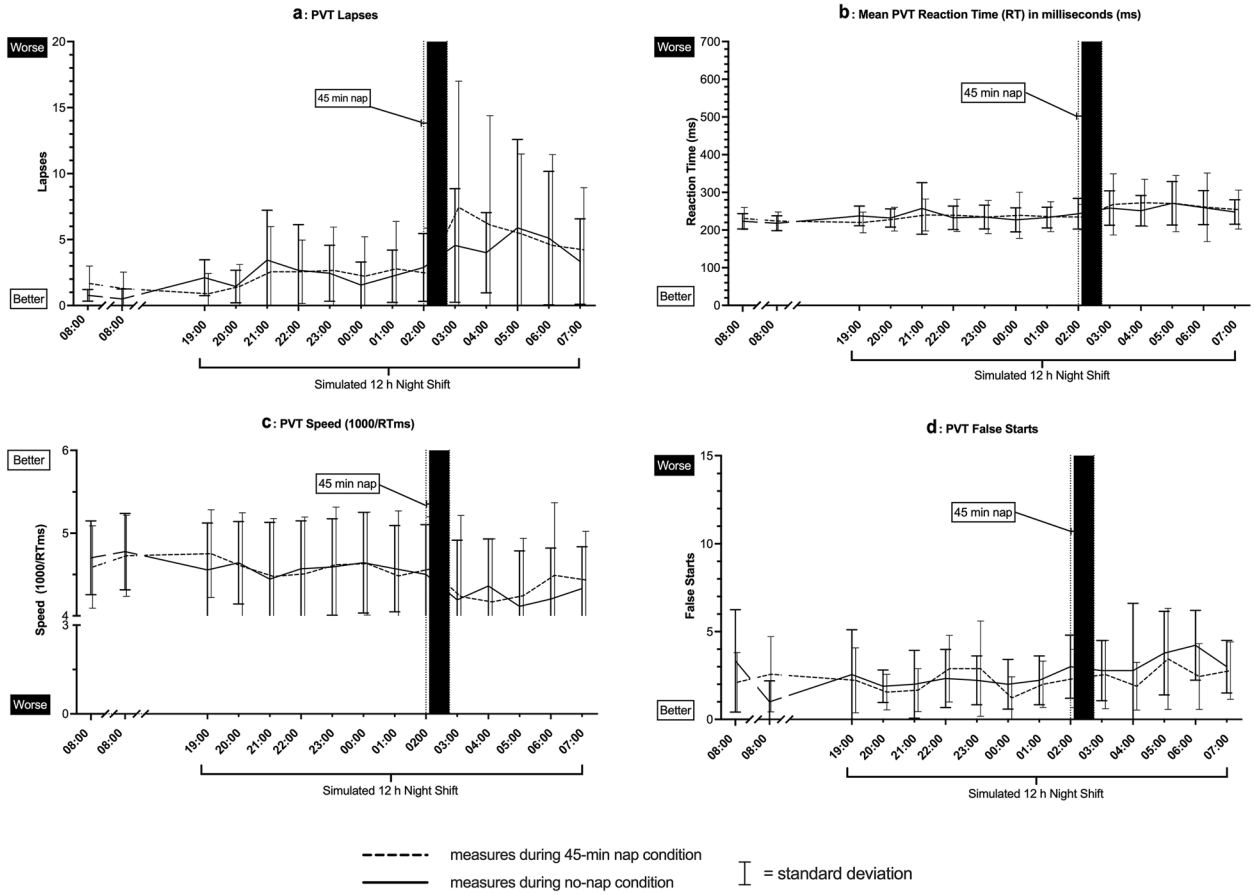

Fig. 4 Hourly PVT performance during simulated night shift by nap condition

for future research involving simulated night shifts with short 45 min or similar duration nap opportunities.

While numerous methods exist for assessing the endothelial health (an important preclinical indicator of cardiovascular health) [17], non-invasive devices measuring PAT and FMD are likely more feasible and attractive to employers and worksite wellness advocates concerned with the cardiovascular health of shift workers. Our findings support feasibility of PAT for this purpose, yet additional research is needed. Future field-based research should consider employee/shift worker willingness to arrive to work early, stay late, or schedule time to visit the employer or a contract organization to obtain baseline and follow-up measures of endothelial function. Second, the costs associated with initial purchase of non-invasive devices and the required disposables needed to complete testing are substantial. Without funding from external grant mechanisms or from internal investment (in-kind funding), few researchers will have the capability to investigate the effect of night shift work on endothelial function with large and diverse samples. In terms of translating research to practice, a sizeable body of evidence may be needed to result in widespread use of these techniques in the workplace for employee health and wellness programming.

