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**Title:** Performance Nutrition for Physician Trainees Working Overnight Shifts: A Randomized Controlled Trial

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Performance Nutrition for Physician Trainees Working Overnight Shifts: A Randomized Controlled Trial

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Data: No outside data sources were used and all data presented in this study were collected by study authors. The raw data for this study are strictly confidential and to protect the privacy of study participants are not available for sharing.
Abstract

Purpose

To compare acute effects of 2 dietary interventions with usual dietary habits on physician trainees’ alertness during overnight shifts.

Method

This registered, controlled, block-randomized crossover trial (NCT03698123) was conducted between October 2018 and May 2019 at Stanford Medicine. Physician trainees working at least 3 overnight shifts during a 1-week period were recruited. During the first overnight shift, participants followed their usual dietary habits. During the intervention nights (low carbohydrate-to-protein ratio and high carbohydrate-to-protein ratio interventions), participants received healthy dinners, snacks, water, and, upon request, caffeinated beverages, at the beginning of their shifts and were instructed to eat meals before 10 p.m. The sequence of interventions on the second and third nights were block-randomized across study weeks. Outcome measures (a priori) were overnight changes in validated measures of specific neurobehavioral dimensions: psychomotor vigilance, sensory-motor speed, working memory, and risk decision-making, as well as self-reported sleepiness and work exhaustion.

Results

Sixty-one physician trainees participated in this study. Compared to usual dietary habits, overnight changes in psychomotor vigilance scores (scale 0–1,000) improved by 51.02 points (95% confidence interval [CI]: 12.08, 89.96); sleepiness (scale 1–7) improved by 0.69 points (95% CI: 0.33, 1.05) under the low carbohydrate-to-protein ratio intervention. Compared to usual dietary habits, overnight changes in sleepiness (scale 1–7) improved by 0.61 points (95% CI: 0.25, 0.96) under the high carbohydrate-to-protein ratio intervention. Neither intervention had
beneficial effects relative to usual dietary habits with respect to sensory-motor speed, working memory, risk decision-making, or work exhaustion. There were no differences in outcomes between low carbohydrate-to-protein ratio and high carbohydrate-to-protein ratio interventions.

**Conclusions**

Dietary interventions may mitigate negative effects of physician trainee sleep deprivation during overnight shifts. Future studies are warranted to further examine the effectiveness of nutritional strategies on physician alertness during overnight shifts.
Over the last 2 decades, occupational factors that influence the performance and well-being of physician trainees have received increased attention.\textsuperscript{1–5} As a result, a number of duty hour restrictions have been mandated by accreditation bodies attempting to improve physician trainees’ well-being and patient safety.\textsuperscript{6} In addition to duty hours, other aspects of work and learning environments that contribute to physician trainee fatigue and impaired patient safety, learning experience, and work performance during shifts (e.g., intensity of work, interruptions, poor teamwork, insufficient breaks) have also been investigated.\textsuperscript{7–11} Nutritional factors, including timing\textsuperscript{12,13} and composition\textsuperscript{14–21} of individuals meals, have an acute effect on sleepiness and cognitive performance. For instance, the carbohydrate-to-protein ratio of a meal may affect postprandial fatigue, alertness, and cognitive performance.\textsuperscript{14–16,20,21} With respect to meal timing, laboratory studies simulating overnight shifts suggest that eating a meal between the hours of 10 p.m. and 6 a.m. is associated with decreased alertness, impaired cognitive performance, increased work errors, delayed response times, and increased attention lapses.\textsuperscript{12,13,20} In addition, physicians experiencing hunger or dehydration report irritability, frustration, light-headedness, tremor, nausea, and difficulty with concentrating and decision-making.\textsuperscript{22} There is also evidence that hydration affects cognitive performance.\textsuperscript{23–26} For example, a study of physicians and nurses found that those who were dehydrated exhibited poorer short-term memory compared with those who were well hydrated.\textsuperscript{26} A number of studies report that physician trainees experience major challenges with eating at regular times and accessing healthy meals, snacks, and drinks during overnight shifts.\textsuperscript{27–31} Although the 2020 Accreditation Council for Graduate Medical Education (ACGME) Common Program Requirements mandate postgraduate training programs attend to fatigue mitigation and mention “maintaining a healthy diet” as a dimension to consider,\textsuperscript{32} to our knowledge the utility
of nutritional interventions as a fatigue mitigation strategy have not been adequately studied or widely employed. Physician trainees are required to learn new concepts quickly, be alert and attentive, and have impeccable judgment and decision-making abilities, often in fast-paced and high-stress settings. All these abilities can be compromised by nutritional factors.\textsuperscript{22,31,33,34} Furthermore, several studies have shown that short- and long-term intake of refined sugar and high saturated fat, fast food, and junk foods—types of food commonly available during resident overnight shifts—impairs reaction times and lapses, episodic memory, and learning ability in healthy adults.\textsuperscript{26,35–38} Similarly, high glycemic index meals (e.g., added sugar) have been shown to result in postprandial sleepiness and decreased sleep onset time.\textsuperscript{19,39} These factors exacerbate the negative impact of sleep deprivation and negatively affect the learning ability of physician trainees and, potentially, patient safety during night shifts.

