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Supplementary methods:

1. ANS data collection and processing

Autonomic data acquisition

Physiological assessments were performed between 9 am and 4 pm. ECG and respiration signals were acquired using custom hardware and software systems. Approximately 30 minutes after feeding, ECG leads were placed on three anatomical locations on infant's body namely, left abdominal, left and right scapula. A respiratory inductance belt (Ambulatory Monitoring Inc.) was placed around the infant's chest. ECG and respiration signals were acquired at 500, and 20 Hz, respectively. Blood pressure (NP) was measured using a clinical monitor (CASMED 740 Vital Signs Monitor). The BP cuff (width = 3–5 cm) was placed around the infant's leg below the left knee. The distance from the middle of the cuff to the level of the heart was measured to allow for computation of hydrostatic pressure, while infants were in the 45^{o} head-up position (0.8 mmHg/cm). A video camera filmed the infant's face during the protocol.

Assessment protocol

Newborn infants were tested 12–96 hours after delivery (the distributions of hours of life across the two sites was different, please see Table 1). In NP, the physiological assessments occurred before discharge from the hospital. On the contrary, in SA infants were discharged <24 hours after delivery. Therefore, at this site, infants returned to testing facilities at either Tygerberg or Karl Bremer Hospital 48–96 hours after birth. The standardized protocol consisted of ECG, respiration and BP recorded during a 10-minutes baseline period and in response to three rapid (~3–5 seconds) 45^{0} head-up tilts (a clinometer was attached to the basinet to measure the baby's tilt position), while the infant was in the prone position. The prone position was chosen as it is a long-recognized SIDS risk sleeping[1].

Data processing

An extensive description of the pipeline used for physiology processing is described in the following. Firstly, electrical line noise was filtered (50 Hz and 60 Hz for SA and NP, respectively). Next, ECG and respiratory tracings were subjected to automated peak detection via custom algorithms. Marks were manually corrected when necessary; the quality of the ECG was generally excellent thus, few minutes per file were required to edit the automatic peak detection marking. Marking of breaths was more time-consuming due to the presence of movement artefacts. Research assistants were trained on these marking procedures until they achieved 80% concordance on training records. Signals from the clinometer were also marked to denote start and stop times for the head-up tilt sequences.

Sleep state coding

Cardiorespiratory variables differ as a function of sleep state. Accordingly, prior to analyses of physiological data, an algorithm was used for coding active or quiet sleep states (AS and QS) based on breathing rate variability. Details on the state coding method and its validation were published elsewhere[2]. This coding was supplemented by the behavioral (awake, crying or fussy) recorded simultaneous with physiological signals.

Data cleaning

The designed preprocessing pipeline consisted of multiple steps. Data cleaning consisted of removing periods of noisy ECG, which are difficult to mark and are generally associated with excessive infant movements. R-wave marking during such segments can produce RR intervals which are not within a physiological range. For RRi analyses, values shorter than 0.3 seconds

(200 bpm) or greater than 0.75 seconds (80 bpm) were excluded from further computations. Beat-to-beat changes in RRi greater than 60 msec (~20 bpm at HR=140 bpm) were excluded. Breath-to-breath intervals shorter than 0.5 seconds (120 breaths/minute) or greater than 2.0 seconds (30 breaths/minute) were excluded. Systolic and diastolic BP values were excluded when the pulse rate derived from the BP monitor differed by more than 10 bpm from the closest preceding ECG-derived HR.

Derived variables (Baseline)

Mean and median values for physiological variables were computed for each of ten one-minutes epochs prior to two baseline BP measurements and initiation of the sequence of three head-up tilts. For each minute, mean and median R-wave to R-wave intervals (RRi) were computed, and from the median RRi, mean heart rate (HR) was computed. Also computed were standard deviations of RRis (SD-RRi), the square root of the mean of the squared successive differences in RRis (rMSSD) and, from spectral analyses, high-frequency variability in RRi (HF-RRi). HF-RRi and rMSSD were taken as indirect indices of parasympathetic modulation of HR. RRi spectra were calculated for each minute using an interval method for computing Fourier transforms. Prior to computing these spectra, the mean of the RRi series was subtracted from each value in the series and the residual series was filtered using a Hanning window. Estimates of spectral power were adjusted to account for power attenuation produced by the Hanning filter. Also, mean and median breath-to-breath intervals were computed. From these signals, breathing rates as well as standard deviations of breath-to-breath intervals (SD-BBi) were estimated. For each heart and respiratory measure, median values across epochs within each sleep state were the final baseline estimates. At the end of the baseline period, two BP measures were taken over a course of about 2 minutes. All summary variables were computed separately for AS and QS epochs.

Derived variables (Head-up tilt)

For each of the cardiorespiratory variables described above, changes in response to head-up tilting were computed. For HR and breathing rate change scores, median values during the 30-seconds period immediately before each tilt were subtracted from median values during the last minute in the head-up position (~45 seconds after reaching the head-up position). After returning to the flat position, 165 seconds elapsed before the next head-up tilt, a time determined to be sufficient for all variables to return, on average, to baseline. Medians over the three tilts are reported. For HR, acute responses to tilts were also computed as maximum HR – minimum HR during the first 15 seconds in the head-up position. The median maximum–minimum HR over the three tilts is reported. The pretilt values for systolic and diastolic BP were obtained ~90 seconds before tilts and the head-up BP values were taken just before returning to the horizontal position. Median changes in BP over the three tilts are reported. The three tilts occurred according to predefined protocol times. Sleep state for each tilt was defined as the state the infant was in during the 30-second baseline preceding each tilt.

2. Exposure imputation and exposure clustering

Missing Data Imputation. For all pregnant women in the Safe Passage Study, daily drinking and smoking data were collected for the last reported drinking day and 30 days prior. For estimates of alcohol consumption, out of 3.2 million person-days of observation, data were missing for 0.36 million (11.4%) days. We excluded subjects with more than 200 days missing and subjects who did not have any alcohol consumption data in the first trimester from the imputation analyses. For estimates of smoking, out of 0.47 million person-weeks, data were missing for 0.13 person-weeks (27.7%). We classified smoking status accurately in 93% of randomly deleted segments, and, for 86% segments imputed data were within +/-1 cigarette/day of the actual. Missing exposure data was imputed using a nonparametric machine learning algorithm called the k nearest neighbor algorithm (kNN)[3].

Alcohol and Smoking Cluster Analysis. In order to discern relationships between different patterns of PAE and PTE during pregnancy on newborn brain activity, we utilized clustering techniques to characterize maternal drinking and smoking behaviors. We have previously published the cluster analysis of alcohol consumption during pregnancy in the Safe Passage Study[4]. In brief, the R-package **clValid**[5] was utilized with an internal validation so the authors could simultaneously evaluate several clustering methods to aid in the authors' determination the most appropriate method and number of clusters based on diverse figures of merit, such as connectivity measures, the Dunn index, and silhouette measures. Based on these metrics and human decision making, finite mixture models were implemented using the R-package **mclust**[6] from derived daily alcohol consumption data for 10,279 participants in the Safe Passage Study. We utilized six features for the alcohol cluster analysis: the sum of standard drinks per day in trimesters 1, 2, and 3 and binge drinking events (≥ 4 drinks on a given day) in trimesters 1, 2, and 3. Ten alcohol trajectory groups were previously defined with one group consisting of non-drinkers (n=5,915)[7]. Hierarchical clustering was implemented using the R-packages **hclust**[8] and **agnes**[5] for 10,941 participants with available smoking information to define smoking cluster groups from four features: average cigarettes smoked per week in trimesters 1, 2, and 3, in addition to a quit smoking variable which was defined as < 1 average cigarettes per week in trimesters 2 and 3. The distance metric was Euclidean and linkage method was Ward's minimum variance method. Women having a total trimester-level average cigarette consumption <1 had that corresponding value set to zero. For the remaining 5,155 participants, any outliers for each feature were winsorized and assigned with a value equal to the *Mean* + (4*SD). Lastly, features utilized for the cluster analysis were z-scored to obtain a zero-mean and unitary-variance. We defined five smoking trajectory groups with one group consisting of non-smokers (n=5,786). For some alcohol and smoking exposure cluster cross-tabulations, there were small N's which also had ANS outcome data. Therefore, in the present analysis we collapsed the PASS alcohol and smoking cluster groups.

Supplemental Table S1: Characteristics of the study population (n=6985) by smoking groups

	Moderate to high continuous N=1100	Low continuous N=1799	Quit early N=298	Non-smoker N=3788
	N[1] (%) or mean (SD)	N[1] (%) or mean (SD)	N[1] (%) or mean (SD)	N[1] (%) or mean (SD)
Maternal characteristics				
Maternal age, years	26.0 (5.9)	23.8 (5.5)	24.0 (5.3)	26.5 (5.5)
Marital status				
Married/cohabiting	519 (47.2)	1012 (56.3)	142 (47.7)	1145 (30.2)
Unmarried	581 (52.8)	787 (43.7)	156 (52.3)	2643 (69.8)
Education				
Primary school education	113 (10.3)	144 (8.0)	11 (3.6)	91 (2.4)
Some high school education	715 (65.0)	1207 (67.1)	117 (39.3)	1179 (31.1)
High school completed	204 (18.5)	315 (17.5)	87 (29.2)	801 (21.1)
Higher than high school	67 (6.1)	133 (7.4)	83 (27.9)	1714 (45.2)
Employment status				
Employed	323 (29.4)	463 (25.7)	135 (45.3)	2176 (57.4)
Unemployed	777 (70.6)	1336 (74.3)	163 (54.7)	1612 (42.6)
BMI, kg/m^2				
<18.5	74 (6.7)	113 (6.3)	12 (4.0)	149 (3.9)
18.5-25	515 (46.8)	919 (51.1)	106 (35.6)	1515 (40.0)
25- 30	268 (24.4)	407 (22.6)	81 (27.2)	1078 (28.5)
30+	243 (22.1)	360 (20.0)	99 (33.2)	1046 (27.6)
Parity				
Nulliparous	305 (27.7)	722 (40.1)	132 (44.3)	1355 (35.8)
Parity 1	334 (30.4)	526 (29.2)	86 (28.9)	1256 (33.1)
Parity 2	254 (23.1)	303 (16.8)	35 (11.7)	693 (18.3)
Parity >3	207 (18.8)	248 (13.8)	45 (15.1)	484 (12.8)
Mode of delivery				

	Normal and assisted delivery	973 (88.5)	1571 (87.3)	228 (76.5)	3112 (82.2)
	Cesarean section	126 (11.5)	226 (12.6)	70 (23.5)	675 (17.8)
Crowding index		1.6 (0.9)	1.5 (1.0)	1.1 (0.8)	1.0 (0.8)
Depression, Edinburgh Depression Score		12.9 (6.2)	12.0 (6.2)	8.5 (5.7)	7.9 (5.9)
Infant characteristics					
Birth weight, g		3059.0 (440.8)	3137.2 (465.7)	3418.0 (493.3)	3399.6 (483.8)
Gestational age, weeks		39.3 (1.1)	39.3 (1.1)	39.5 (1.1)	39.5 (1.1)
Sex					
	Female	562 (51.1)	921 (51.2)	149 (50.0)	1935 (51.1)
	Male	538 (48.9)	878 (48.8)	149 (50.0)	1853 (48.9)
Hours of life at measurement		57.0 (54.6)	54.3 (48.8)	38.7 (48.5)	42.0 (52.0)

Supplemental Table S2: Characteristics of the study population (n=6616) by drinking groups

