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The Influence of Habitual Physical Activity and Sedentary Behavior on Objective and Subjective Hot Flashes at Midlife

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ABSTRACT:

The years surrounding the transition to menopause are marked by multiple challenges to health. Hot flashes are a commonly reported symptom of women at this time and their frequency has been associated with disease risk. Regular physical activity and reduced sedentary time are recommended for health and wellbeing. However, the effect of physical activity and sedentary behavior on hot flashes remains unclear. OBJECTIVE: The purpose of this study was to evaluate relationships between physical activity, sedentary time and hot flashes during both waking and sleeping periods using concurrent objective and subjective measures of hot flashes in midlife women. METHODS: Women aged 45-55 (n=196) provided self-reported data on physical activity and underwent 24-hours of hot flash monitoring using sternal skin conductance. Participants used event marking and logs to indicate when hot flashes were perceived. Wake and sleep periods were defined by actigraphy. Mean ambient temperature and humidity were recorded during the study period. Generalized linear regression modeling was used to evaluate the effect of physical activity types and sedentary time on hot flash outcomes. Isotemporal substitution modeling was used to study the effect of replacing sedentary time with activity variables on hot flash frequency. RESULTS: Modeled results indicated that increasing sitting by one hour was associated with a 7% increase in the rate of objectively measured but not subjectively reported hot flashes during sleep. Replacing one hour of sitting with one hour of vigorous activity was associated with a 100% increase in subjectively reported but not objectively measured waking hot flashes. There was little evidence for an effect of temperature or humidity on any hot flash outcome. CONCLUSIONS: These data provide support for relations between sedentary time, physical activity and hot flashes and highlight the importance of using objective and subjective assessments to better understand the 24-hour hot flash experience.

KEY WORDS:

Physical activity, sedentary time, hot flashes, hot flash measurement, isotemporal substitution modeling

Introduction

The years surrounding the final menstrual period are associated with hallmark symptoms such as hot flashes. Hot flashes (a.k.a. hot flushes) are a sudden heat dissipation response leading to increased heart rate, vasodilation of the skin and sweating experienced by approximately 80% of people who undergo menopause[1–3]. The mechanism underlying hot flashes is not completely understood but appears to involve disruption of the hypothalamic thermoregulatory control center via hypertrophy and activity of KNDy (kisspeptin/neurokinin B/dynorphin) neurons as estradiol levels fall[4–6]. Hot flashes can be bothersome, decrease quality of life, and have been related to cardiovascular disease risk[7–12].

Physical activity is known to positively influence health, wellness, and risk for multiple diseases. Physical activity, particularly moderate and vigorous activity, involves thermoregulation to alleviate metabolic heat production[13]. Further, thermoregulatory capacity can be modulated by exercise training resulting in a lowered sweating threshold[14–16]. The relationship between physical activity and hot flash experience is complex and remains unclear[17]. Acute exercise has been shown to trigger hot flashes[18]. However, while habitual physical activity may reduce the severity of hot flashes[19–21] the available data are equivocal with studies reporting some[22–25] and no[26–28] association with the number of hot flashes. Data from randomized controlled trials of exercise training interventions are also mixed[14,16,29–35]. One potential explanation for the lack of consistent findings may be due to the methodology of hot flash measurement. Most of these studies evaluating the effect of habitual physical activity on hot flash experience exclusively employed various self-report measures excluding one[25].

Hot flashes can be measured subjectively via self-report methods such as diaries, and objectively, using devices that measure changes in skin conductance[36,37]. Concordance between the two methods varies and there are advantages and disadvantages to both methods[36,38,39]. Objective measures show a physiological response and are important as some people have objective hot flashes and no corresponding subjective experience. Some people report feeling hot flashes when no physiological response is recorded by sternal skin conductance measures. Subjective reports can be influenced by recall bias, affect, and expectation but represent a person's experience. On the other hand, objective assessment carries a burden of constant instrumentation for ambulatory monitoring. Objective measures are independent of perception, attention, or attitudes toward hot flashes[40]. Therefore, objective measures are particularly helpful to assess hot flashes during sleep periods as subjective reports during sleeping hours can be influenced by whether the hot flash is accompanied by an awakening and/or awareness. Subjective hot flashes are commonly underreported during sleep[37,39,41]. Nevertheless, different factors contribute to the experience of subjective and objective hot flashes. Therefore, improved understanding of the hot flash experience likely involves both types of hot flash measurement.

Sedentary behavior is common as the Women's Health Study reported that women under the age of 65 spent 9.4hrs or 63.5% of their waking time sedentary[42]. Sedentary behavior has associations with negative health outcomes for women that are independent of time spent in physical activity[43,44]. Some evidence suggests that sedentary time is associated with more severe self-reported menopause symptoms, including hot flashes[45]. However, no studies have specifically evaluated the effect of sedentary behavior on objective and subjective hot flash experience.

The aim of this analysis was to determine the relationships between physical activity, sedentary time and subjective and objective hot flashes during waking and sleeping periods in midlife women around the menopausal transition. We also modeled the effect of increasing sitting time and replacing time sitting with physical activity on hot flashes via isotemporal substitution modeling.

Methods:

Design

Data from this analysis were collected as part of a larger study on the relationship between brown adipose tissue and hot flashes. The study was designed to evaluate the ambulatory 24-hour hot flash experience in a sample of midlife women. Data collection occurred from 2019 to 2023 during the cooler months in Western Massachusetts (between October and April). Participants completed a single laboratory visit where they completed questionnaires, including a physical activity questionnaire, underwent laboratory measures, and were instrumented with hot flash, physical activity and temperature monitors, which they wore continuously for 24-hours.