Unfortunately, medical training often limits one’s ability to adhere to optimal nutritional behaviors.\textsuperscript{27,31,40,41} For example, 66\% of surveyed first-year residents identified irregular meal times as one of the main work-related challenges faced during the first year of residency—more prevalent than heavy workload (64\%), and second only to long work hours (75\%).\textsuperscript{28} On the other hand, physician trainees who reported that their nutritional needs were met during on-call shifts rated themselves higher on well-being indices, including lower rates of burnout.\textsuperscript{42} To our knowledge, only one study has assessed the effects of dietary factors on physician performance.\textsuperscript{43} In a small nonrandomized pre–post study, Lemaire and colleagues found that providing healthy meals and drinks to physicians during daytime shifts resulted in improved cognitive performance on the dietary intervention day.\textsuperscript{43} To date, no randomized-controlled trials have assessed the acute effects of dietary interventions on the alertness and sleepiness of physician trainees during overnight shifts. In addition, no studies have assessed the combined...
effects of night shift food composition, timing, and fluid intake on alertness and sleepiness of physician trainees, nor the feasibility and suitability of dietary interventions in the health care settings where physicians’ differing on-call schedules, lifestyles, and dietary preferences make interventions challenging.

In this randomized-controlled trial, we compared the acute effects of 2 standardized dietary interventions with usual dietary habits on overnight changes in neurobehavioral performance, self-reported sleepiness and work exhaustion among physician trainees working overnight shifts. Our 2 hypotheses were that compared to usual dietary habits, 2 standardized dietary interventions would mitigate the negative effects of sleep deprivation on neurobehavioral performance, self-reported sleepiness, and work exhaustion of physician trainees during nighttime duty; and that among the 2 standardized dietary interventions, the low carbohydrate-to-protein ratio intervention would further minimize the negative effects of sleep deprivation on neurocognitive performance, self-reported sleepiness, and work exhaustion of physician trainees during nighttime duty relative to the high carbohydrate-to-protein ratio intervention.

Method

Design, setting, and participants

This block-randomized crossover trial was conducted during 9 weeks between October 2018 and May 2019. The Stanford University Institutional Review Board approved the study protocol prior to starting recruitment. This study was registered at clinicaltrials.gov (clinicaltrials.gov/ct2/show/NCT03698123, NCT03698123). Prior to participation, we obtained written informed consent from all participants. Participants received a $100 e-gift card upon completion of the study. This study was named the Superheroes Nutrition Study by study staff to reflect the extraordinary work that physician trainees do.
Residents and fellows, in all training years, working overnight shifts at the Stanford Health Care or Stanford Children’s Health hospitals on at least 3 nights during a 1-week period were eligible to participate in this study. Although the majority of participants were on rotations involving 12- to 14-hour overnight shifts, we also included participants with longer shifts, up to 24 hours. Exclusion criteria were any food allergy, prior anaphylactic reaction to food, or other dietary restrictions that the catering kitchen could not accommodate (e.g., gluten free, ketogenic, halal, or kosher diets). We recruited participants through brief presentations at grand grounds and resident conferences, printed and digital flyers, email invitations via program directors and chief residents, and referrals from other study participants (volunteer sample). Blinding the study participants and those assessing outcomes was not possible, however, all statistical analyses conducted by the first author (M.S.M.) were independently verified by a biostatistician (H.W.) who was blinded to the intervention assignments. In addition, although study participants knew the goal of the study was to test the impact of nutritional strategies on cognitive performance, sleepiness, and work exhaustion during overnight shifts, they did not know that the macronutrient ratio of the meals was specifically being designed and compared.

**Interventions**

Each participant contributed data over 3 overnight shifts during a 1-week interval. During the first night shift (usual dietary habits), we asked participants to eat and drink as they normally would during a night shift and record the time and amount of all food, fluid, and caffeine they consumed. Participants completed a paper baseline survey providing demographic characteristics (age, gender, height, weight, specialty) and average hours of sleep per 24 hours during the previous week. After completing the study assessments at the beginning of the shift on the first night, we provided participants with a 2-page handout summarizing the potential benefits of
staying hydrated, eating healthy meals and snacks, and avoiding food intake after 10:00 p.m., along with a copy of their signed consent form in a pocket folder. The contents of the handout were not reviewed with participants on the nights of the usual dietary habits intervention.