	Moderate to high continuous N=1061	Low continuous N=247	Quit early N=2129	Non-drinker N=3179
	N[1] (%) or mean (SD)	N[1] (%) or mean (SD)	N[1] (%) or mean (SD)	N[1] (%) or mean (SD)
Maternal characteristics				
Maternal age, years	25.4 (5.8)	24.5 (6.0)	25.7 (5.4)	25.9 (5.9)
Marital status				
Married/cohabiting	564 (53.2)	137 (55.5)	766 (36.0)	1130 (35.5)
Unmarried	497 (46.8)	110 (44.5)	1363 (64.0)	2049 (64.5)
Education				
Primary school education	87 (8.1)	15 (6.0)	53 (2.4)	171 (5.3)
Some high school education	664 (62.6)	158 (64.0)	721 (33.9)	1426 (44.9)
High school completed	197 (18.6)	43 (17.4)	428 (20.1)	674 (21.2)
Higher than high school	113 (10.7)	31 (12.6)	926 (43.5)	906 (28.5)
Employment status				

	Employed	338 (31.9)	75 (30.1)	1194 (56.1)	1393 (43.8)
	Unemployed	723 (68.1)	172 (69.6)	935 (43.9)	1786 (56.2)
BMI, kg/m^2					
	<18.5	57 (5.4)	14 (5.6)	101 (4.7)	154 (4.8)
	18.5-25	546 (51.5)	120 (48.6)	934 (43.9)	1260 (39.6)
	25- 30	254 (23.9)	73 (29.6)	574 (27.0)	849 (26.7)
	30+	204 (19.2)	40 (16.2)	520 (24.4)	916 (28.8)
Parity					
	Nulliparous	366 (34.5)	98 (39.7)	881 (41.4)	1007 (31.7)
	Parity 1	325 (30.6)	82 (33.2)	700 (32.9)	986 (31.0)
	Parity 2	203 (19.1)	41 (16.6)	352 (16.5)	630 (19.8)
	Parity >3	167 (15.7)	26 (10.5)	196 (9.2)	556 (17.5)
Mode of delivery					
	Normal and assisted delivery	941 (88.8)	223 (90.3)	1730 (81.3)	2651 (83.4)
	Cesarean section	119 (11.2)	24 (9.7)	399 (18.7)	525 (16.5)
Crowding index		1.5 (1.1)	1.6 (1.0)	1.0 (0.8)	1.2 (0.9)
Depression, Edinburgh Depression Score		12.4 (6.3)	12.6 (6.0)	8.2 (6.1)	9.2 (6.3)
Infant characteristics					
Birth weight, g		3120.6 (468.4)	3094.0 (481.0)	3367.8 (482.4)	3311.9 (495.1)
Gestational age, weeks		39.4 (1.1)	39.4 (1.1)	39.5 (1.1)	39.4 (1.1)
Sex					
	Female	565 (53.3)	121 (49.0)	1075 (50.5)	1622 (51.0)
	Male	496 (46.7)	126 (51.0)	1054 (49.5)	1557 (49.0)
Hours of life at measurement		55.3 (48.6)	52.6 (22.1)	41.2 (43.3)	47.3 (58.3)

Supplemental Table S3: Distribution of alcohol and smoking categories, and the number and percent of subjects in each exposure category by site

Exposure category	Exposure Information			South Africa N (%)	Northern Plains N (%)
	Trimester 1	Trimester 2	Trimester 3		
Smoking category	**Average Cigarettes/ week, mean (SD)**				
Non-smokers	0.014 (0.08)	0.003 (0.04)	0.009 (0.06)	1572 (39)	2216 (76)
Quit early	8.81 (9.92)	0.07 (0.19)	0.11 (0.22)	99 (2)	199 (7)
Low continuous	15.72 (10.28)	15.40 (10.79)	14.33 (10.32)	1442 (35)	357 (12)
Moderate to high continuous	48.31 (21.71)	51.71 (25.53)	47.09 (25.29)	959 (24)	141 (5)
Drinking category	**Drinks/ trimester, mean (SD)**				
Non-drinkers	0.04 (0.16)	0.02 (0.10)	0.01 (0.07)	1779 (48)	1400 (48)
Quit early	8.77 (7.41)	0.12 (0.58)	0.04 (0.26)	865 (23)	1264 (44)
Low continuous	2.41 (3.83)	2.27 (2.71)	1.85 (1.25)	218 (6)	29 (1)
Moderate to high continuous	40.89 (60.08)	16.12 (28.27)	7.46 (16.88)	857 (23)	204 (7)

Supplemental Table S4: Distribution of autonomic parameters at baseline

	Northern Plains		South Africa	
ANS measures	Mean (SD)	Interquartile Range (25%-75%)	Mean (SD)	Interquartile Range (25%-75%)
HR (bpm, AS)	126.94 (11.92)	119.36, 133.94	126.2 (12.5)	118.1— 133.9
HR (bpm, QS)	122.13 (11.22)	114.22, 129.13	121. 8 (12.2)	112.9 – 129.9
RMSSD (s, AS)	0.011 (0.005)	0.006, 0.013	0.014 (0.007)	0.009-0.013
RMSSD (s, QS)	0.011 (0.006)	0.006, 0.015	0.016 (0.007)	0.009-0.014
SD-RRi (s, AS)	-1.64 (0.20)	-1.77, -1.51	-1.58 (0.19)	-1.71, -1.44
SD-RRi (s, QS)	-1.77 (0.24)	-19.4, -1.62	-1.68 (0.23)	-1.83, -1.53
breaths/min, (AS)	55.65 (11.44)	47.21, 61.81	58.22 (13.85)	48.66-56.79
breaths/min, (QS)	45.34 (9.80)	37.81, 50.98	47.07 (11.88)	39.02-44.80
Systolic BP (mmHg, AS)	77.82 (13.87)	70.00, 83.00	87.74 (12.46)	79.00-95.00
Systolic BP (mmHg, QS)	78.35 (11.68)	71.00, 82.00	88.16 (11.28)	81.00-94.00
Diastolic BP (mmHg, AS)	46.74 (11.63)	40.00. 51.00	54.80 (10.27)	48.00-61.00
Diastolic BP (mmHg, QS)	45.54 (7.87)	41.00, 49.00	54.77 (9.17)	49.00-60.00

Supplemental Table S5: Association of prenatal smoking with ANS measures at baseline in South Africa.

(Infants whose mothers did not smoke during pregnancy formed the reference group. Results with p-values <0.10 are bolded.)

	Non-smoker Mean (95%CI)	Quit early Mean difference (95%CI) P value	Low continuous Mean difference (95%CI) P value	Moderate to high continuous Mean difference (95%CI) P value
Active sleep				
HR (bpm)	125.72 (124.74, 126.69)	1.64 (-1.50, 4.77) (0.30)	0.22 (-0.96, 1.42) (0.70)	-0.17 (-1.56, 1.22) (0.81)
log_{10}SD-RRi (s)	-1.59 (-1.60, 1.57)	-0.03 (-0.08, 0.01) (0.17)	0.01 (-0.006, 0.03) (0.19)	**0.02 (0.002, 0.04) (0.02)**
log_{10}RMSSD (s)	-1.89 (-1.91, -1.88)	**-0.08 (-0.14, -0.03) 0.003**	0.004 (-0.02, 0.02) (0.68)	0.02 (-0.006, 0.04) (0.14)
Breaths/min	56.90 (55.81, 57.99)	-1.42 (-5.03, 2.18) (0.44)	0.60 (-0.73, 1.95) (0.37)	**2.00 (0.43, 3.56) (0.01)**
Systolic blood pressure (mmHg)	87.71 (86.26, 89.15)	-0.09 (-4.73, 4,53) (0.96)	0.39 (-1.36, 2.15) (0.66)	1.15 (-0.89, 3.20) (0.26)
Diastolic blood pressure (mmHg)	54.39 (53.20, 55.57)	0.12 (-3.68, 3.92) (0.95)	1.04 (-0.39. 2.48) (0.15)	1.30 (-0.37, 2.98) (0.12)
Low frequency power of HRV	-6.23 (-6.31, -6.15)	-0.03 (-0.13, 0.06) (0.49)	0.02 (-0.017, 0.059) (0.27)	**0.04 (0.00082, 0.09) (0.045)**
High frequency power of HRV	-6.74 (-6.81, -6.67)	**-0.11 (-0.22, -0.009) (0.03)**	0.001 (-0.04, 0.04) (0.95)	0.03 (-0.017, 0.07) (0.21)
Ratio of low and high frequency power of HRV	0.51 (0.42, 0.59)	0.08 (-0.017, 0.18) (0.104)	0.02 (-0.017, 0.05) (0.28)	0.013, (-0.031, 0.057) (0.56)
Quiet sleep				
HR (bpm)	120.49 (118.79, 122.18)	0.23 (-5.57, 6.04) (0.93)	0.63 (-1.53, 2.79) (0.57)	0.66 (-1.87, 3.19) (0.60)
log_{10}SD-RRi (s)	-1.70 (-1.73, -1.67)	0.01 (-0.09, 0.12) (0.80)	0.01 (-0.03, 0.05) (0.49)	0.03 (-0.02, 0.07) (0.28)
log_{10}RMSSD (s)	-1.84 (-1.88, -1.81)	**-0.11 (-0.22, -0.001)**	**-0.007 (-0.04, 0.03)**	0.007 (-0.04, 0.05) (0.75)

		(0.05)	(0.73)	
Breaths/min	46.51 (44.95, 48.08)	-3.86 (-9.21, 1.48) (0.15)	-046 (-2.47, 1.53) (0.64)	1.64 (-0.70, 3.99) (0.16)
Systolic blood pressure (mmHg)	87.10 (84.94, 89.26)	1.39 (-5.55, 8.35) (0.69)	0.75 (-2.00, 3.52) (0.58)	0.34 (-3.53, 2.84) (0.83)
Diastolic blood pressure (mmHg)	54.47 (52.72, 56.22)	0.34 (-5.30, 5.99) (0.12)	0.12 (-2.12, 2.35) (0.91)	-1.71 (-4.29, 0.86) (0.19)
Low frequency power of HRV	-6.27 (-6.35, -6.20)	0.041 (-0.208, 0.29) (0.74)	0.04 (-0.043, 0.14) (0.29)	0.09 (-0.018, 0.2) (0.102)
High frequency power of HRV	-6.68 (-6.74, -6.62)	-0.16 (-0.37, 0.039) (0.11)	-0.04 (-0.11, 0.035) (0.29)	-0.005 (-0.09, 0.08) (0.90)
Ratio of low and high frequency power of HRV	0.40 (0.33, 0.48)	0.206 (-0.04, 0.46) (0.11)	**0.08 (-0.006, 0.18) (0.06)**	0.08 (-0.02, 0.19) (0.14)

Supplemental Table S6: Association of prenatal smoking with ANS measures at baseline in Northern Plains

(Infants whose mothers did not smoke during pregnancy formed the reference group. Results with p-values <0.10 are bolded.)