Sample

A sample of pre- peri- and postmenopausal individuals, aged 45-55 was recruited from Western Massachusetts. Menopausal stages were categorized according to the STRAW+10 criteria [46]. Briefly, premenopause was defined by regular menstruation, including lighter or heavier or more or less frequent menstruation than normal; perimenopause was defined as menstrual cycles ≥7 days different than normal up to 12 months of amenorrhea; postmenopause was amenorrhea > 12 months. Women taking hormone therapy were excluded. Data were collected from 270 participants. Data from 18 were excluded due to incomplete actigraphy data to characterize hot flashes as waking or sleeping. Participants were only included if they had over 10 hours of hot flash monitor wear time and at least 4 hours of sleeping wear time, excluding 50. An additional 6 participants were excluded for missing the menopausal stage or missing one of the IPAQ activity variables for a total of 196 participants retained in this sample. The study was approved by the Institutional Review Boards of the University of Massachusetts Amherst and the University of Hawaii; all participants gave written consent and written authorization for use of health information.

Measures

Height and weight were measured to calculate Body Mass Index (BMI, kg/m^2). Participants completed a questionnaire that included questions on demographics, general health, and reproductive history.

Habitual physical activity data were collected using the International Physical Activity Questionnaire Short Form (IPAQ-SF) on the day the participants were instrumented with the monitors. The IPAQ asks participants to report, in the past 7 days, the number of days and time spent per day performing moderate and vigorous intensity activities and walking. Participants were asked to only include activities that they did for at least 10 minutes at a time. Participants also recorded time spent sitting in the last 7 days on a weekday. For the isotemporal substitution models, the average number of hours spent in vigorous or moderate activities or walking for each participant was included. The average activity for each day in a category was calculated as (Minutes of that Activity) * (Days of that Activity) * (1/7).

Main outcomes of interest were waking and sleeping hot flashes, considering self-reported and objectively recorded hot flashes separately. Participants wore a Biolog (UFI, Morro Bay, CA) ambulatory sternal skin conductance hot flash monitor with event marking buttons for 24 hours. Silver/silver chloride electrodes were filled with conducting gel[47] and placed 4 inches apart on either side of the sternum and connected to the monitor. Objective hot flashes meeting the established criteria of an increase of 2 micromhos over 30 seconds were recorded by the monitor. Marked hot flashes were also inspected manually and were distinguished from night sweat events, which were not in the scope of the current study. Participants self-reported hot flashes via the buttons on the hot flash monitor, which they were instructed to push upon experiencing a hot flash.

Participants were also provided a paper log and instructed to record hot flashes on the log if pressing the button at the time was not possible or inconvenient (e.g. while driving).

Temperature and humidity were continuously recorded using a GSP-6 data logger (Elitech, San Jose, CA) concurrent with the sternal skin conductance for 24 hours. Participants were instructed to place the monitors under the covers with them at night to provide data related to their microclimate while sleeping. Missing values in temperature and humidity were imputed with the median value across participants. During sleeping hours, 14.6% of participants were missing temperature or humidity data. During the day, 6.06% participants were missing temperature or humidity data. For models considering waking or sleeping hot flashes, the temperature included was the mean across waking or sleeping hours; otherwise, the mean was taken across the entire duration of wear.

During the monitoring period, waking and sleep periods were determined by actigraphy. Participants wore an Actigraph accelerometer (v6.13.4 Firmware v1.9.2, Pensacola, FL) for the 24-hour period with an epoch length of 10 seconds. The times of sleep onset and wake up were estimated using the R package GGIR (version 2.9-0) with the sleep algorithm proposed by Vanhees et al. (2015) to categorize hot flashes and mean temperature and humidity during waking and sleeping periods [48].

Analysis

The primary outcomes considered were the waking and sleeping objective hot flash rates and the waking and sleeping subjective hot flash rates. Each of these outcomes was modeled separately. Generalized linear regression models were used to assess the outcomes of interest. Monitor wear time (in hours) was included as an offset variable in the model, which allows interpretation of the effect of different covariates on the number of hot flashes per monitor wear time period, that is, the hot flash rate.

A common behavioral recommendation made to reduce sedentary time and change health outcomes is to replace sedentary time with physical activity. To study the effect of multiple activity variables on hot flash frequency, an isotemporal substitution paradigm [49] was used. This paradigm is a useful framework for considering multiple physical activity variables in the same model, including time sitting as well as time spent in different intensities of physical activity. An isotemporal substitution model provides an estimation of how replacing one hour of sitting with an hour of some physical activity, for example replacing sitting with vigorous activity, may change the frequency of hot flashes. To obtain this interpretation, the models include the number of hours engaged in walking, moderate activity, and vigorous activity as well as a total activity variable, which is the sum of the time spent sitting, walking, in moderate, and vigorous activity. Including the total activity variable that includes sitting, but not including the time spent sitting as a covariate, allows interpretation of the coefficients of walking, moderate activity, and vigorous activity as estimating the effect of replacing an hour of sitting with each of the other physical activity variables. For generalized linear models with a log link, the interpretation of the coefficients is multiplicative rather than additive.