On the second and third study intervention nights, participants received 1 of the 2 different standardized dietary interventions: low carbohydrate-to-protein ratio or high carbohydrate-to-protein ratio. The composition of the low carbohydrate-to-protein ratio (25% of total calories from protein, 40% from carbohydrates, and 35% from fat) and high carbohydrate-to-protein ratio (12% of total calories from protein, 54% from carbohydrates, and 34% from fat) are provided in Supplemental Digital Appendix 1, at http://links.lww.com/ACADMED/B204. As illustrated there, both intervention meals and snacks were higher in plant-based foods and lower in added sugars than current standard American diets. In addition, about 4% of total calories of the high carbohydrate-to-protein ratio intervention came from added sugars and 5% from saturated fat, and 0% from added sugars and 7% from saturated fat for the low carbohydrate-to-protein ratio intervention, as opposed to the approximate daily average of 42% from added sugars and 12% from saturated fat reported by U.S. adults.

The sequence of low carbohydrate-to-protein ratio and high carbohydrate-to-protein ratio on the second and third study night were block-randomized across study weeks using a computer-generated random-number sequence by the first author (M.S.M.) prior beginning the study, which we conducted in blocks of 4 for 16 weeks. Accordingly, there were 2 possible sequences (see Figure 1): usual dietary habits, then low carbohydrate-to-protein ratio, then high carbohydrate-to-protein ratio (n = 34); or usual dietary habits, then high carbohydrate-to-protein ratio, then low carbohydrate-to-protein ratio (n = 27). A study staff member (M.S.M.) reviewed the potential negative effects of late-night eating and positive effects of hydration on cognitive
performance with each study participant (one-on-one) at the beginning of both intervention nights.

The study was conducted during weeks where at least 3 physician trainees were eligible and able to participate in the study. When schedules permitted, we implemented a $\geq 24$-hour wash-out period between study nights (e.g., participation on Monday, Wednesday, and Friday). More details about the 2 intervention nights are provided in Supplemental Digital Appendix 1, at http://links.lww.com/ACADMED/B204.

**Outcomes and measures**

Outcomes were overnight changes (pre-shift assessment relative to latter part of shift assessment) in validated measures designed to assess psychomotor vigilance, sensory-motor speed, working memory, and risk decision-making, as well as self-reported sleepiness and work exhaustion. On each night of the study, participants completed assessments at the beginning (4:00 – 8:30 p.m.) and in the latter part of the shift (2:00 – 7:00 a.m.). Each study session lasted on average 15 minutes. The time window for the second assessment was selected to occur when the body is prime for sleep and nighttime cognitive performance is maximally impaired.\textsuperscript{12,46,47}

The scores for the 4 primary outcomes (neurobehavioral tests) range from 0 to 1,000, where higher scores are favorable. These 4 tasks were selected by physician authors (M.T.T., L.K., T.D.S.) of this study out of 10 components of the Cognition battery, specifically designed to assess fitness-for-duty during spaceflight and validated in astronaut and highly educated adult populations,\textsuperscript{48,49} for maximum relevance to physician trainees and balanced with minimum time taken away from clinical duties. A brief description of each of these measures is provided below; see Supplemental Digital Appendix 2, at http://links.lww.com/ACADMED/B204, for additional details.
• Psychomotor Vigilance Test (PVT) efficiency scores: The 3-minute PVT measures sustained vigilant attention,\textsuperscript{49,50} a basic requirement for information processing that enables the maintenance of vigilance, selective and focused attention, response persistence, and continuous effort despite changing conditions.\textsuperscript{51} It is considered the criterion standard and most sensitive measure of the neurobehavioral effects of sleep deprivation and neurobehavioral alertness in operational settings.\textsuperscript{5,51–53} The PVT has stable performance and, among the neurobehavioral assessments, is the least prone to learning effects across repeated tests.\textsuperscript{49,54–56}

• Motor Praxis Task (MPT) speed scores: The MPT is a validated neurobehavioral test that takes 30 seconds to complete and assesses sensory-motor speed.\textsuperscript{49,50}

• Fractal 2-Back (F2B) accuracy scores: The F2B is a validated neurobehavioral test that takes 2 minutes to complete and assesses working memory.\textsuperscript{49,50}

• Balloon Analog Risk Task (BART) accuracy (risk-taking) scores: The BART takes 2 minutes to complete and is a validated neurobehavioral test that assesses risk decision-making.\textsuperscript{49,50}

Secondary outcomes were self-reported sleepiness and work exhaustion. We assessed sleepiness using the validated Stanford Sleepiness Scale (SSS) (scale: 1–7; see Supplemental Digital Appendix 2, at http://links.lww.com/ACADMED/B204)\textsuperscript{57} and measured work exhaustion by a modified version of the validated Work Exhaustion Scale of the Stanford Professional Fulfillment Index (scale: 0–4; see Supplemental Digital Appendix 2, at http://links.lww.com/ACADMED/B204).\textsuperscript{58}
Statistical analyses

Analyses were completed using SAS statistical software, version 9.4 for Windows (SAS Institute Inc., Cary, NC). Generalized linear mixed models (PROC GLIMMIX) with random subject effect and linear contrast (a priori) were used to compare the overnight changes in outcomes under the 3 dietary conditions. We calculated least-squares means of overnight change in outcome measures and their standard errors for each condition, as well as differences between conditions as calculated by the PROC GLIMMIX procedure. PROC GLIMMIX automatically handles missing data in dependent variables using a maximum likelihood method and does not delete missing data listwise.