	Non-smoker Mean (95%CI)	Quit early Mean difference (95%CI) P value	Low continuous Mean difference (95%CI) P value	Moderate to high continuous Mean difference (95%CI) P value
Active sleep				
HR (bpm)	127.57 (126.11, 129.03)	0.59 (-1.57, 2.76) (0.58)	-0.55 (-2.34, 1.24) (0.54)	1.20 (-1.36, 3.78) 0.35
log_{10}SD-RRi (s)	-1.62 (-1.65, -1.59)	0.008 (-0.03, 0.04) (0.93)	**-0.02 (-0.05, 0.004) (0.08)**	0.002 (-0.04, 0.04) (0.91)
log_{10}RMSSD (s)	-2.02 (-2.05, -1.99)	0.002 (-0.04, 0.04) (0.93)	-0.015 (-0.05, 0.019) (0.39)	0.007 (-0.04, 0.06) (0.77)
Breaths/min	55.26 (53.82, 56.70)	-1.02 (-3.15, 1.12) (0.34)	1.18 (-0.58, 2.95) (0.18)	**2.38 (-0.15, 4.91) (0.06)**
Systolic blood pressure (mmHg)	75.56 (72.98, 78.14)	1.41 (-2.75, 5.58) (0.50)	-0.16 (-3.34, 3.02) (0.92)	0.87 (-3.88, 5.63) (0.71)
Diastolic blood pressure (mmHg)	47.87 (46.13, 49.61)	-1.55 (-4.15, 1.05) (0.24)	1.03 (-1.24, 3.29) (0.37)	1.43 (-2.49, 5.36) (0.47)
Low frequency power of HRV	-5.85 (-5.90, -5.80)	0.02 (-0.05, 0.09) (0.54)	-0.05 (-0.11, 0.01) (0.104)	0.004 (-0.08, 0.09) (0.91)
High frequency power of HRV	-6.95 (-7.006, -6.89)	-0.009 9-0.09, 0.07) (0.82)	-0.02 (-0.09, 0.04) (0.46)	-0.03 (-0.13, 0.06) (0.45)
Ratio of low and high frequency power of HRV	1.09 (1.04, 1.14)	0.03 (-0.03, 0.107) (0.36)	-0.02 (-0.08, 0.03) (0.39)	0.03 (-0.05, 0.12) (0.41)
Quiet sleep				
HR (bpm)	121.04 (118.99, 123.08)	-1.34 (-4.29, 1.59) (0.36)	-0.31 (-2.85, 2.23) (0.81)	**4.99 (0.55, 9.42) (0.02)**
log_{10}SD-RRi (s)	-1.77 (-1.82, -1.73)	0.07 (0.007, 0.13) (0.02)	-0.06 (-0.11, -0.001) (0.04)	0.004 (-0.09, 0.10) (0.92)
log_{10}RMSSD (s)	-2.01 (-2.06, -1.96)	0.054 (-0.01, 0.12)	-0.039 (-0.09, 0.02)	-0.025 (-0.13, 0.07)

		(0.12)	(0.19)	(0.63)
Breaths/min	44.28 (42.46, 46.09)	-1.55 (-4.16, 1.05) (0.24)	1.03 (-1.24, 3.29) (0.37)	1.43 (-2.49, 5.36) (0.47)
Systolic blood pressure (mmHg)	76.66 (72.16, 81.15)	-1.16 (-5.79, 3.47) (0.62)	0.42 (-3.57, 4.41) (0.83)	2.83 (-4.21, 9.87) (0.42)
Diastolic blood pressure (mmHg)	43.61 (40.65, 46.56)	-0.91 (-3.96, 2.12) (0.55)	-1.02 (-3.64, 1.60) (0.44)	1.73 (-2.89, 6.36) (0.46)
Low frequency power of HRV	-6.24 (-6.33, -6.14)	**0.17 (0.03, 0.31) (0.016)**	**-0.15 (-0.27, -0.03) (0.012)**	-0.03 (-0.24, 0.17) (0.72)
High frequency power of HRV	-6.99 (-7.08, -6.90)	0.06 (-0.06, 0.19) (0.33)	-0.07 (-0.18, 0.04) (0.22)	-0.06 (-0.26, 0.13) (0.52)
Ratio of low and high frequency power of HRV	0.75 (0.65, 0.84)	0.09 (-0.04, 0.23) (0.18)	-0.08 (-0.204, 0.03) (0.15)	0.002 (-0.208, 0.21) (0.98)

Supplemental Table S7: Association of prenatal alcohol with ANS measures at baseline in South Africa

(Infants whose mothers did not drink during pregnancy formed the reference group. Results with p-values <0.10 are bolded.)

	Non- Mean (95%CI)	Quit early Mean difference (95%CI) P value	Low continuous Mean difference (95%CI) P value	Moderate to high continuous Mean difference (95%CI) P value
Active sleep				
HR (bpm)	125.95 (124.95, 126.98)	0.97 (-0.26, 2.22) (0.12)	-1.08 (-3.28, 1.12) (0.33)	0.89 (-0.43, 2.22) (0.18)
log_{10}SD-RRi (s)	-1.58 (-1.60, -1.57)	-0.008 (-0.02, 0.01) (0.39)	-0.008 (-0.04, 0.02) (0.63)	-0.007 (-0.03, 0.01) (0.52)
log_{10}RMSSD (s)	-1.91 (-1.93, -1.89)	-0.003 (-0.024, 0.019) (0.80)	0.02 (-0.019, 0.06) (0.33)	0.004 (-0.02, 0.02) (0.76)
Breaths/min	58.03 (56.87, 59.19)	-1.13 (-2.53, 0.26) (0.11)	-2.01 (-4.48, 0.46) (0.11)	-0.22 (-1.72, 1.27) (0.76)
Systolic blood pressure (mmHg)	87.83 (86.34, 89.31)	0.40 (-1.44, 2.24) (0.66)	0.10 (-3.28, 3.48) (0.95)	0.45 (-1.49, 2.39) (0.64)
Diastolic blood pressure (mmHg)	54.78 (53.56, 56.01)	0.66 (-0.85, 2.16) (0.39)	-0.06 (-2.84, 2.70) (0.96)	0.28 (-1.30, 1.88) (0.72)
Low frequency power of HRV	-5.85 (-5.88, 5.81)	-0.02 (-0.06, 0.01) (0.24)	-0.05 (-0.12, 0.015) (0.12)	-0.02 (-0.06, 0.02) (0.32)
High frequency power of HRV	-6.76 (-6.80, -6.73)	0.008 (-0.03, 0.05) (0.68)	0.04 (-0.02, 0.12) (0.203)	0.015 (-0.03, 0.06) (0.51)
Ratio of low and high frequency power of HRV	0.91 (0.88, 0.94)	-0.03 (-0.07, 0.006) (0.105)	**-0.11 (-0.18, -0.04)** **(0.002)**	**-0.03 (-0.08, 0.004)** **(0.07)**
Quiet sleep				
HR (bpm)	122.60 (120.70, 124.49)	0.34 (-1.89, 2.54) (0.76)	**-4.50 (-8.26, -0.74)** **(0.01)**	**-2.76 (-5.26, -0.25)** **(0.03)**
log_{10}SD-RRi (s)	-1.69 (-1.72, -1.65)	0.01 (-0.03, 0.05) (0.56)	-0.03 (-0.09, 0.04) (0.44)	0.02 (-0.2, 0.07) (0.30)
log_{10}RMSSD (s)	-1.89 (-1.92, -1.85)	0.01 (-0.03, 0.05)	0.009 (-0.61, 0.08)	0.04 (-0.004, 0.09) (0.07)

		(0.61)	(0.79)	
Breaths/min	46.21 (44.45, 47.95)	-1.31 (-3.38, 0.77) (0.21)	0.09 (-3.36, 3.56) (0.95)	-0.22 (-2.54, 2.09) (0.84)
Systolic blood pressure (mmHg)	88.82 (86.55, 91.08)	-1.76 (-4.59, 1.07) (0.69)	-3.00 (-7.59, 1.58) (0.19)	-0.27 (-3.33, 2.78) (0.86)
Diastolic blood pressure (mmHg)	55.05 (53.21, 56.89)	-1.53 (-3.83, 0.75) (0.18)	-2.82 (-6.55, 0.90) (0.13)	0.78 (-1.69, 3.25) (0.53)
Low frequency power of HRV	-6.23 (-6.31, -6.15)	0.04 (-0.05, 0.14) (0.36)	-0.08 (-0.24, 0.08) (0.32)	0.04 (-0.06, 0.14) (0.46)
High frequency power of HRV	-6.74 (-6.81, -6.67)	0.017 (-0.06, 0.09) (0.67)	-0.05 (-0.18, 0.08) (0.45)	0.08 (-0.008, 0.17) (0.07)
Ratio of low and high frequency power of HRV	0.51 (0.42, 0.59)	0.02 (-0.07, 0.12) (0.62)	-0.02 (-0.19, 0.13) (0.75)	-0.03 (-0.14, 0.07) (0.51)

Supplemental Table S8: Association of prenatal alcohol with ANS measures at baseline in Northern Plains. (Infants whose mothers did not drink during pregnancy formed the reference group.)

	Non- Mean (95%CI)	Quit early Mean difference (95%CI) P value	Low continuous Mean difference (95%CI) P value	Moderate to high continuous Mean difference (95%CI) P value
Active sleep				
HR (bpm)	126.92 (125.78, 128.06)	0.29 (-0.81, 1.40) (0.60)	3.42 (-1.83, 8.67) (0.20)	0.13 (-2.06, 2.32) (0.90)
log_{10}SD-RRi (s)	-1.64 (-1.66, -1.63)	**-0.0007 (-0.02, 0.02) (0.93)**	0.07 (-0.02, 0.15) (0.14)	-0.005 (-0.04, 0.03) (0.78)
log_{10}RMSSD (s)	-2.03 (-2.06, -2.01)	-0.008 (-0.03, 0.013) (0.45)	0.045 (-0.05, 0.14) (0.39)	0.009 (-0.03, 0.05) (0.65)
Breaths/min	55.77 (54.64, 56.89)	0.81 (-0.28, 1.90) (0.14)	1.13 (-4.05, 6.30) (0.66)	-1.44 (-3.61, 0.73) (0.19)
Systolic blood pressure (mmHg)	78.69 (76.57, 80.82)	-0.75 (-2.77, 1.26) (0.46)	-7.00 (-16.16, 2.16) (0.13)	-2.67 (-6.54, 1.21) (0.17)

Diastolic blood pressure (mmHg)	47.87 (46.13, 49.61)	0.34 (-1.15, 1.84) (0.65)	-4.67 (-11.13, 1.78) (0.15)	2.18 (-0.51, 4.87) (0.11)
Low frequency power of HRV	-5.89 (-5.93, -5.85)	-0.003 (-0.04, 0.03) (0.85)	0.16 (-0.01, 0.35) (0.06)	-0.02 (-0.1009, 0.05) (0.52)
High frequency power of HRV	-7.01 (-7.06, -6.97)	-0.004 (-0.04, 0.03) (0.82)	0.15 (-0.04, 0.35) (0.13)	0.05 (-0.02, 0.14) (0.17)
Ratio of low and high frequency power of HRV	1.11 (1.08, 1.15)	0.002 (-0.03, 0.03) (0.91)	0.01 (-0.15, 0.19) (0.83)	-0.08 (-0.15, -0.007) (0.03)
Quiet sleep				
HR (bpm)	122.54 (120.83, 124.25)	0.32 (1.36, 2.00) (0.70)	-4.77 (-12.07, 2.51) (0.19)	1.78 (-1.24, 4.80) (0.24)
log_{10}SD-RRi (s)	-1.76 (-1.80, -1.73)	-0.01 (-0.05, 0.03) (0.53)	0.06 (-0.10, 0.21) (0.46)	-0.04 (-0.11, 0.02) (0.19)
log_{10}RMSSD (s)	-2.01 (-2.05, -1.97)	-0.018 (-0.058, 0.020) (0.34)	0.049 (-0.122, 0.22) (0.57)	-0.030 (-0.101, 0.040) (0.40)
Breaths/min	45.04 (43.52, 46.56)	0.34 (-1.15, 1.84) (0.65)	-4.67 (-11.13, 1.78) (0.15)	2.18 (-0.51, 4.87) (0.11)
Systolic blood pressure (mmHg)	79.43 (76.71, 82.14)	0.99 (-3.73, 1.73) (0.47)	-9.08 (-25.93, 7.77) (0.29)	1.10 (-3.54, 5.74) (0.64)
Diastolic blood pressure (mmHg)	46.24 (44.45, 48.02)	-1.50 (-3.29, 0.29) (0.10)	-11.09 (-22.18, -0.02) (0.04)	1.88 (-1.17, 4.94) (0.22)
Low frequency power of HRV	-6.27 (-6.35, -6.19)	-0.006 (-0.08, 0.07) (0.86)	0.22 (-0.12, 0.56) (0.21)	-0.09 (-0.23, 0.04) (0.19)
High frequency power of HRV	-7.004 (-7.08, -6.92)	-0.04 (-0.12, 0.03) (0.23)	0.05 (-0.26, 0.38) (0.72)	-0.04 (-0.17, 0.09) (0.52)
Ratio of low and high frequency power of HRV	0.71 (0.63, 0.79)	0.03 (-0.04, 0.11) (0.33)	0.16 (-0.17, 0.506) (0.33)	-0.04 (-0.18, 0.09) (0.51)