In addition to the isotemporal substitution models, to enable comparisons to previous literature where this paradigm was not used, the relationships between each hot flash rate and the weekly MET hours and weekly hours sitting were modeled with the same relevant covariates included in the isotemporal substitution models.

To handle overdispersion in the hot flash count data, negative binomial and generalized Poisson regression were considered[50]. Furthermore, since zeros in the number of hot flashes could reflect sampling zeros, that is, zeros that resulted because we didn't happen to observe a hot flash in the 24 hour period of observation, or structural zeros, where the participant never experienced hot flashes, zero-inflated models, which accommodate these distinct sources of zeros, [51] were considered.

Final models were selected based on the Bayesian Information Criterion (BIC) in conjunction with inspection of diagnostic plots of the randomized quantile residuals using the DHARMa package[52]. A discussion of model selection is included in the Supplement. See Supplementary Table 1 for the BIC values for the isotemporal substitution models and Supplementary Table 2 for the BIC values for models considering the weekly MET hours.

Based on examination of the BIC values and residual diagnostics for the isotemporal substitution models, a zero-inflated Poisson was used to model the overall subjective and objective hot flashes, the objective and subjective waking hot flashes, and the objective sleeping hot flashes. For the subjective sleeping hot flashes, the zero-inflated negative binomial was most appropriate. For the models considering total MET hours and total hours sitting, a zero-inflated generalized Poisson was used to model the overall subjective and objective total hot flashes, subjective waking hot flashes, and the objective sleeping hot flashes. For the objective waking hot flashes, a zero-inflated Poisson was the best fit, and for the subjective sleeping hot flashes the negative binomial was the best fit.

Models were fitted with the R package glmmTMB, version 1.1.7[53]. Code for reproducing these analyses is available upon request.

Results:

Women were distributed across the 3 menopausal stages, had an average age of 51, BMI of 26, well-educated, and mostly non-smokers. Participants spent a median of 7 hours daily sitting (IQR 4.4-9.0 hours), 30 minutes walking (IQR 13-60 minutes), 11 minutes engaging in moderate activity (IQR 0-29 minutes), and 9 minutes engaging in vigorous activity (IQR 0-26 minutes) according to the IPAQ (Table 1). Variable distributions for the IPAQ are found in Supplementary Figure 1.

The average monitoring period was 20±3.2 (SD) hours. Objective and subjective hot flash rates for waking and sleeping periods are found in Figure 1. Hot flash counts are found in Table 1. Objective hot flashes were more highly correlated with subjective hot flashes during waking hours than during sleeping hours (Figure 2).

<u>Isotemporal Model Results</u>

Waking Hot Flashes: The coefficient estimates from the model with the outcome as subjective waking hot flashes demonstrate that, with other covariates held constant, replacing one hour of sitting with one hour of vigorous activity was associated with a 100% increase in the hot flash rate (Table 2a and Figure 3a, $p = 0.010$). BMI was significantly positively associated with subjective waking hot flashes (Table 2a and Figure 3a, $p=0.038$). These same relationships were not found with objective waking hot flashes. Postmenopausal stage was significantly and strongly associated with objective (OR 3.3, $p<0.001$) and subjective (OR 4.5, $p<0.001$) hot flashes compared with premenopausal stage. There was no significant influence of temperature or humidity on waking hot flashes of either type.

Sleeping Hot Flashes: A central finding was the relationship between time sitting and objective sleeping hot flashes. In the isotemporal substitution paradigm, the coefficient for 'total activity' is interpreted as the effect of the variable omitted. Modeling results indicated that, provided all other coefficients were held constant, increasing sitting by an hour was associated with a 7% increase in the rate of objectively measured sleeping hot flashes (Table 2b and Figure 3b, $p=0.01$). There were no significant relationships between physical activity and subjectively assessed sleeping hot flashes. Peri- (OR 2.64, p=0.014) and postmenopausal (OR 3.85, p<0.001) status were significantly associated with subjectively reported sleeping hot flashes but not objectively measured sleeping hot flashes. Sleeping hot flashes were not significantly related to temperature or humidity.

Total Hot Flashes: Combining day and night hot flashes did not result in any significant effects of any physical activity variables. There was weak evidence for an effect of sitting on the overall objective hot flash rate, where increasing time sitting by an hour was associated with a 5% increase in the total hot flash rate but this was not significant (Table 2c and Figure 3c, p=0.078). Postmenopausal stage was associated with greater odds of objectively measured (OR 1.99, p=0.002) and subjectively (OR 3.31, p <0.001) reported hot flashes compared with premenopausal stage. Neither total objective or subjective hot flashes were significantly related to temperature or humidity.

Traditional Model Results

When considering the models with weekly time sitting and total MET hours per week where we did not use the isotemporal substitution paradigm (Table 3), the results corroborate the trend observed in the isotemporal substitution models that increasing time sitting was associated with an increase in the sleeping objective hot flash rate (Table 3b, p=0.013). Postmenopausal stage was associated with a greater odds of objective waking (OR 3.25, p<0.001), subjective waking (OR 4.04, p<0.001), subjective sleeping (OR 3.35, p=0.003), objective total (OR 1.98, p=0.002) and subjective total (OR 3.33, p<0.001) hot flashes. Similar to the isotemporal model, body mass index was associated with the odds of higher subjective waking hot flashes (OR 1.25, p=0.05). There was no support for modeled effects of humidity or temperature for any type of hot flash.