Another reason additional research is needed is existence of potentially conflicting or unexpected results from this laboratory-based experimental study and from prior research. A study by Garu and colleagues used PAT to determine the impact of sleep loss and night shift work on endothelial function [23]. They performed 3 measures prior to a daylight shift (baseline measures) followed by three measures after a night shift. They reported no differences between baseline and post-night shift measures. Our findings are like Garu and colleagues, showing no differences from baseline to post-night shift in either nap condition. When compared to findings from other studies assessing endothelial function before and after night shift work with FMD, findings and conclusions differ from our findings and those of Garu and colleagues [25, 43]. Specifically, these prior studies with FMD techniques show declines in endothelial function in response to night shift work [25, 43]. One possible explanation is that our study sample included young and generally healthy

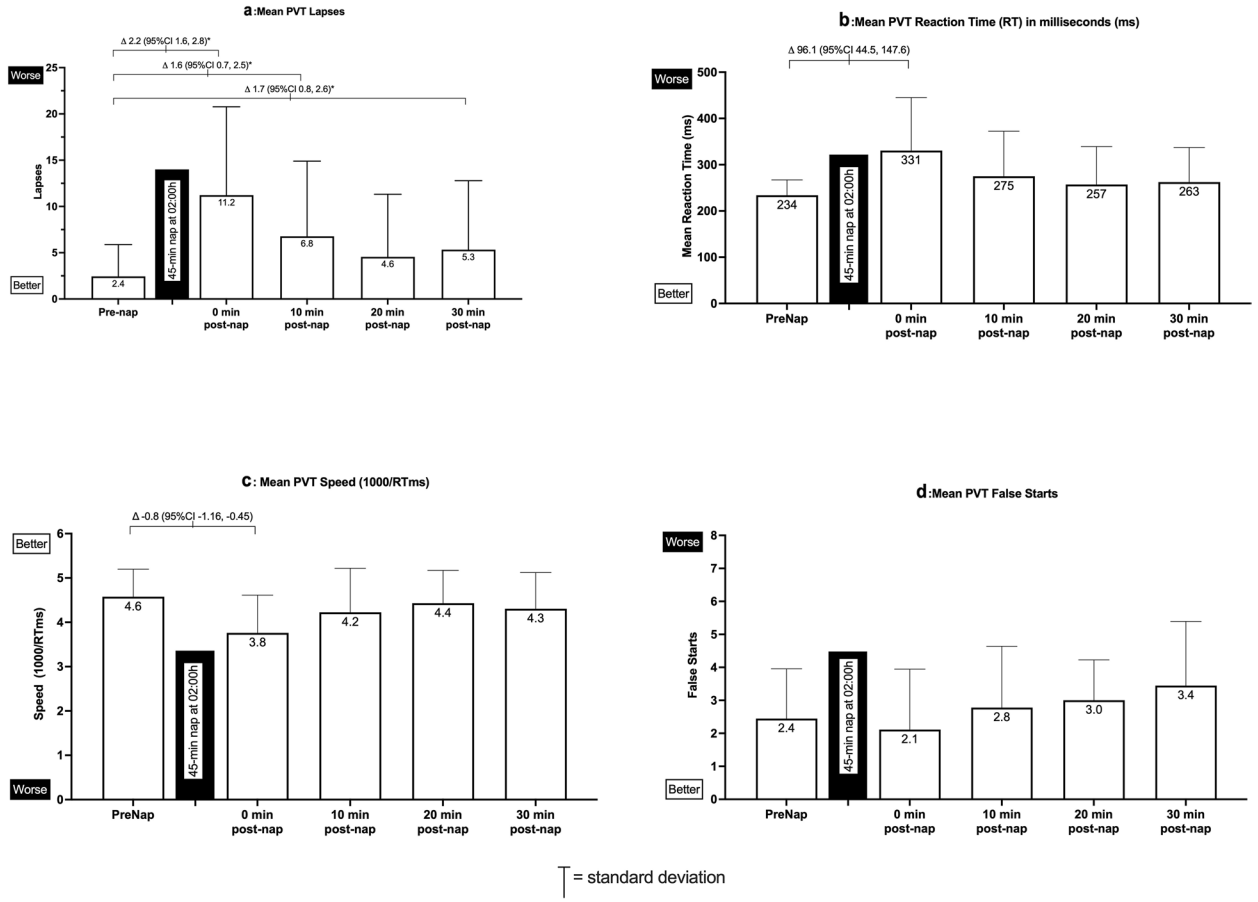

Fig. 5 PVT performance pre- and immediately post-45-min nap opportunity

volunteers, whereas these other studies were isolated to shift workers whose cumulative experience with night shift work may contribute to acute changes in endothelial function not detectable in non-shift workers. Another explanation is that the 2 methods of measurement (FMD and PAT) simply quantify different aspects of endothelial function (one macrovascular and the other microvascular), and our interpretation of these measures may need to differ or be qualified by mechanistic processes not yet fully understood. These and other questions are not only raised by our findings but also by previous research assessing the relationship between FMD and PAT and showing results that conflict [32, 44–46]. Future research that tests protocols like the one used in our study and includes measurements with FMD and PAT may help to clarify confusion and guide decisions on which of the 2 methods is most appropriate for specific research questions and populations.