We had set the success rate for feasibility of this program at a retention rate of over 80%. Currently there is no established minimal clinically important difference for the PVT efficiency score, therefore, prior to the start of the trial based on pooled evidence from previous studies, the study protocol defined an intervention effective, relative to usual dietary habits, if it resulted in a >20% improvement in PVT performance. Based on our power calculation, with a total of 50 participants entering the study, the probability that a treatment difference would be detected at a 2-sided 0.05 significance level was 90%. All tests were 2-sided with type I error rates of 0.05. Standardized coefficients were calculated by centering to the grand mean and dividing by the grand standard deviation of each variable.

Results

Of the 114 physician trainees who expressed interest in participating in the study, 61 (60 residents and 1 clinical fellow) enrolled (54%) (Figure 1). Table 1 summarizes participants’ characteristics. There were no significant differences between subject characteristics such as age, body mass index, gender distribution between the 2 randomized sequence groups. Sixty-one
participants completed 182 of the potential 183 pre/post shift study assessments (missing data for 1 PVT score for a pre-shift session on the first study night); we thus analyzed data for all 61 participants. All 61 participants completed the study (100% retention). Among these, 23 out of 61 (38%) had at least a 24-hour washout period between each condition, and 31 (51%) had at least a 24-hour washout between low carbohydrate-to-protein ratio and high carbohydrate-to-protein ratio interventions. All washout periods were at least 18 hours. Among the 61 participants, 5 (8%) reported sleeping during usual dietary habits night (range: 20–150 minutes; median: 0), 4 (7%) reported sleeping during low carbohydrate-to-protein ratio night (range: 60–300 minutes; median: 0) and 5 (8%) reported sleeping during high carbohydrate-to-protein ratio night (range: 30–90 minutes; median: 0). There were no significant differences between minutes of sleep among the 3 study nights. In terms of shift length, 1 (2%) physician trainee was on a 24-hour shift and 2 (3%) were on 20-hour shifts every other night that started between 4:00 and 7:00 p.m. All other physician trainees (95%) were on rotations requiring overnight shifts ranging from 12 to 14 hours in duration. On the usual dietary habits night, the majority of participants ate sporadically and frequently during their overnight shifts, with 32 (52%) eating a meal or large snack (≥ 300 calories) after 10:00 p.m. On high carbohydrate-to-protein ratio night 13% and on low carbohydrate-to-protein ratio night 20% of participants ate their meals or snacks (≥ 300 calories) after 10:00 p.m. None of the study participants ate non-study meals on high carbohydrate-to-protein ratio and low carbohydrate-to-protein ratio intervention nights. During high carbohydrate-to-protein ratio and low carbohydrate-to-protein ratio nights, 1 and 3 participants, respectively, ate less than half of their meals, due to aversion to ingredients in the meals (2), feeling ill (1), and lack of time due to clinical work needs (1). With respect to hydration, the number of subjects reporting fluid intake
≥ 1,000 ml during their overnight shift was 9 of 61 (15%) on the usual dietary habits night, 32 (52%) on high carbohydrate-to-protein ratio, and 26 (43%) on low carbohydrate-to-protein ratio.

**Primary outcomes: Neurobehavioral performance**

Table 2 displays least squares means for primary outcomes (scales: 0–1,000). Compared to usual dietary habits condition, overnight changes in psychomotor vigilance (PVT) scores had a statistically significant improvement by 51.02 points (standard error [SE] = 19.67, \( P = .011, \) 95% confidence interval [CI]: 12.08, 89.96) under the low carbohydrate-to-protein ratio intervention. There were no statistically significant differences for overnight changes in psychomotor vigilance scores between usual dietary habits and the high carbohydrate-to-protein ratio intervention, or between low carbohydrate-to-protein ratio and high carbohydrate-to-protein ratio interventions.

Working memory scores (F2B) improved by 101.5 points during the first night of the study (usual dietary habits) (Table 2). This improvement was significantly larger than both high carbohydrate-to-protein ratio and low carbohydrate-to-protein ratio interventions (Table 2). Neither of the dietary interventions had any beneficial effects relative to usual dietary habits with respect to sensory-motor speed and risk decision-making (Table 2).