Discussion:

Hot flashes are frequently reported by women in the years around the transition to menopause. Currently there is insufficient evidence to determine whether physical activity can be considered a treatment for hot flashes [54,55] which could be in part due to the lack of concurrent objective and subjective hot flash monitoring in these studies. Our data are some of the first to reveal that subjectively reported and objectively measured hot flashes and those occurring during waking and sleeping periods have different relationships with sedentary and physical activity behavior. We found that greater time sitting was significantly associated with greater objectively measured hot flashes during sleeping periods. Isotemporal substitution modeling revealed that replacing one hour of sitting with vigorous activity was associated with an increase in subjectively reported but not objectively measured waking hot flashes. These results improve our understanding of the role of habitual physical activity and sedentary time on the 24-hr hot flash experience and reveal important considerations related to hot flash assessment for future studies.

Sedentary behavior has been related to more subjectively reported severe menopausal symptoms including hot flushes[45]. Herein we report that greater amounts of time spent sitting was associated with objectively measured sleep period hot flashes. While we report a relatively small increase in hot flashes, our study population was less sedentary and more active than average in the United States[56], and the effect may be larger when considering a broader population. Hot flashes that occur during sleep periods can be particularly bothersome as they may cause sleep disruptions[57–59]. Objectively measured hot flashes during sleep have also been associated with white matter hyperintensities, a potential indicator of small vessel disease[11], pronounced declines in heart rate variability around hot flashes[12,60], and lower verbal memory[61]. While there are currently no studies on sedentary behavior and objective sleep period hot flashes, a randomized 6-month unsupervised aerobic exercise training trial showed reduced subjective reports of hot flashes during sleep in the exercise group compared with controls[62]. Notably, we did not find a similar relation between sedentary time and subjectively reported sleep period hot flashes. Our analysis indicated that correlations between objective and subjective hot flashes were lower during the sleep period compared with the wake period (r=0.423 vs. 0.775) which may reflect underreporting subjective hot flashes during sleep. Underreporting of hot flashes during sleep is common[38] and, according to the symptom perception theory, hot flashes can be undetected at night due to reduced awareness[40,63]. Therefore, objective measures of hot flashes during sleep periods may be an important tool to appropriately capture the symptom experience and reduce type II errors.

There are many health benefits attributed to physical activity and negative outcomes related to sedentary behavior. In addition to the health outcomes related to objective hot flashes during sleep periods mentioned above, objective and subjective hot flashes have been associated with subclinical cardiovascular disease risk[8,10,64–66]. Practitioners often suggest replacing sedentary time with physical activity to improve health and reduce the risk of disease. We used isotemporal substitution modeling to evaluate the replacement of sedentary time with walking, moderate or vigorous activity to evaluate the effect on hot flash experience. We found replacing sedentary time with vigorous activity was related to higher waking subjectively reported but not objectively measured hot flashes. In an analysis from a Study of Women Across the Nation (SWAN) cohort[67] using objective and subjective monitoring, investigators showed that people with higher self-reported habitual physical activity, via the Kaiser Physical Activity Survey, had a higher odds of subjectively reported hot flashes that were not corroborated with an objectively measured hot flash over a 24-hr period (OR=1.27, 95% CI=1.13-1.41). Another study showed that women who reported high amounts of physical activity between ages 35-40 were more likely to report a higher number of hot flashes during their peri and postmenopausal years[68]. The relationship between more vigorous exercise and subjective hot flashes could be explained by the symptom perception theory[63]. Vigorous exercise may cause changes to attentional focus from external to internal body sensations, increased somatization, heightened experience of the somatic symptoms of sweating and attribution of sweating sensations to hot flashes[40]. Alternatively, individual variation in sweating with hot flashes has been reported[69,70]. It is possible that sternal skin conductance does not adequately measure differences in sweating patterns that occur with hot flashes in response to vigorous exercise. Further, objective and subjective measures might assess two different aspects of the hot flash construct, that is, physiological correlates and the perceptual correlates of hot flashes[38–40], and the correlates of these constructs may vary with the intensity of physical activity. Nevertheless, if hot flash experience is related to disease risk, it is imperative that further studies clarify the relationships between objectively measured vs. subjectively reported hot flashes, physical activity, and disease risk.

Other results reported herein regarding BMI are notable. In this analysis, higher BMI was only related to higher waking subjective but not objective hot flash rates, and there were no significant effects of BMI on sleeping or total hot flashes. The relation between hot flashes and BMI has been mixed, and the majority of studies have used self-reported hot flashes or vasomotor symptoms (VMS). For example, longitudinal data from the Midlife Women's Health Study found no relationship between change in BMI and self-reported hot flashes[71]; however, a weight loss intervention showed reduced hot flash reporting in the weight loss group compared with controls[72]. It is possible that the relationship between BMI and self-reported hot flashes changes through the transition as the SWAN study found a relationship between VMS and BMI early in menopause but not later stages[73]. Using objective monitoring, Thurston, et al. showed in women aged 54-63 that the relationship between BMI and hot flashes was modified by age where BMI was negatively associated with objective hot flashes in older women[72]. Our data add to this literature, showing that in a sample that is younger (aged 45-55) and overweight (BMI, 26 kg/m^2), positive relationships of hot flashes with BMI were only apparent with subjective daytime hot flashes.