Supplemental Table S9: Association of prenatal smoking with mean changes in cardiorespiratory variables in response to 45º head-up tilts in South Africa. (Infants whose mothers did not smoke during pregnancy formed the reference group)

	Non-smoker Mean (95%CI)	Quit early Mean difference (95%CI) (P value)	Low continuous Mean difference (95%CI) (P value)	Moderate to high continuous Mean difference (95%CI) (P value)
Active sleep				
Δ sustained HR (bpm)	2.45 (1.87, 3.03)	-1.10 (-2.98, 0.77) (0.24)	-0.09 (-0.78, 0.61) 0.79)	-0.07 (-0.89, 0.76) (0.87)
Δ acute HR (bpm)	24.16 (23.31, 25.01)	**-2.64 (-5.42, 0.13) (0.06)**	0.88 (-0.14, 1.90) (0.08)	**1.37 (0.17, 2.57) (0.02)**
Δ rMSSD-RRi (s)	-0.54 (-0.89, -0.19)	0.029(-1.10, 1.16) (0.95)	0.23 (-0.19, 0.66) (0.28)	-0.34(-0.84, 0.16) (0.18)
Δ change in breathing (breaths/min)	-3.90 (-4.68, -3.12)	0.66 (-1.99, 3.31) (0.62)	1.29 (0.33, 2.23) (0.008)	0.39 (-0.72, 1.49) (0.49)
Δ systolic blood pressure (mmHg)	-5.15 (-5.92, -4.38)	1.45 (-0.97, 3.87) (0.23)	0.71 (-0.20, 1.64) (0.12)	0.01 (-1.09, 1.11) (0.98)
Δ diastolic blood pressure (mmHg)	-5.56 (-6.30, -4.82)	-1.75 (-4.06, 0.56) (0.13)	0.25 (-0.63, 1.14) (0.57)	-0.08 (-1.13, 0.98) (0.88)
Quiet Sleep				
Δ sustained HR (bpm)	3.84 (3.08, 4.61)	1.16 (-1.48, 3.79) (0.38)	-0.11 (-1.03, 0.83) (0.82)	0.58 (-0.52, 1.67) (0.30)
Δ acute HR (bpm)	23.61 (22.43, 24.78)	-3.10 (-7.14, 0.93) (0.13)	-0.26 (-1.69, 1.16) (0.71)	0.29 (-1.38, 1.97) (0.72)
Δ rMSSD-RRi (s)	-1.28 (-1.78, -0.78)	-1.64 (-3.39, 0.10) (0.06)	0.11 (-0.49, 0.71) (0.73)	0.12 (-0.59, 0.82) (0.75)
Δ change in breathing (breaths/min)	-1.94 (-2.74, -1.14)	0.35 (-2.56, 3.26) (0.81)	-0.77 (-.1.75, 0.21) (0.12)	-0.34 (-1.49, 0.80) (0.55)
Δ systolic blood pressure (mmHg)	-4.84 (-5.70, -3.98)	2.43 (-0.57, 5.43) (0.11)	0.03 (-1.01, 1.08) (0.94)	0.52 (-0.69, 1.74) (0.39)
Δ diastolic blood pressure (mmHg)	-5.62 (-6.41, -4.83)	0.75 (-2.00, 3.51) (0.59)	0.05 (-0.90, 1.01) (0.91)	0.53 (-0.57, 1.64) (0.34)

Supplemental Table S10: Association of prenatal smoking with mean changes in cardiorespiratory variables in response to 45° head-up tilts in Northern Plains. (Infants whose mothers did not smoke during pregnancy formed the reference group)

	Non-smoker Mean (95%CI)	Quit early Mean difference (95%CI) (P value)	Low continuous Mean difference (95%CI) (P value)	Moderate to high continuous Mean difference (95%CI) (P value)
Active sleep				
Δ sustained HR (bpm)	2.59 (1.67, 3.52)	-0.29 (-1.67, 1.09) (0.68)	-0.91 (-2.08, 0.25) (0.12)	-0.90 (-2.59, 0.79) (0.29)
Δ acute HR (bpm)	21.74 (20.63, 22.86)	0.18 (-1.45, 1.81) (0.83)	1.28 (-0.13, 2.68) (0.07)	0.14 (-2.01, 2.04) (0.98)
Δ rMSSD-RRi (s)	-0.65 (-1.08, -0.23)	0.63 (-.002, 1.27) (0.05)	0.41 (-.13, 0.95) (0.13)	0.80 (0.02, 1.58) (0.04)
Δ change in breathing (breaths/min)	-2.96 (-3.94, -1.96)	-0.003 (-1.50, 1.49) (0.99)	-0.16 (-1.43, 1.12) (0.81)	-0.44 (-2.31, 1.43) (0.64)
Δ systolic blood pressure (mmHg)	-8.20 (-10.17, 6.23)	3.76 (0.84, 6.68) (0.01)	0.52 (-2.02, 3.05) (0.68)	-1.97 (-5.72, 1.77) (0.30)
Δ diastolic blood pressure (mmHg)	-7.72 (-9.36, -6.06)	4.34 (1.90, 6.79) (0.0005)	2.57 (0.51, 4.63) (0.02)	-1.33 (-4.46, 1.81) (0.40)
Quiet Sleep				
Δ sustained HR (bpm)	3.14 (1.95, 4.33)	0.75 (-1.12, 2.61) (0.43)	-0.89 (-2.52, 0.74) (0.28)	0.30 (-2.13, 2.73) (0.81)
Δ acute HR (bpm)	20.84 (19.22, 22.46)	-1.35 (-3.95, 1.25) (0.30)	1.13 (-1.06, 3.32) (0.31)	0.06 (-3.25, 3.36) (0.97)
Δ rMSSD-RRi (s)	-0.98 (-1.61, -0.35)	-0.68 (-1.67, 0.31) (0.18)	-0.18 (-1.05, 0.68) (0.68)	0.73 (-0.56, 2.02) (0.26)
Δ change in breathing (breaths/min)	-4.16 (-5.37, -2.95)	0.32 (-1.42, 2.07) (0.71)	0.85 (-0.72, 2.41) (0.29)	-0.46 (-2.79, 1.87) (0.69)
Δ systolic blood pressure (mmHg)	-4.89 (-7.18, -2.62)	-1.91 (-5.52, 1.70) (0.30)	0.62 (-2.49, 3.74) (0.69)	-0.17 (-4.97, 4.62) (0.94)
Δ diastolic blood pressure (mmHg)	-5.64 (-7.43, -3.86)	-1.16 (-3.99, 1.66) (0.41)	1.71 (-0.69, 4.12) (0.16)	-1.92 (-5.67, 1.83) (0.31)

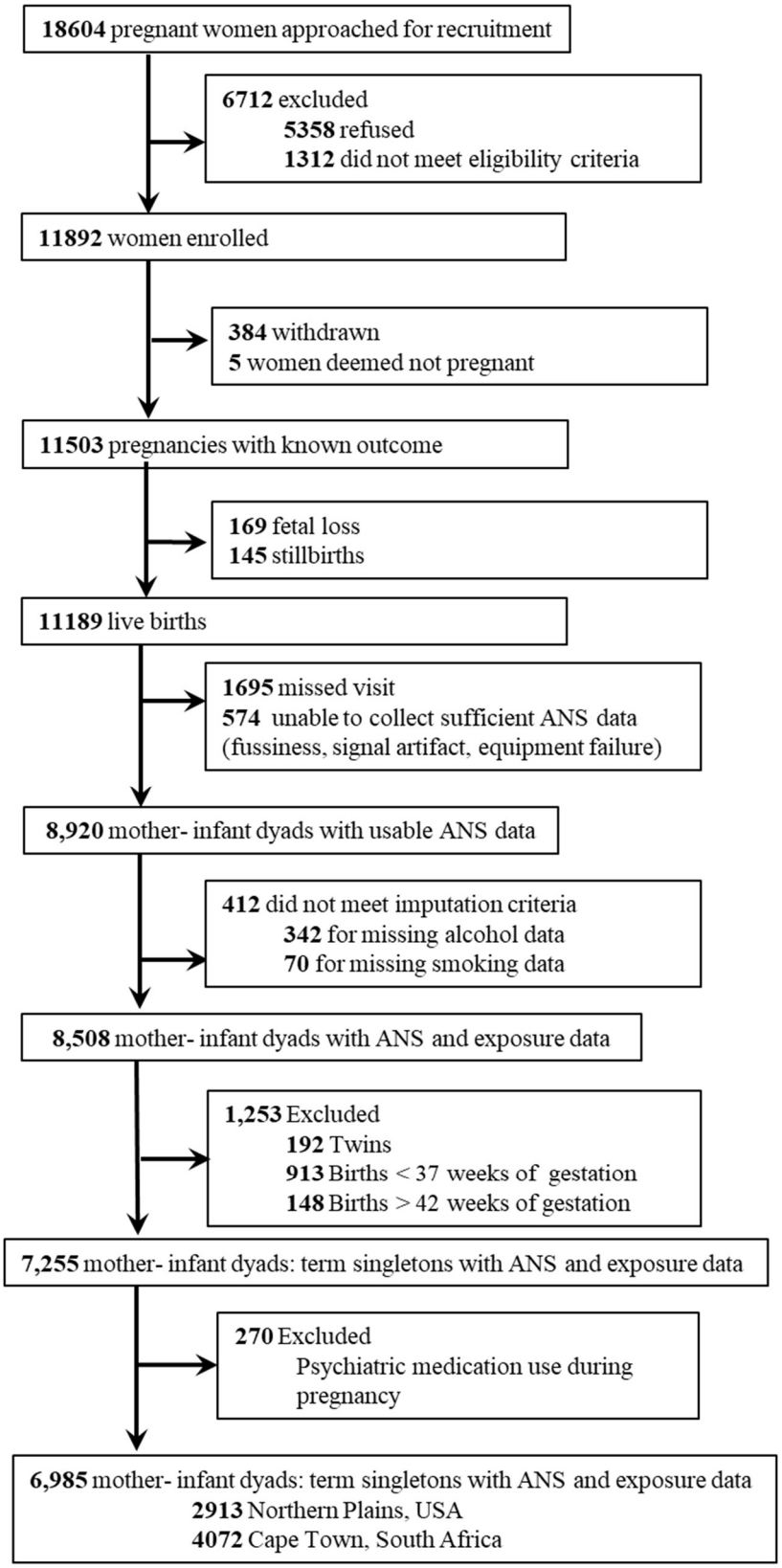
Supplemental Table S11: Association of prenatal drinking with mean changes in cardiorespiratory variables in response to 45º head-up tilts in South Africa. (Infants whose mothers did not drink during pregnancy formed the reference group)