**Secondary outcomes: Self-reported sleepiness and work exhaustion**

Table 2 displays least squares means for secondary outcomes. Compared to the usual dietary habits condition, overnight changes in self-reported sleepiness (scale: 1–7) improved by 0.69 point (SE = 0.18, \( P < .001, \) 95% CI: 0.33, 1.05) under low carbohydrate-to-protein ratio intervention and by 0.61 points (SE= 0.18, \( P = .001, \) 95% CI: 0.25, 0.96) under the high carbohydrate-to-protein ratio intervention. There were no differences in overnight changes in self-reported sleepiness between low carbohydrate-to-protein ratio and high carbohydrate-to-
protein ratio interventions. There were no statistically significant differences in overnight changes in work exhaustion between the 3 conditions (Table 2).

**Discussion**

With this study, we have compared the effects of 2 standardized dietary interventions with usual dietary habits of physician trainees on overnight changes in neurobehavioral performance, self-reported sleepiness, and work exhaustion. Consistent with our first hypothesis, our findings suggest that overnight declines in psychomotor vigilance, a criterion standard and the most sensitive measure of the neurobehavioral effects of sleep deprivation, were mitigated under the low carbohydrate-to-protein ratio dietary intervention where the average PVT score was slightly higher at the end of the shift (18.9 points improvement) compared to decline in PVT observed under the usual dietary habits condition (32.1 points decline). Although currently there is no established minimal clinically important difference for PVT efficiency score, that the low carbohydrate-to-protein ratio dietary intervention abrogated the overnight decline in PVT observed under usual dietary conditions is striking. We also found that the increase in self-reported sleepiness was smaller under both low carbohydrate-to-protein ratio and high carbohydrate-to-protein ratio interventions relative to usual dietary habits. There was a 0.69-point worsening in SSS scores on usual dietary habits night in the latter part of the shift assessments. Although there is no established minimal clinically important difference for SSS scores, we found no overnight changes in these scores on the low carbohydrate-to-protein ratio night and a mean of only 0.08-point worsening on the high carbohydrate-to-protein ratio night, again suggesting that the dietary interventions abrogated the overnight increase in sleepiness. Neither dietary intervention had beneficial effects on sensory-motor speed, working memory, risk decision-making, or self-reported work exhaustion. We found that there was a large
improvement in working memory score (F2B) on the first night (usual dietary habits) that was statistically significantly larger than overnight changes in both the high carbohydrate-to-protein ratio and low carbohydrate-to-protein ratio interventions. Based on lack of physiological plausibility and findings of other studies that either show that F2B performance improved on the first shift and that, unlike the PVT, the F2B test is prone to improvements over time due to learning and practice effects, we believe that this improvement was mostly likely due to learning effects with F2B assessment that happened between first and second assessments on the first night. Contrary to our second hypothesis, there were no differences in study outcomes between low carbohydrate-to-protein ratio and high carbohydrate-to-protein ratio interventions. Although multiple studies have demonstrated the negative impact of overnight shifts on psychomotor vigilance in physicians using the PVT, few studies have evaluated the effects of various interventions on PVT performance in hospital settings. A study comparing flexible and standard duty-hour programs among first-year residents found no differences in psychomotor vigilance outcomes. A single-center randomized, crossover trial in a surgical intensive care unit found nurses exposed to a high illuminance (1,500–2,000 lx) white light for 10 hours had lower subjective sleepiness on the SSS at the end of the night shift (2.6 ± 0.2 versus 3.0 ± 0.2)—a difference smaller than observed with both the low carbohydrate-to-protein ratio and high carbohydrate-to-protein ratio interventions we analyzed. We found no differences in psychomotor vigilance outcomes as measured by the PVT. A randomized crossover study comparing the effects of a fatigue countermeasure program, focused on sleep health and shift scheduling, with a “jet lag diet” program in emergency physicians did not show any statistically significant differences between decline in psychomotor vigilance measured by the PVT between the 2 conditions. A nonrandomized pre–post study by Lemaire and colleagues examined the...
effects of a dietary intervention including 6 small healthy meals provided to physicians at scheduled breaks either at the doctors’ lounge or at their practice location on their daytime composite scores of speed and accuracy for simple reaction time tests and found higher (favorable) scores on the dietary intervention day compared to baseline (220 versus 209, \( P = .01 \)).

In our study, the improved performance on the low carbohydrate-to-protein ratio intervention compared to usual dietary habits is consistent with other studies demonstrating that lower carbohydrate-to-protein ratio in a meal is associated with improved alertness, potentially by altering brain levels of tryptamines and catecholamines. On the other hand, we did not find a clear difference between the low carbohydrate-to-protein ratio and high carbohydrate-to-protein ratio interventions for any study outcomes. It is noteworthy that even the high carbohydrate-to-protein ratio meal had much lower sugar content, where only 4% of total calories came from added sugars, compared to an average 42% of total calories from sugar reported by U.S. adults.