Overall, using continuous ambulatory localized monitoring, this analysis shows no support for an effect of temperature and humidity on hot flash experience on a sample of women in Western Massachusetts during non-summer months (October-April). While increasing ambient temperature and humidity would be hypothesized to be a trigger of hot flashes based on the theory of reduced thermoneutral zone[18], previous work has also shown the lack of a clear relationship between the ambient temperature and humidity and hot flashes[70]; however, further investigation is needed to determine whether acute changes in temperature and humidity are more relevant for hot flash experience rather than the mean temperature and humidity levels across the entire day or night. It is also possible that temperature and humidity become more relevant contributors to the hot flash experience during the warmer spring and summer months.

This work is not without limitations. First, physical activity was assessed from a subjective IPAQ report. There are notable concerns related to the validity of the IPAQ with regard to the overestimation of activity levels [75,76]. Future studies could employ objective physical activity measures to capture habitual activity levels. Another limitation is that monitoring for hot flashes only occurred over one 24-hour period. As hot flash experience may have day to day variability, additional monitoring periods would benefit this research. We also must interpret these findings with the recognition that the coefficients measure associations and not causal relationships. The participants did not undergo an exercise intervention, and as a result, we can only state the estimated change in hot flash rate associated with a change in each physical activity variable. That said, this work provides motivation for further validation via clinical studies to evaluate the effect of structured changes in activity.

Conclusion:

Overall, these data indicate that sedentary time and physical activity are associated with the 24-hour hot flash experience as increasing sitting by one hour was associated with a 7% increase in the rate of objectively measured but not subjectively reported hot flashes during sleep. Replacing one hour of sitting with one hour of vigorous activity was associated with a 100% increase in the subjectively reported but not objectively measured waking hot flashes. These results highlight the importance of considering sedentary behavior along with physical activity in studies evaluating hot flashes and have important implications for measurement considerations for future studies as type of symptom measure and time of day can influence hot flash outcomes.

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Figure Legends:

Figure 1: Hot Flash Rate by Hot Flash Type. Rates are calculated as the number of hot flashes during the wear period over the length of wear time. Participant data were included if minimum wear time was 10 hours of monitor wear time and at least 4 hours of sleeping wear time.

Figure 2: Comparing Subjective and Objective Hot Flashes for Sleeping and Waking Periods. Hot flashes measured during sleep periods had a lower correlation than hot flashes measured during waking periods. Hot flashes were counts recorded within a 24-hour wear time; the hot flash rate is the number of hot flashes experienced over the wear time when the participant was waking or sleeping.

Figure 3: 95% Confidence Intervals for the Coefficient Estimates of Isotemporal Substitution Models for (a) Waking, (b) Sleeping, and (c) Total Hot Flashes. Exact estimates for all covariates are shown in Table 3.

Supplemental Digital Content

File: R2 Revised Supplement.pdf

Contents

Table updated

Table 1: Participant Characteristics

Characteristic	N=196
Menopausal Stage, n (%)	
Premenopausal	35 (18%)
Perimenopausal	84 (43%)
Postmenopausal	77 (39%)
Activity Variables	
Sitting (Hours)	7.0 (4.4, 9.0)
Walking (Minutes)	30 (13, 60)
Moderate Activity (Minutes)	11 (0, 29)
Vigorous Activity (Minutes)	9 (0, 26)
BMI, kg/m^2 (IQR)	26 (23, 32)
Age, years (IQR)	51 (49, 53)
Smoking Status, n (%)	
Does Not Smoke	188 (96%)
Smokes	8 (4.1%)
Education, n (%)	
High School or Less	11 (5.6%)
Some College or College Graduate	82 (41.8%)
Higher than College Education	103 (52.6%)
Hot Flash Counts, median (IQR)	
Sleeping Subjective	0 (0.0, 1.0)

Waking Subjective	0 (0.0, 2.3)
Sleeping Objective	2 (0.0, 3.0)
Waking Objective	1 (0.0, 3.0)
Monitor Wear Duration (Hours)	20.9 (19.7, 22.1)

Table 2: Odds Ratio Estimates for Isotemporal Substitution Models: Estimating the Change in Hot Flash Associated with Replacing One hour of Sitting

(a) Waking Hot Flashes

Variable	Estimate	P-value
Objective Waking Hot Flashes		
Walking	0.871	0.087
Moderate Activity	1.100	0.112
Vigorous Activity	1.040	0.795
Total Activity	0.982	0.545
Mean Humidity	0.886	0.155
Mean Temperature	1.010	0.899
BMI	0.877	0.125
Perimenopausal	1.710	0.076
Postmenopausal	3.310	<0.001 (***)
Subjective Waking Hot Flashes		
Walking	1.050	0.549
Moderate Activity	1.050	0.376
Vigorous Activity	2.060	0.01 (**)
Total Activity	1.010	0.773
Mean Humidity	0.857	0.089

Table 2: Odds Ratio Estimates for Isotemporal Substitution Models: Estimating the Change in Hot Flash Associated with Replacing One hour of Sitting

(a) Waking Hot Flashes

Variable	Estimate	P-value
Mean Temperature	0.954	0.67
BMI	1.270	0.038 (*)
Perimenopausal	1.990	0.075
Postmenopausal	4.470	<0.001 (***)

(b) Sleeping Hot Flashes

Variable	Estimate	P-value
Objective Sleeping Hot Flashes		
Walking	0.979	0.628
Moderate Activity	0.938	0.282
Vigorous Activity	0.835	0.232
Total Activity	1.070	0.00994 (**)
Mean Humidity	1.020	0.718
Mean Temperature	1.030	0.684
BMI	0.886	0.083