	Non-drinker Mean (95%CI)	Quit early Mean difference (95%CI) (P value)	Low continuous Mean difference (95%CI) (P value)	Moderate to high continuous Mean difference (95%CI) (P value)
Active sleep				
Δ sustained HR (bpm)	2.14 (1.54, 2.74)	-0.57 (-0.74, 0.73) (0.99)	-0.25 (-1.53, 1.05) (0.70)	0.23 (-0.56, 1.02) (0.56)
Δ acute HR (bpm)	23.90 (23.02, 24.78)	-0.37 (-1.45, 0.71) (0.49)	1.21 (-0.66, 3.08) (0.20)	-0.18 (-1.32, 0.96) (0.76)
Δ rMSSD-RRi (s)	-0.56 (-0.9, -0.19)	-0.12 (-0.56, 0.33) (0.60)	0.29 (-0.49, 1.0) (0.46)	-0.19 (-0.67, 0.28) (0.41)
Δ change in breathing (breaths/min)	-3.51 (-4.34, -2.66)	0.25 (-0.74, 1.24) (0.62)	1.02 (-0.70, 2.73) (0.24)	-0.53 (-1.59, 0.53) (0.32)
Δ systolic blood pressure (mmHg)	-5.04 (-5.82, -4.26)	-0.30 (-1.27, 0.66) (0.54)	0.66 (-1.08, 2.42) (0.45)	1.37 (0.34, 2.41) (0.009)
Δ diastolic blood pressure (mmHg)	-6.46 (-7.20, -5.72)	0.54 (-0.37, 1.09) (0.33)	0.56 (-1.11, 2.23) (0.51)	0.91 (-0.08, 1.91) (0.07)
Quiet Sleep				
Δ sustained HR (bpm)	4.72 (3.88, 5.56)	-0.45 (-1.40, 0.52) (0.36)	-1.39 (-3.14, 0.35) (0.11)	-0.02 (-1.05, 1.02) (0.97)
Δ acute HR (bpm)	23.17 (21.88, 24.45)	-1.22 (-2.69, 0.24) (0.10)	0.17 (-2.53, 2.87) (0.89)	-0.25 (-1.81, 1.32) (0.75)
Δ rMSSD-RRi (s)	-1.65 (-2.21, -1.10)	0.41 (-0.22, 1.03) (0.20)	-0.26 (-1.39, 0.86) (0.65)	-0.05 (-0.72, 0.62) (0.87)
Δ change in breathing (breaths/min)	-1.65 (-2.57, -0.73)	-0.49 (-1.49, 0.50) (0.33)	-0.59 (-2.36, 1.19) (0.51)	-0.82 (-1.91, 0.26) (0.13)
Δ systolic blood pressure (mmHg)	-3.83 (-4.78. -2.88)	0.03 (-1.06, 1.11) (0.96)	-0.64 (-2.62, 1.34) (0.52)	-0.45 (-1.59, 0.70) (0.44)
Δ diastolic blood pressure (mmHg)	-5.17 (-6.03, -4.31)	-0.12 (-1.12, 0.87) (0.81)	0.17 (-1.6, 1.98) (0.85)	-0.47 (-1.52, 0.57) (0.37)

Supplemental Table S12: Association of prenatal drinking with mean changes in cardiorespiratory variables in response to 45º head-up tilts in both Northern Plains. (Infants whose mothers did not drink during pregnancy formed the reference group)

	Non-drinker Mean (95%CI)	Quit early Mean difference (95%CI) (P value)	Low continuous Mean difference (95%CI) (P value)	Moderate to high continuous Mean difference (95%CI) (P value)
Active sleep				
Δ sustained HR (bpm)	2.16 (1.42, 2.91)	-0.42 (-1.13, 0.28) (0.23)	0.01 (-3.3, 3.3) (0.99)	0.01 (-1.40, 1.44) (0.97)
Δ acute HR (bpm)	21.64 (20.75, 22.52)	-0.12 (-0.96, 0.73) (0.78)	1.65 (-2.33, 5.63) (0.42)	0.38 (-1.33, 2.08) (0.66)
Δ rMSSD-RRi (s)	-0.003 (-0.35, 0.34)	-.09 (-.42, 0.24) (0.59)	-.79 (-2.32, 0.73) (0.31)	0.11 (-.55, 0.77) (0.73)
Δ change in breathing (breaths/min)	-4.73 (-5.54, -3.92)	0.77 (0.003, 1.54) (0.05)	5.49 (1.96, 9.02) (0.002)	0.25 (-1.31, 1.81) (0.76)
Δ systolic blood pressure (mmHg)	-7.42 (-9.05, -5.79)	0.70 (-0.83, 2.23) (0.36)	-1.71 (-8.62, 5.19) (0.62)	0.21 (-2.88, 3.30) (0.89)
Δ diastolic blood pressure (mmHg)	-6.37 (-7.72, 5.02)	0.08 (-1.19, 1.35) (0.89)	-0.90 (-4.78, 6.81) (0.72)	-0.90 (-3.49, 1.68) (0.49)
Quiet Sleep				
Δ sustained HR (bpm)	2.56 (1.54, 3.58)	-0.23 (-1.19, 0.74) (0.64)	1.09 (-3.13, 5.32) (0.61)	1.62 (-0.28, 3.51) (0.09)
Δ acute HR (bpm)	20.65 (19.26, 22.05)	-0.09 (-1.41, 1.23) (0.89)	0.68 (-5.07, 6.41) (0.81)	0.01 (-2.61, 2.62) (0.99)
Δ rMSSD-RRi (s)	-0.50 (-1.04, 0.04)	0.43 (-0.09, 0.94) (0.10)	-1.76 (-4.01, 0.47) (0.12)	-0.70 (-1.71, 0.30) (0.16)
Δ change in breathing (breaths/min)	-3.13 (-4.10, -2.16)	0.25 (-0.69, 1.18) (0.61)	4.55 (0.19, 8.91) (0.04)	0.87 (-0.92, 2.66) (0.34)
Δ systolic blood pressure (mmHg)	-6.02 (8.01, -4.03)	-0.56 (-2.49, 1.37) (0.57)	1.10 (-6.86, 9.08) (0.78)	2.48 (-1.29, 6.25) (0.19)
Δ diastolic blood pressure (mmHg)	-7.09 (-8.63, -5.54)	0.39 (-1.12, 1.89) (0.61)	-0.35 (-6.59, 5.89) (0.91)	4.36 (1.41, 7.30) (0.004)

Supplemental Figure S1: Flow chart of study sample selection



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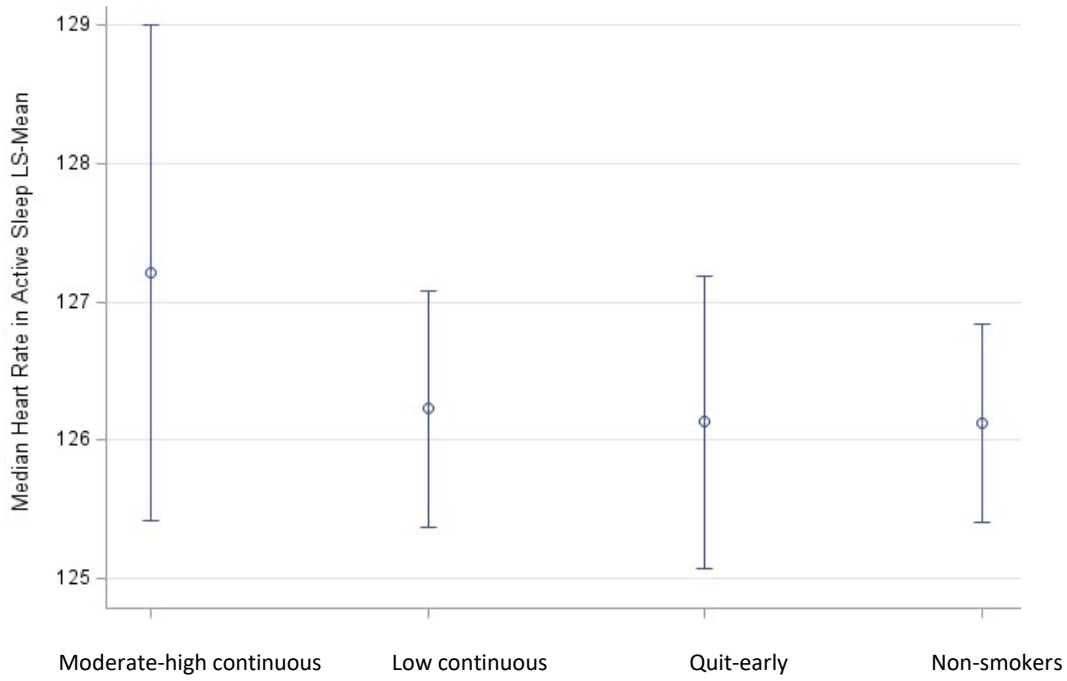
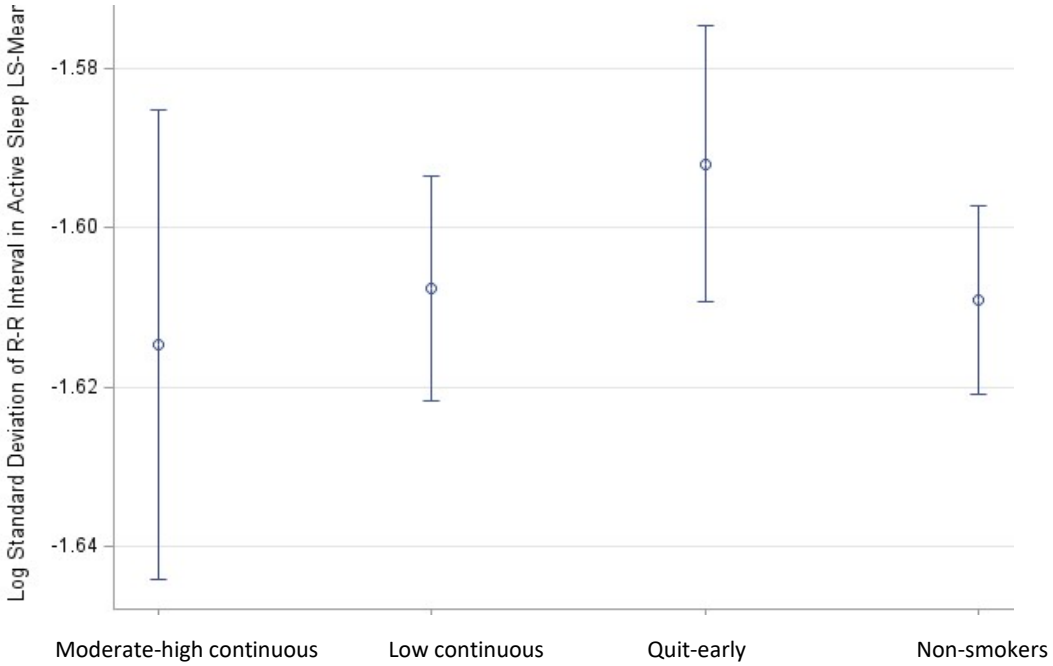
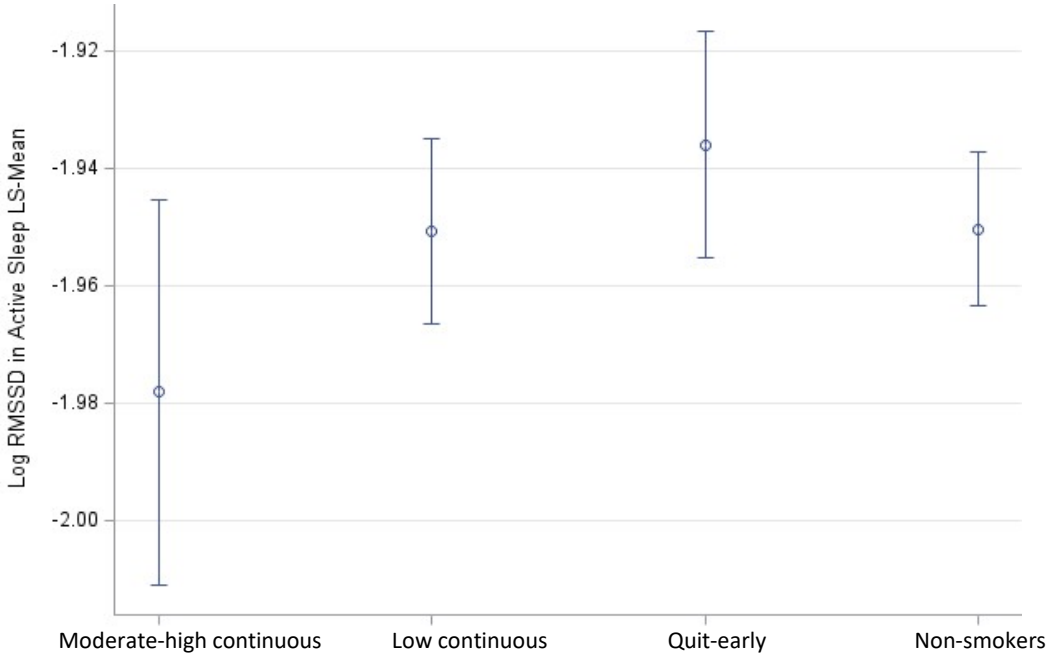