There is evidence that high glycemic index meals (e.g., with added sugar) result in postprandial sleepiness and decreased sleep onset time. We also found that educating study participants about the potential negative effects of late-night eating and positive effect of hydration on cognitive performance resulted in greater likelihood of consuming meals prior to 10:00 p.m. and consuming more water throughout the shift. Studies conducted outside medical settings have also shown that combining nutrition education with provision of healthy and free foods improves healthy eating behaviors. Although many physicians are aware of the importance of nutrition and hydration for their long term well-being, lack of awareness about the acute effects of meals on cognitive performance, limited time to take nutrition and hydration breaks, and limited or no access to healthy food and snack options at hospital cafeterias and patient areas during night shift
or weekends challenge their ability to maintain healthy eating behaviors. Health care organizations can facilitate healthy eating behaviors among physicians by providing nutrition education on acute effects of diet on cognitive performance, creating policies that promote regular nutrition and hydration breaks, and improving access to healthy and affordable food choices at workplaces. We are providing a summary of recommendations based on existing evidence in Table 3, which could be considered as part of residency program efforts to adhere to the ACGME Common Program Requirement to mitigate fatigue.

Our study is subject to a number of limitations. First, although we assessed changes in multiple neurobehavioral dimensions, we could not assess all dimensions due to time demands and unpredictable work schedules. Second, similar to other studies we found that some of the neurobehavioral tests (the MPT, F2B, and BART) appear to be prone to improvements in scores over time due to learning and practice effects, which may explain large improvements, compared to other study nights, in the scores of these tests on the first night of the study (usual dietary habits). Third, there were variation in dimensions that we could not control (e.g., actual shift duration, patient census, patient acuity, number of admissions, whether participants were able to sleep) across study nights and these might have influenced the outcome measures. Fourth, due to the unpredictability of clinical work duties, we could not rigidly standardize the timing of the later shift assessment to be consistent on all 3 study nights. Fifth, although we randomized which dietary intervention night came first, we standardized usual dietary habits to be the first night of the study for all participants due to concern that the nutrition education regarding the importance of healthy eating, hydration, and meal timing on the 2 intervention nights might alter usual dietary habits. Sixth, the study was not designed to assess in what ways changes in sleepiness and neurobehavioral outcomes translate into patient care outcomes. Finally, the study was
powered to detect changes in PVT scores, a primary study outcome, and may have not had
enough power to detect changes in the other assessment scores (MPT, F2B, and BART). Due to
structure of the shifts and scheduling, we were not able to uniformly implement the protocol’s
recommended ≥ 24-hour washout period between conditions. However, it is unlikely that a
timeframe shorter than 24-hours (which was always at least 18 hours) between study meals
would have affected study results. The majority of related studies suggest that the effects of
meals on cognitive performance and sleepiness are most pronounced up to 4 hours after ingestion
of a meal,19-21,65 and the metabolic effects of nighttime meal consumption can last longer,66 or
until morning.67
Our study also has several strengths. To our knowledge, this is the first controlled study
assessing the effects of nutritional factors on physician performance during overnight shifts in
real-life settings. We used the PVT as one of our primary outcomes as it is considered a suitable
performance assessment for real-life situations where continuous vigilant attention and timely
responses are essential53 and prior research indicates repeated testing does not affect the PVT
performance.49,54-56 We included physician trainees from different specialties and believe that
these findings are generalizable to other academic medicine graduate medical education
programs. We also believe our findings on nutritional composition, timing, and hydration are
likely generalizable to practicing physicians working overnight shifts. While trainee physician
participation in randomized controlled trials is challenging due to time constraints, concern for
interrupting patient flow, and unpredictable work schedules, we were able to successfully recruit
a large number of participants, all of whom completed the study. The 100% retention rate among
our participants is also strong evidence of program feasibility for testing future nutrition
interventions in physician trainees.
Sleep deprivation is an inherent occupational risk for physician trainees. Consequences of sleep deprivation include increased sleepiness, disorientation, significant fatigue, and difficulty concentrating and learning, all of which may have a negative effect on learning, performance and well-being of physician trainees as well as the quality of patient care during overnight shifts. To our knowledge, we report here the first controlled trial of a dietary intervention on neurobehavioral performance and sleepiness among physician trainees working overnight shifts. Our preliminary findings highlight nutritional strategies as one potential approach that graduate medical education leaders and program directors can use to mitigate learner sleepiness and deterioration in alertness during overnight shifts. This may in turn improve the learning experience, work performance, and well-being of physician trainees and the quality of patient care. At the end of 2020, the Stanford Graduate Medical Education program, in collaboration with Stanford WellMD Center, launched an enduring program to provide free healthy meals for physician trainees during overnight shifts using operational funds. The program has received multiple gratitude notes and positive subjective feedback from physician trainees. Future studies are warranted to address the limitations of this preliminary study, and to examine the individual effects of meal timing, meal composition, and fluid intake; their dose response effects on mitigating the detrimental effects of sleep deprivation on alertness of physicians during overnight shifts; and ways changes in physician alertness during overnight shifts translate into patient care outcomes. Given that the PVT is one of the most validated performance assessment tools for real-life situations and is least influenced by learning or aptitude, we recommend PVT in future studies of nutrition and alertness. We hope that future studies further detail the importance of nutrition on optimal learning, performance, and well-being of physician trainees and the safety and quality of patient care they provide.
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Figure Legends