Variable	Estimate	P-value
Perimenopausal	1.000	0.998
Postmenopausal	1.220	0.361
Subjective Sleeping Hot Flashes		
Walking	0.963	0.665
Moderate Activity	0.924	0.419
Vigorous Activity	0.954	0.814
Total Activity	1.010	0.87
Mean Humidity	1.150	0.247
Mean Temperature	0.978	0.86
BMI	0.997	0.982
Perimenopausal	2.640	0.0141 (*)
Postmenopausal	3.850	<0.001 (***)

(c) Total Hot Flashes

Variable	Estimate	P-value
Objective Total Hot Flashes		
Walking	0.945	0.304
Moderate Activity	1.000	0.933
Vigorous Activity	0.991	0.967

Variable	Estimate	P-value[a]
Total Activity	1.050	0.078
Mean Humidity	0.956	0.465
Mean Temperature	1.030	0.603
BMI	0.896	0.121
Perimenopausal	1.260	0.316
Postmenopausal	1.990	0.0022 (**)
Subjective Total Hot Flashes		
Walking	1.010	0.945
Moderate Activity	1.050	0.425
Vigorous Activity	1.010	0.955
Total Activity	0.995	0.872
Mean Humidity	0.954	0.549
Mean Temperature	1.000	0.992
BMI	1.140	0.187
Perimenopausal	1.710	0.076
Postmenopausal	3.310	<0.001 (***)

[a]BMI; Body Mass Index. (***) indicates $p \leq 0.001$, (**) indicates $p \leq 0.01$, (*) indicates $p \leq 0.05$

Table 3: Odds Ratio Estimates for Modeling the Weekly MET Hours and Weekly Hours Sitting

(a) Waking Hot Flashes

Variable	Estimate	P-value[a]
Objective Waking Hot Flashes		
Total MET Hours	0.999	0.44
Time Sitting (Hours)	0.997	0.52
Mean Humidity	0.867	0.103
Mean Temperature	1.010	0.92
BMI	0.897	0.204
Perimenopausal	1.730	0.0697
Postmenopausal	3.250	<0.001 (***)
Subjective Waking Hot Flashes		
Total MET Hours	1.000	0.113
Time Sitting (Hours)	1.000	0.913
Mean Humidity	0.843	0.073
Mean Temperature	0.965	0.775
BMI	1.250	0.051
Perimenopausal	1.720	0.148
Postmenopausal	4.040	<0.001 (***)

(b) Sleeping Hot Flashes

Variable	Estimate	P-value
Objective Sleeping Hot Flashes		
Total MET Hours	1.000	0.892
Time Sitting (Hours)	1.010	0.0128 (*)
Mean Humidity	1.010	0.857
Mean Temperature	1.040	0.586
BMI	0.885	0.084
Perimenopausal	1.030	0.897
Postmenopausal	1.260	0.278
Subjective Sleeping Hot Flashes		
Total MET Hours	0.999	0.597
Time Sitting (Hours)	0.999	0.828
Mean Humidity	1.080	0.55

Mean Temperature	1.060	0.655
BMI	1.080	0.527
Perimenopausal	2.180	0.0554
Postmenopausal	3.350	0.00267 (**)

(c) Total Hot Flashes

Variable	Estimate	P-value
Objective Total Hot Flashes		
Total MET Hours	1.000	0.468
Time Sitting (Hours)	1.010	0.0664
Mean Humidity	0.950	0.396
Mean Temperature	1.030	0.638
BMI	0.901	0.138

Perimenopausal	1.270	0.299
Postmenopausal	1.980	0.00222 (**)
Subjective Total Hot Flashes		
Total MET Hours	1.000	0.678
Time Sitting (Hours)	0.999	0.84
Mean Humidity	0.949	0.505
Mean Temperature	0.996	0.959
BMI	1.140	0.185
Perimenopausal	1.740	0.065
Postmenopausal	3.330	<0.001 (***)

[a]BMI; Body Mass Index. (∗∗∗) indicates p≤ 0.001, (∗∗) indicates p≤0.01, (∗) indicates p≤0.05