Bearing in mind that our study was not powered to detect specific change in RHI or lnRHI or difference between the 2 conditions tested, the data in study are worthy of further exploration. Specifically, previous research would suggest that RHI and lnRHI scores in the condition with no sleep would show a movement towards lower scores during follow-up measures compared to baseline, whereas the scores from baseline to follow-up in the condition with a nap would show the opposite [24]. Future research should include larger study samples to evaluate if such patterns emerge, as suggested from prior research [24], and seek to detect clinically meaningful differences between groups. One challenge that we foresee with planning future studies is the lack of evidence defining what is and is not a clinically meaningful change in endothelial function as measured by PAT.

We observed a substantial impairment in vigilant attention immediately after the 45-min nap, consistent with the phenomenon of sleep inertia [47]. This impairment, which lasted up to 10 min after the sleep opportunity, was expected given that approximately half the sample was in deep sleep in the last 5 min of the nap opportunity [48]. Our study highlights that while naps of this length may be investigated to explore the potential benefits for cardiovascular health outcomes, it is important to simultaneously consider the cognitive

performance impacts of sleep inertia, especially when translated to safety–critical operational settings.

Our study includes several limitations as well as strengths. First, the size of our study sample is small, which was purposeful due to a lack of resources, specifically funding. The lack of a statistically justified sample size is a limitation. Second, we used a simple coin flip procedure for randomization of condition order. This approach has been criticized by some as biased given the opportunity for manipulation [49]. Future studies involving larger samples should consider alternative, more robust methods. Third, statistical tests applied to small samples, like paired *t*-tests, may produce biased or inaccurate findings. We evaluated normality of select measures prior to use of select tests such as the Shapiro–Wilk tests. While tests like the Shapiro–Wilk are often recommended for small samples (e.g., < 50) [50], the risk of these tests being underpowered with small samples remains. Fourth, while we incorporated adjustments to linear mixed models and generalized estimating equations to account for our small sample size and potential for overdispersion, risk of biased parameter estimates remain a concern. Finally, our study sample included young and generally healthy adults. Future studies of experienced shift workers (rather than non-shift workers) would be beneficial and provide direct evidence for researchers and employers devoted to the health and safety of shift workers in search of the best available evidence germane to their settings and needs.

In this laboratory-based study, we demonstrate feasibility of non-invasive PAT measurement pre- and post-night shift work with high compliance and low attrition. The latter may be due, in part, to the relatively high remuneration for participation. We also provide data regarding the acute impact of night shift work (with and without napping) on endothelial function. We found that neither night shift work without sleep and night shift work with a 45-min nap had an impact on non-invasive indicators of endothelial function. Our findings conflict with findings from previous research and thus raise questions about how best to assess endothelial function when in relation to night shift work. Future, adequately powered studies are needed to confirm feasibility and determine if selected non-invasive techniques for assessing endothelial function are affected by night shift work and on-shift interventions like napping.

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None.

Authors' contributions
Authors PDP, DH, LSW, and SER conceived of the study aims and study design. Authors PDP, DGLR, TSO, SEM, and LSW executed the study protocol and data acquisition. All authors (PDP, CJH, TSO, SEM, DGLR, DH, MDW, LSW, and SER) were involved in analysis, interpretation, and review of data synthesis and reporting. All authors approved the final version for publication.

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Data availability
The data supporting this research study is available based on University of Pittsburgh policies and reviewed on a case-by-case basis.

Declarations

Ethics approval and consent to participate
The University of Pittsburgh Institutional Review Board approved this study on June 14, 2022, and assigned ID no. STUDY22040156. The study protocol was registered with ClinicalTrials.gov on June 23, 2022, and assigned ID no. NCT05436951. The first participant was consented on July 12, 2022.

Consent for publications
Not applicable. No individual data presented.

Competing interests
The authors declare that they have no competing interests.

Author details
[1]Department of Emergency Medicine, School of Medicine, University of Pittsburgh, PA, Pittsburgh 15261, USA. [2]Emergency Medicine Program, Department of Community Health Services and Rehabilitation Science, School of Health and Rehabilitation Sciences, University of Pittsburgh, PA, Pittsburgh 15261, USA. [3]Fatigue Countermeasures Laboratory, San José State University, CA, San José 95192, USA. [4]Division of Sleep and Circadian Disorders, Brigham and Women's Hospital, MA, Boston 02115, USA. [5]Division of Sleep Medicine, Harvard Medical School, MA, Boston 02115, USA. [6]Department of Exercise and Nutrition Sciences, School of Public Health and Health Professions, University at Buffalo, NY, Buffalo 14214, USA. [7]Department of Medicine, University of Pittsburgh, PA, Pittsburgh 15261, USA.

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