Figure 1

CONSORT flow diagram, from a randomized controlled trial comparing effects of 2 dietary interventions with usual dietary habits on alertness of physician trainees during overnight shifts, Stanford Health Care and Stanford Children’s’ Health hospitals, October 2018–May 2019. Abbreviations: HCP, high carbohydrate to protein ratio condition; LCP, low carbohydrate to protein ratio condition.
### Table 1

Characteristics of 61 Physician Trainees, From a Randomized Controlled Trial Comparing Effects of 2 Dietary Interventions With Usual Dietary Habits on Alertness During Overnight Shifts, Stanford Health Care and Stanford Children’s Health Hospitals, October 2018–May 2019

<table>
<thead>
<tr>
<th>Demographic information</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender, frequency (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>31 (50.8)</td>
</tr>
<tr>
<td>Male</td>
<td>30 (49.2)</td>
</tr>
<tr>
<td><strong>Specialty, frequency (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Internal medicine</td>
<td>28 (45.9)</td>
</tr>
<tr>
<td>Pediatrics</td>
<td>11 (18.0)</td>
</tr>
<tr>
<td>Other(^a)</td>
<td>15 (24.6)</td>
</tr>
<tr>
<td>General surgery</td>
<td>7 (11.5)</td>
</tr>
<tr>
<td><strong>Age in years, range; mean (SD)</strong></td>
<td>27–36; 29.7 (2.2)</td>
</tr>
<tr>
<td><strong>Weight in kg, range; mean (SD)</strong></td>
<td>47.6–99.8; 66.8 (13.3)</td>
</tr>
<tr>
<td><strong>Height in cm, range; mean (SD)</strong></td>
<td>152.4–190.5; 170.0 (9.4)</td>
</tr>
<tr>
<td><strong>BMI, range; mean (SD)</strong></td>
<td>18.6–35.4; 23.0 (3.3)</td>
</tr>
<tr>
<td><strong>Average hours of sleep per 24</strong></td>
<td>5.5–9.0; 6.8 (0.7)</td>
</tr>
<tr>
<td><strong>hours in the past week, range;</strong></td>
<td></td>
</tr>
<tr>
<td><strong>mean (SD)</strong></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: SD, standard deviation.
\(^a\)Other specialties were anesthesiology, neurology, obstetrics–gynecology, and psychiatry.
### Table 2

Overnight Changes in Primary and Secondary Outcomes for 61 Physician Trainees, From a Randomized Controlled Trial Comparing Effects of 2 Dietary Interventions With Usual Dietary Habits on Alertness During Overnight Shifts, Stanford Health Care and Stanford Children’s Health Hospitals, October 2018–May 2019

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Least-squares means</th>
<th>$P$ value $^c$ for contrasts</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>UDH</td>
<td>HCP</td>
</tr>
<tr>
<td><strong>Primary outcomes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychomotor vigilance (PVT) (scale: 0–1,000)</td>
<td>32.12</td>
<td>-1.82</td>
</tr>
<tr>
<td>Sensory-motor speed (MPT) (scale: 0–1,000)</td>
<td>-1.03</td>
<td>-0.66</td>
</tr>
<tr>
<td>Working memory (F2B) (scale: 0–1,000)</td>
<td>-101.46</td>
<td>9.26</td>
</tr>
<tr>
<td>Risk decision-making (BART) scale: (0–1,000)</td>
<td>-54.59</td>
<td>16.82</td>
</tr>
<tr>
<td><strong>Secondary outcomes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stanford self-reported sleepiness (scale: 1–7)</td>
<td>-0.69</td>
<td>-0.08</td>
</tr>
<tr>
<td>Work exhaustion (scale: 0–4)</td>
<td>-0.07</td>
<td>-0.04</td>
</tr>
</tbody>
</table>

Abbreviations: UDH, usual dietary habits; HCP, high carbohydrate-to-protein ratio intervention; LCP, low carbohydrate-to-protein ratio intervention; SE, standard error; PVT, Psychomotor Vigilance Test; MPT, Motor Praxis Task; F2B, Fractal 2-Back; BART, Balloon Analog Risk Task.

$^a$Least-squares means of overnight changes (beginning of the shift values minus latter part of the shift values). Smaller values (more negative) are favorable and indicate improvement in neurobehavioral performance tasks (primary outcomes). Larger (more positive) values are favorable and indicate improvement in sleepiness and work exhaustion (secondary outcomes).

$^b$P values are reported for the a priori contrasts. Bold values indicate statistical significance where $P < .05$.