Figure 1

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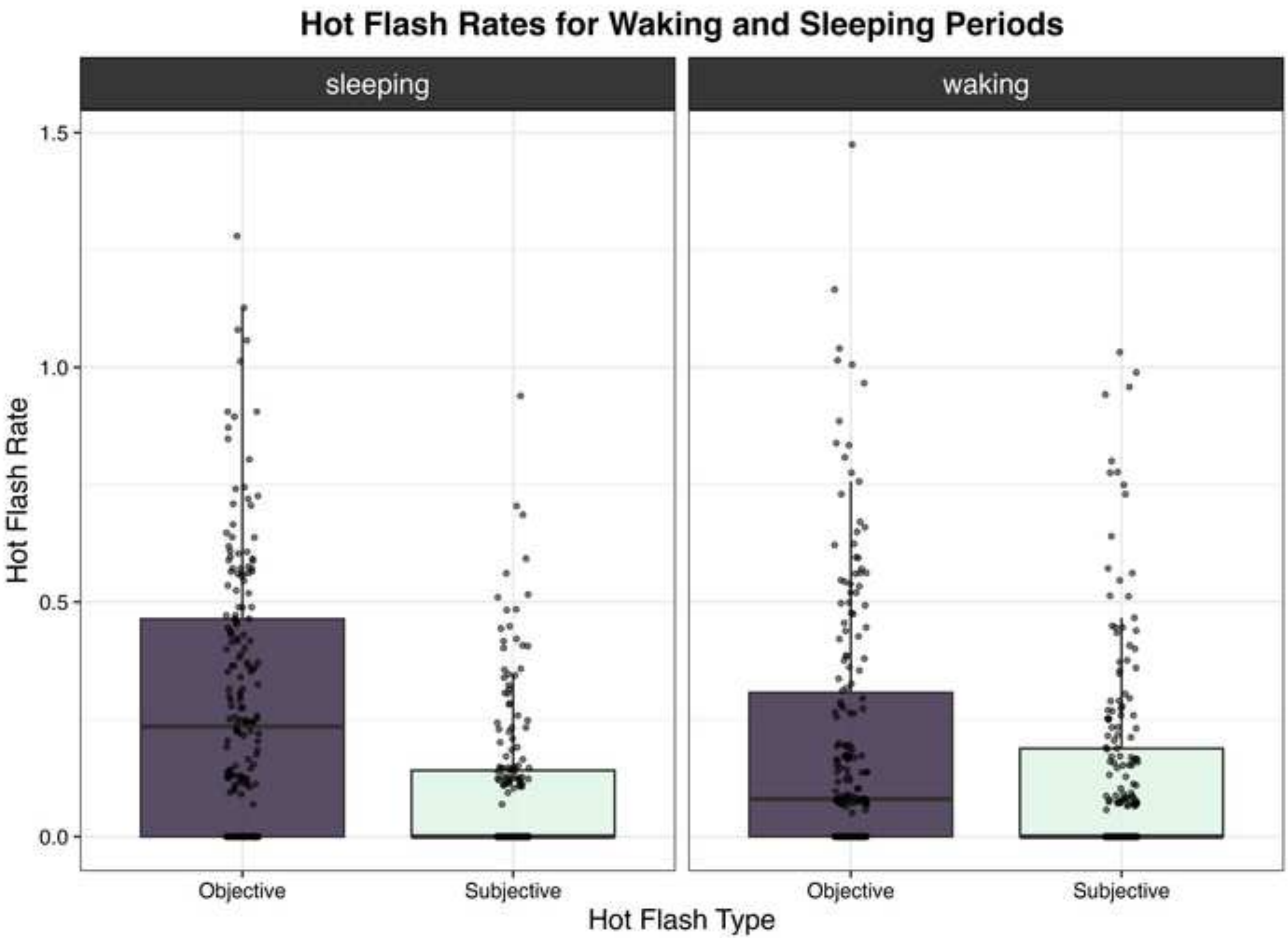

Figure 2

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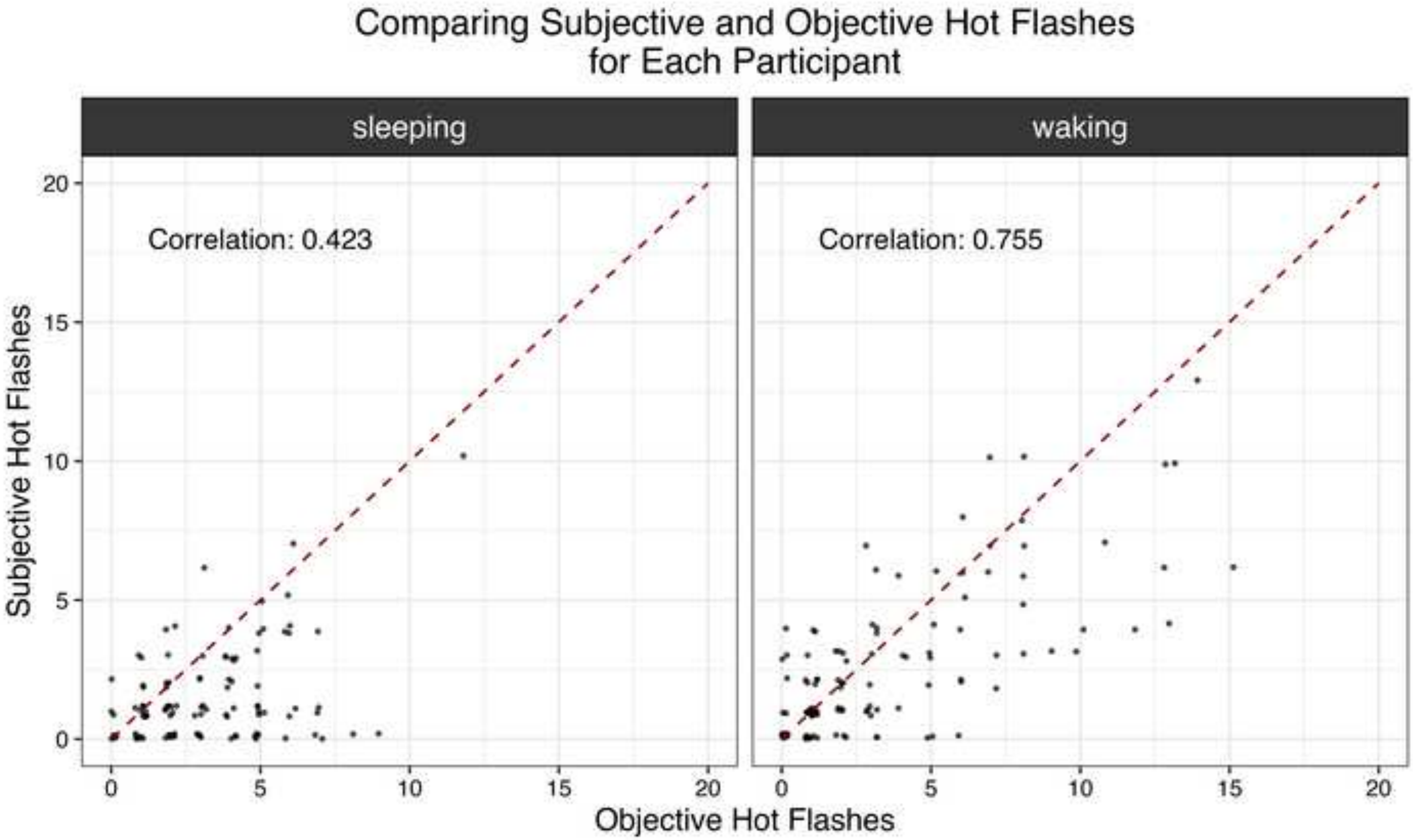