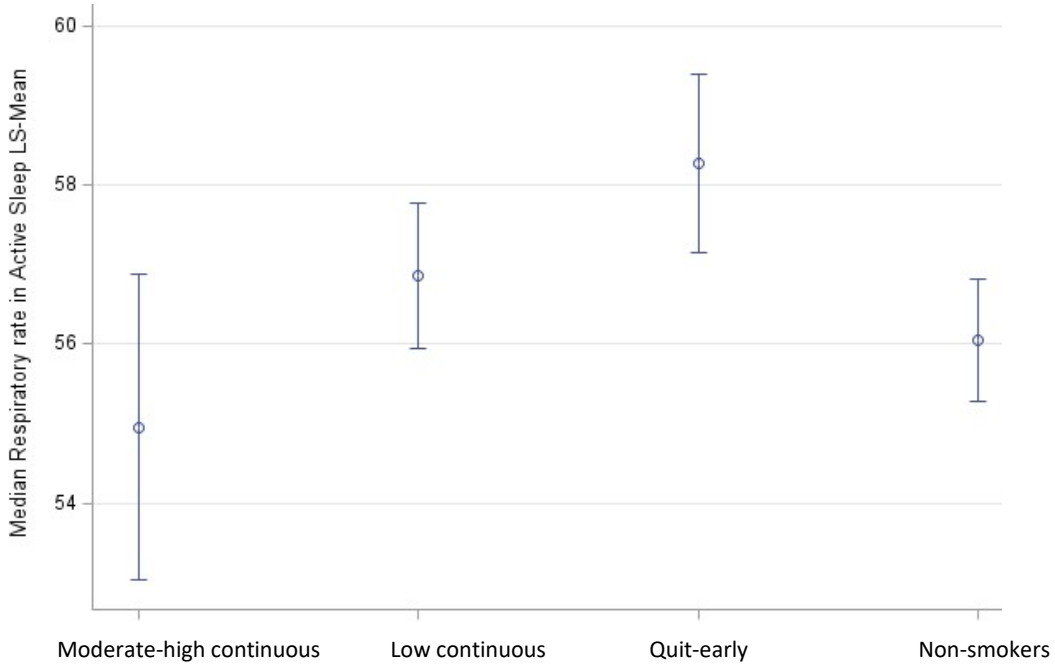
Supplemental Figure S2: Marginal means of median heart rate for each smoking groups in active sleep, both study sites



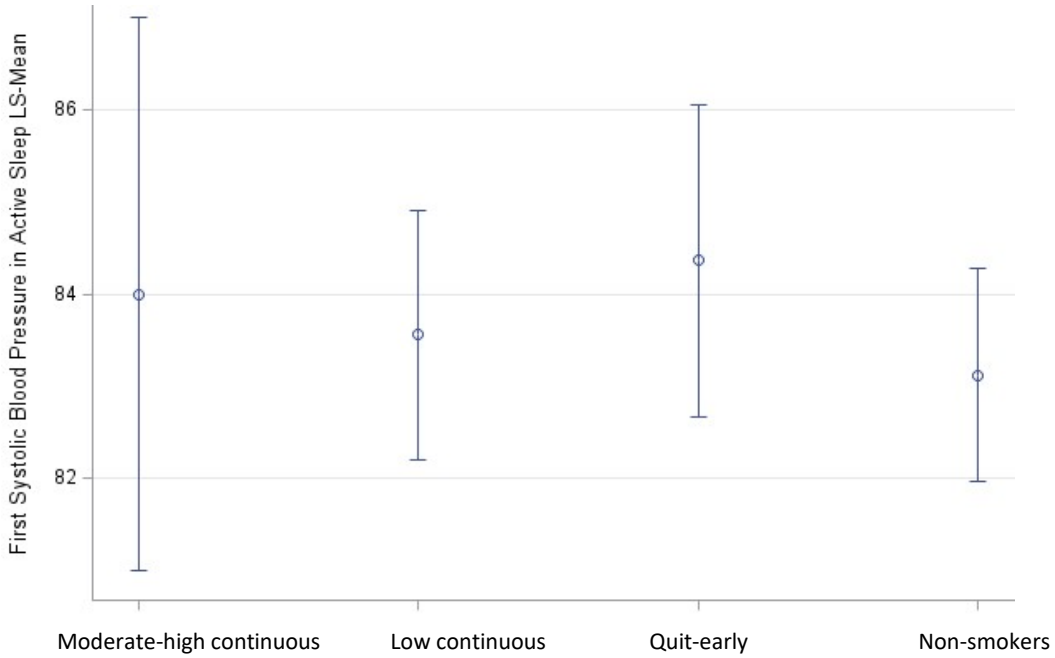
Supplemental Figure S3: Marginal means $\log_{10}$SD-RRi for each smoking groups in active sleep, both study sites



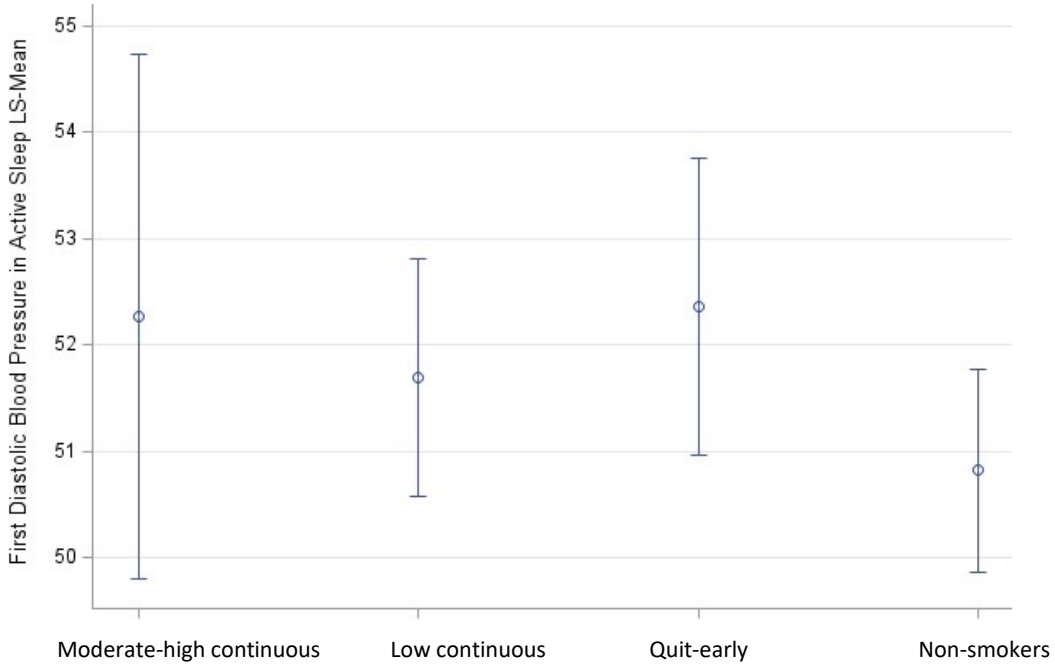
Supplemental Figure S4: Marginal means of Log RMSSD for each smoking groups in active sleep, both study sites



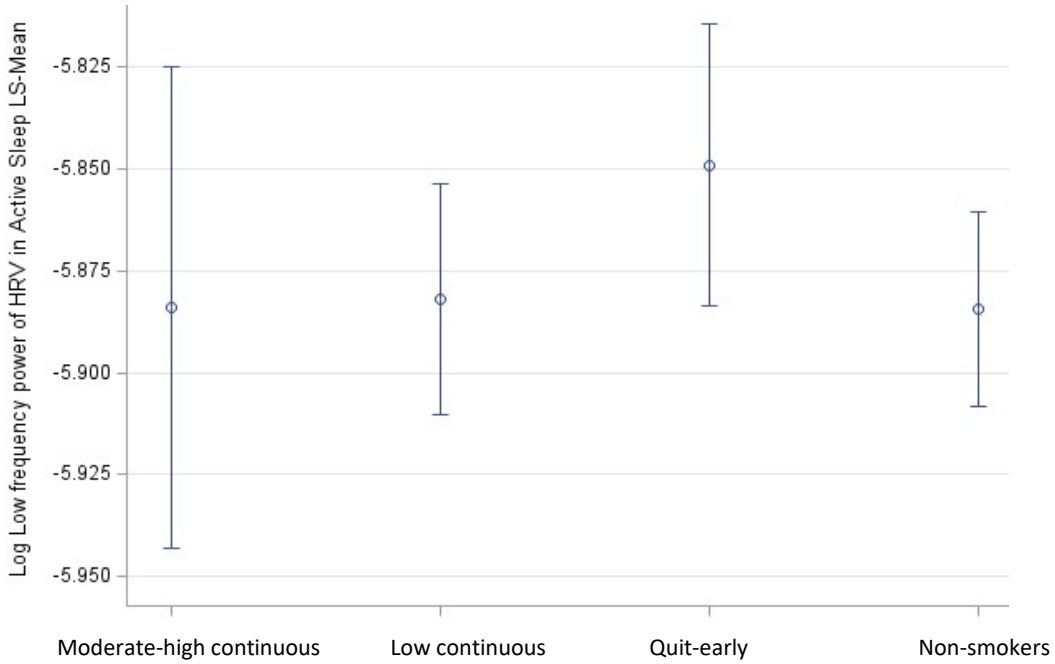
Supplemental Figure S5: Marginal means of median respiratory rate for each smoking groups in active sleep, both study sites