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### Table 3

**Performance Nutrition Recommendations for Physician Trainees Working Overnight Shifts Based on Existing Evidence and Findings From a Randomized Controlled Trial Comparing Effects of 2 Dietary Interventions With Usual Dietary Habits on Alertness During Overnight Shifts, Stanford Health Care and Stanford Children’s Health Hospitals, October 2018–May 2019**

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Rationale(^a)</th>
<th>Tactics to foster implementation</th>
</tr>
</thead>
</table>
| Keep hydrated           | In addition to findings of this study, there is convincing evidence that being hydrated is associated with improved mood, cognitive performance, and alertness and reduced sleepiness.\(^{23,25,26,72–74}\) | Individuals:  
  - Drink water, tea, and coffee during a nightshift in order to fulfill daily fluid intake requirements.\(^{75}\)  
  - Aim for at least 3 and ideally 6 glasses of plain water a day.\(^{76}\)  
    That said, individual water requirements vary and the simplest way to assess hydration status is to use urine color chart developed and validated by Armstrong et al.\(^{77,78}\)  
  - In order to overcome dehydration while regulating frequent visits to restrooms, drink small amounts of fluids frequently throughout the shift and, during the day, consume fruits and vegetables, which contain fluid that is gradually released.  

  Organizations:  
  - Ensure the number and locations of water fountains meet physician trainees needs.  
  - Provide free and portable water bottles at mealtimes as an alternative to sugar-sweetened beverages.  
  - Provide education on importance of hydration on work performance.  

| Pay attention to meal timing | There is convincing evidence that, compared to the morning, eating late at night or during night shifts results in unfavorable cognitive performance, metabolic response, and energy expenditure.\(^{12,13,21,79–84}\) The | Individuals:  
  - During overnight shifts, eat meals before start of the night shift and before 10 p.m.  

  Organizations:  
  - Provide physician trainees healthy meals at the beginning of each overnight shift.  

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\(^{a}\) The rationale indicates evidence and findings from a randomized controlled trial comparing effects of 2 dietary interventions with usual dietary habits on alertness during overnight shifts, Stanford Health Care and Stanford Children’s Health Hospitals, October 2018–May 2019.
Negative affect on metabolism is observed as early as eating at 8 p.m. Pay attention to meal size and composition. Many studies have shown that the size of the meal, fat content, and ratio of carbohydrate to protein in meals can acutely affect postprandial cognitive performance.\(^{15-17,85}\) Large meals that are low in protein and high in both fat and carbohydrates may slow down reaction times and result in higher self-reported fatigue and sleepiness.\(^{15,16,19,35-38,86-92}\)

- Provide education that eating meals during overnight shifts may impair work performance.
- During night shifts, choose dinners with higher protein and lower carbohydrate and fat contents. One suggestion for a balanced meal is to include 20–30 g of protein, 40–60 g of complex carbohydrates, and 20–30 g of fat with less than 7 g of saturated fat and no added sugars.
- After completing the shift, consuming a meal with higher carbohydrate content 2–4 hours before bedtime may shorten sleep onset latency.
- Limit consumption of drinks and foods with added sugar and saturated fat.

Individuals:

- During night shifts, choose dinners with higher protein and lower carbohydrate and fat contents. One suggestion for a balanced meal is to include 20–30 g of protein, 40–60 g of complex carbohydrates, and 20–30 g of fat with less than 7 g of saturated fat and no added sugars.
- After completing the shift, consuming a meal with higher carbohydrate content 2–4 hours before bedtime may shorten sleep onset latency.
- Limit consumption of drinks and foods with added sugar and saturated fat.

Organizations:

- Improve access to free or affordable fruits, vegetables, protein sources (low in saturated fat), and whole grains.
- Limit access to sugar-sweetened beverages, foods, and snacks high in added sugar and saturated fat.
- Provide education about the importance of meal size and composition on work performance.

\(^{a}\)These recommendations could also be considered as part of residency program efforts to adhere to the Accreditation Council for Graduate Medical Education Common Program Requirement to mitigate fatigue.\(^{32}\)
Figure 1

Screened

Assessed for eligibility assessment (n = 110)

Excluded (n = 4)
- Reasons (n = 4, not interested in study foods)

Assessed for eligibility (n = 110)

Excluded (n = 39)
- Not meeting inclusion criteria (n = 3)
- Declined to participate (n = 1)
- Other reasons (n = 35, not working at least 3 nights during study weeks or conflict with study)

Randomized (n = 61)

Allocated to intervention (n = 34, sequence: LCP-HCP)
- Received allocated intervention (n = 34)
- Did not receive allocated intervention (n = 0)

Allocated to intervention (n = 27, sequence: HCP-LCP)
- Received allocated intervention (n = 27)
- Did not receive allocated intervention (n = 0)

Follow-Up

Lost to follow-up (n = 0)
Discontinued intervention (n = 0)

Assessment

Assessed for objective 1 (n = 34)
Assessed for objective 2 (n = 34)

Assessed for objective 1 (n = 27)
Assessed for objective 2 (n = 27)