Figure 3

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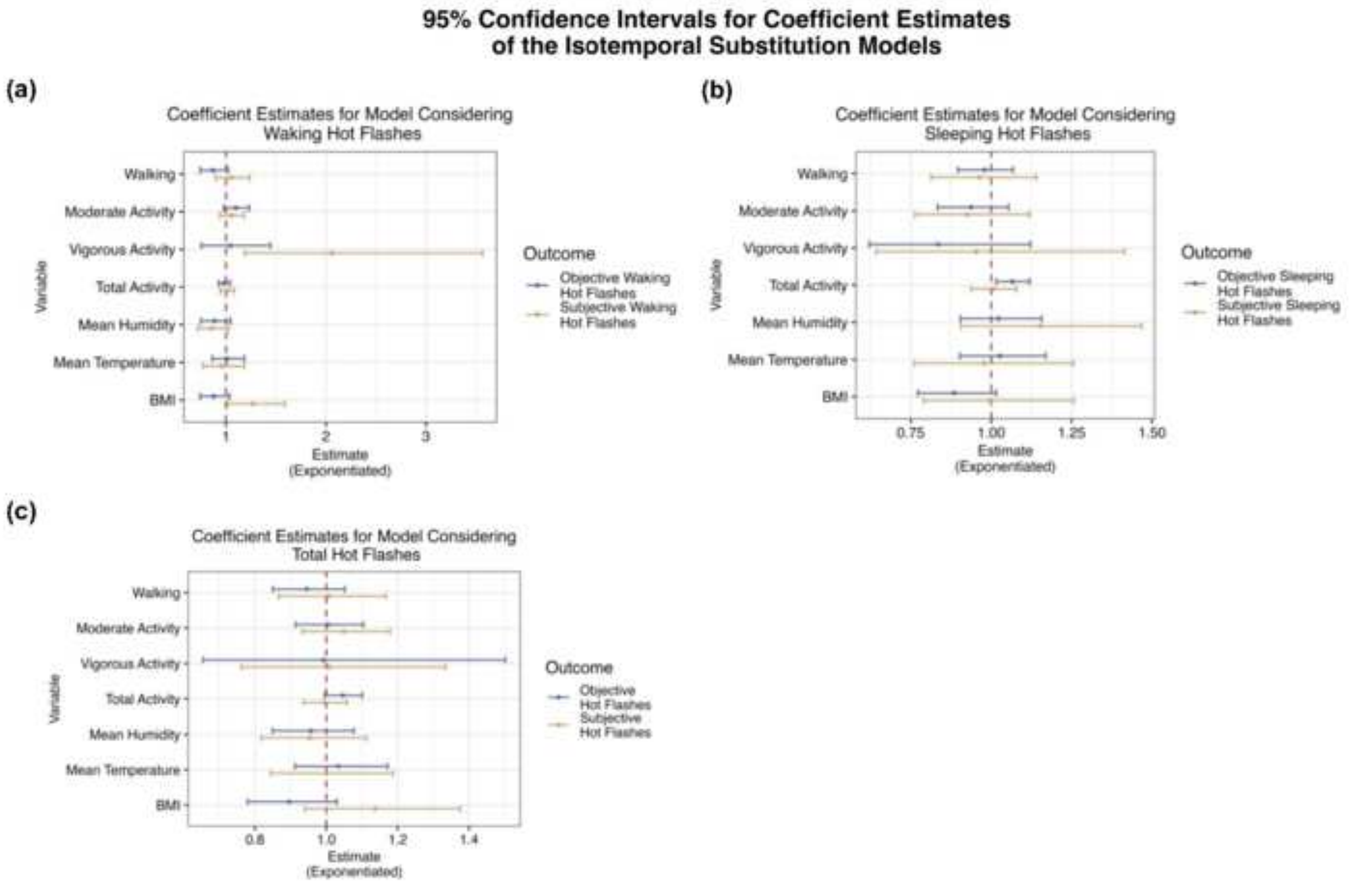

Two sentence summary

In this sample, isotemporal substitution modeling was used to show that sedentary time and physical activity were associated with the 24-hour hot flash experience as increasing sitting by one hour was associated with a 7% increase in the rate of objectively measured but not subjectively reported hot flashes during sleep. Replacing one hour of sitting with one hour of vigorous activity was associated with a 100% increase in subjectively reported but not objectively measured waking hot flashes.