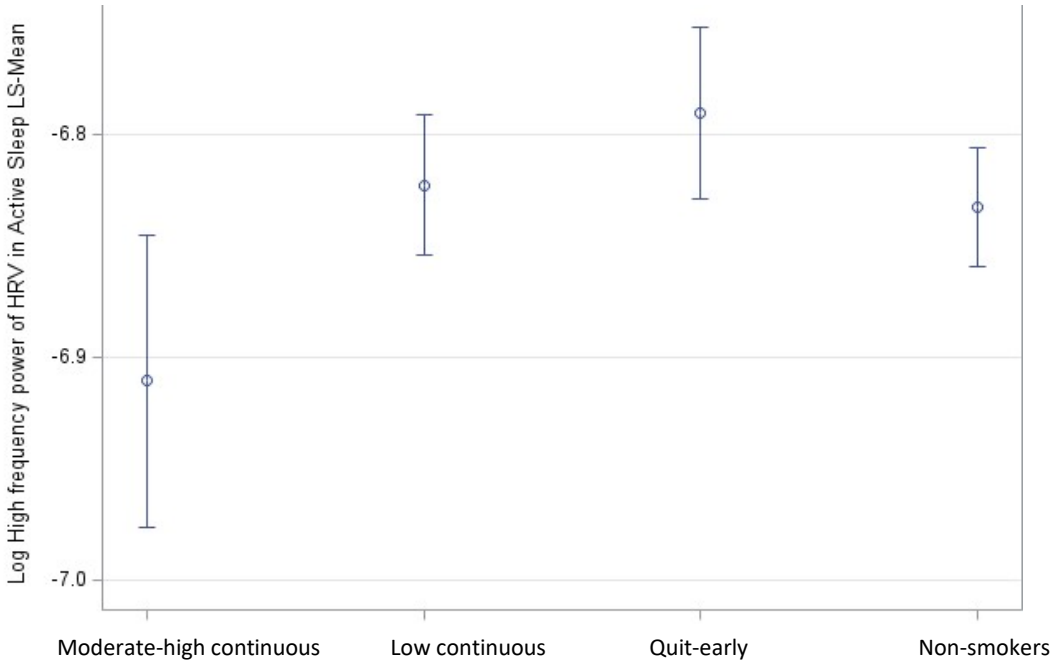
Supplemental Figure S6: Marginal means of systolic blood pressure for each smoking groups in active sleep, both study sites



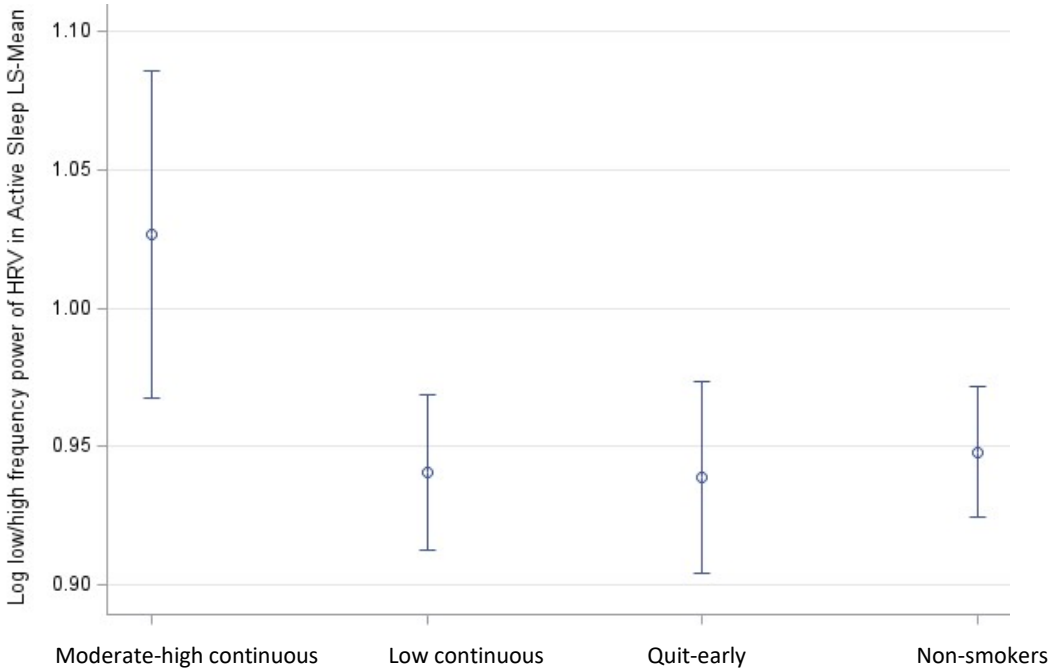
Supplemental Figure S7: Marginal means of diastolic blood pressure for each smoking groups in active sleep, both study sites



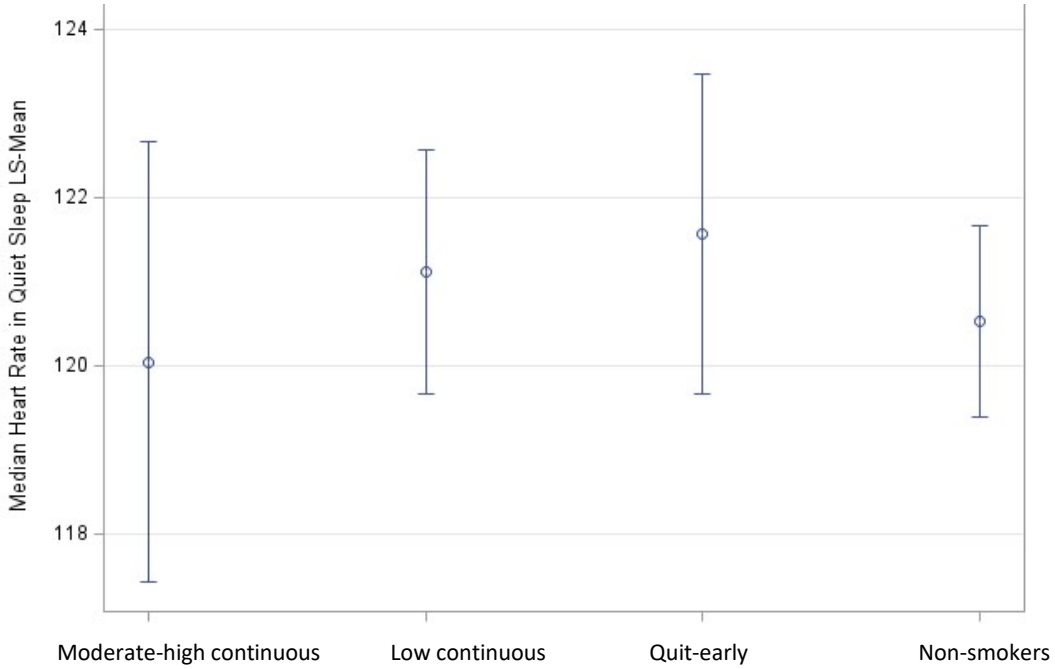
Supplemental Figure S8: Marginal means log low frequency power of HRV for each smoking groups in active sleep, both study sites



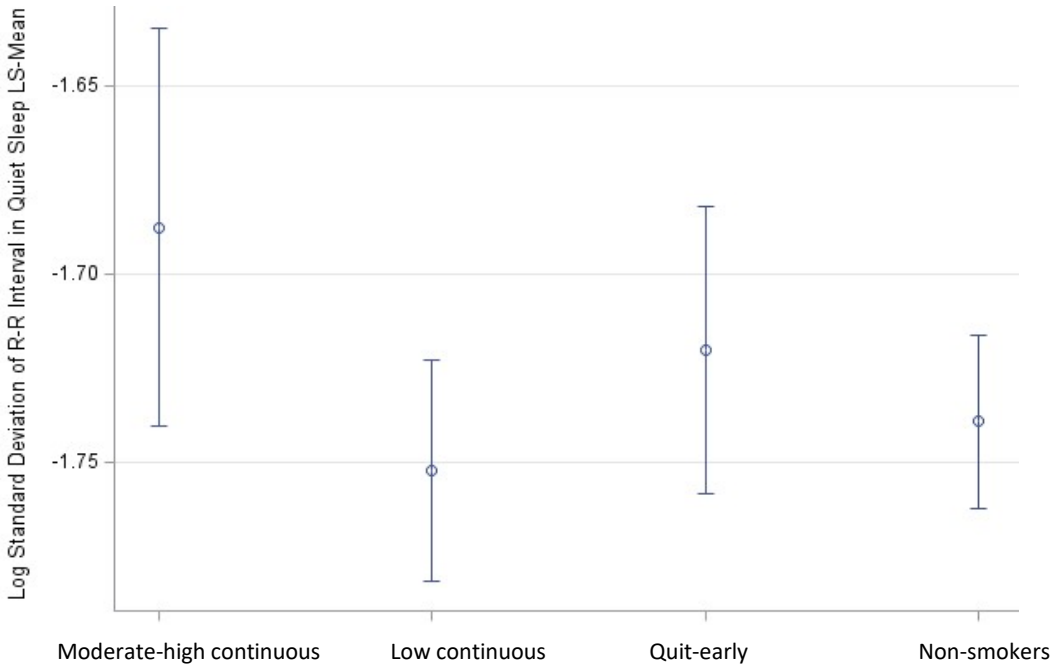
Supplemental Figure S9: Marginal means log high frequency power of HRV for each smoking groups in active sleep, both study sites



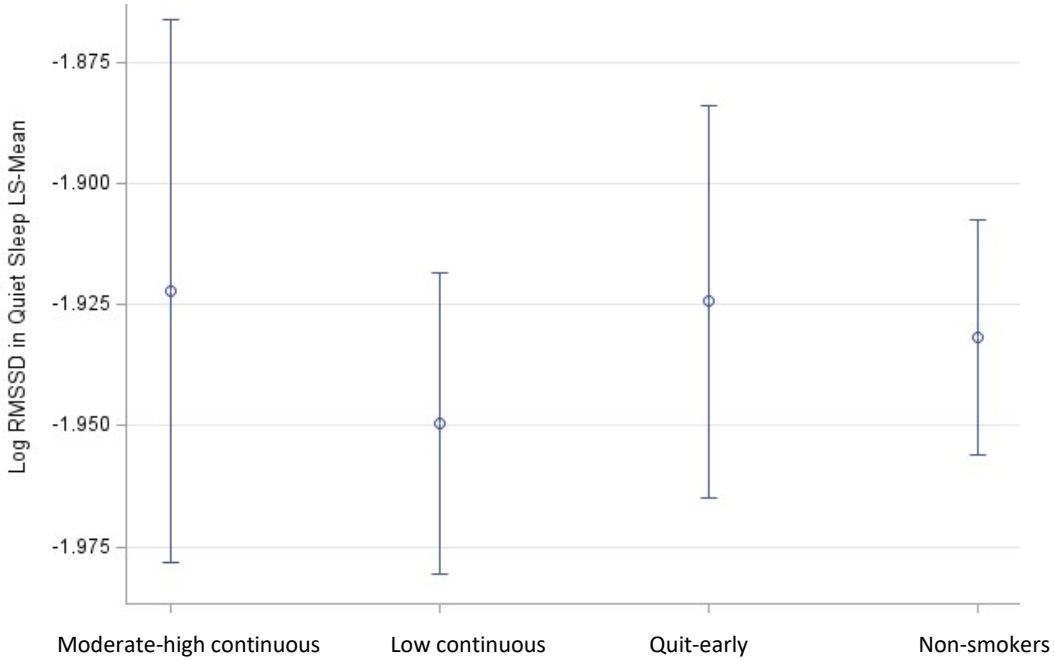
Supplemental Figure S10: Marginal means of ratio of low to high frequency power of HRV for each smoking groups in active sleep, both study si



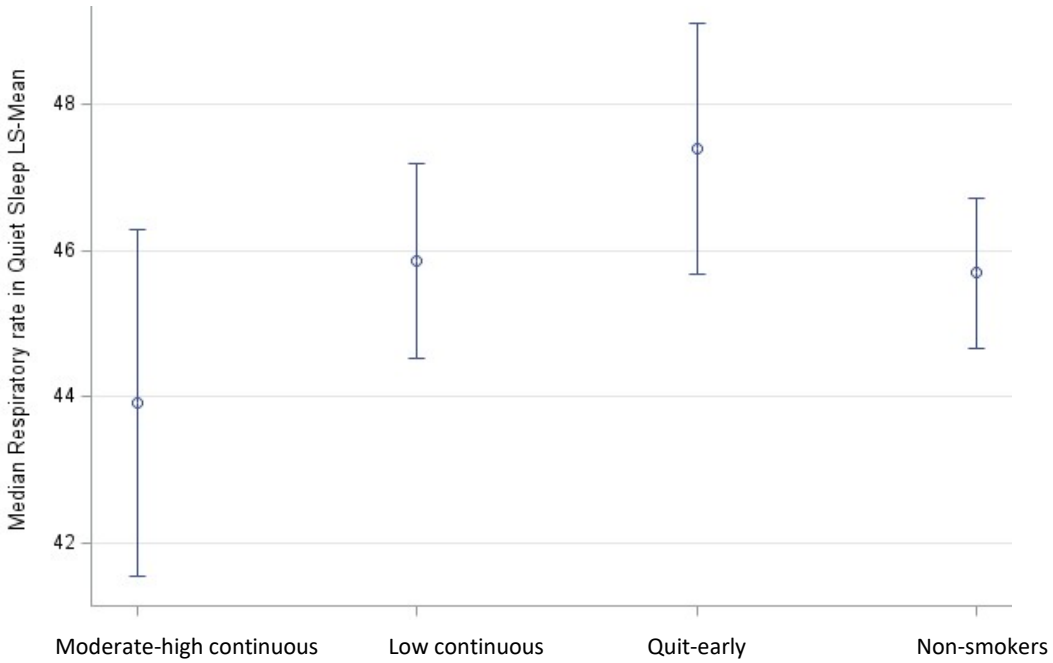
Supplemental Figure S11: Marginal means of median heart rate for each smoking groups in quiet sleep, both study sites



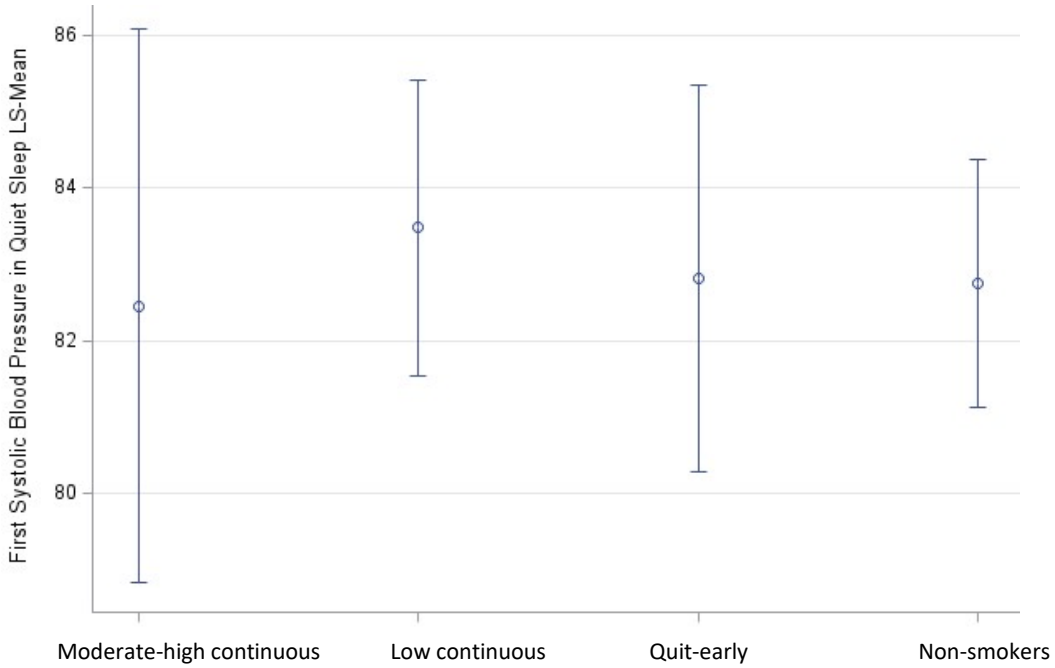
Supplemental Figure S12: Marginal means log_{10}SD-RRi for each smoking groups in quiet sleep, both study sites



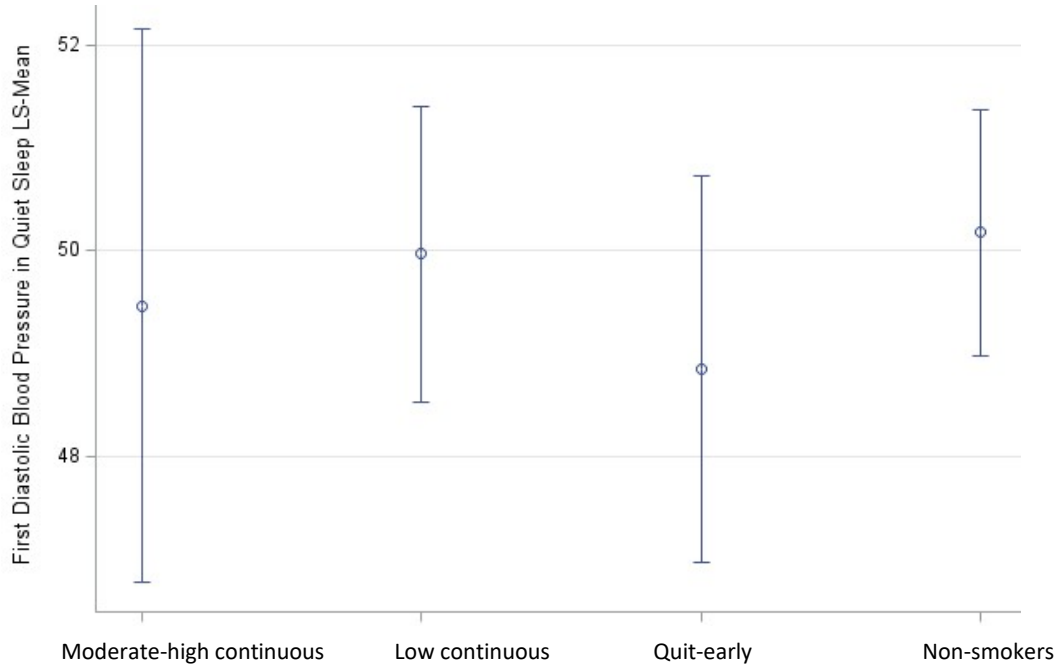
Supplemental Figure S13: Marginal means of Log RMSSD for each smoking groups in quiet sleep, both study sites



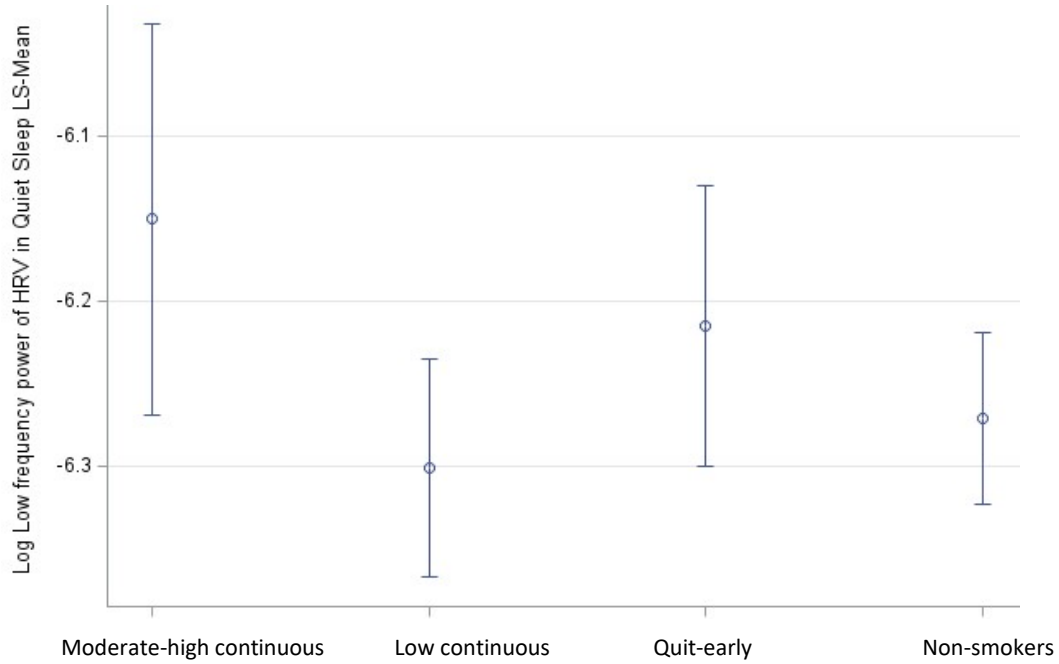
Supplemental Figure S14: Marginal means of median respiratory rate for each smoking groups in quiet sleep, both study sites



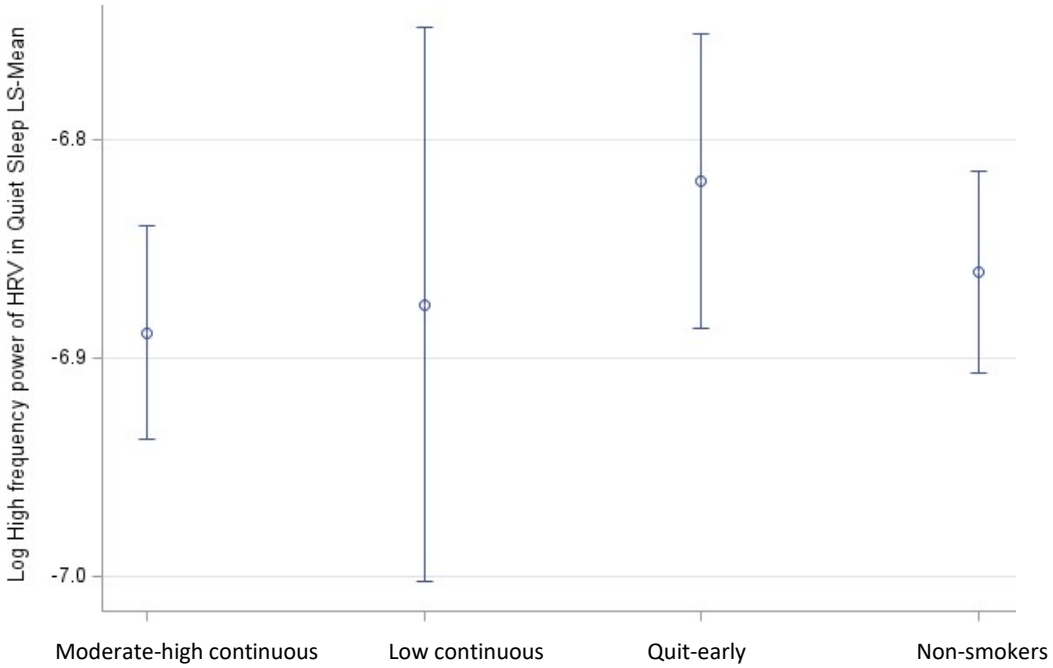
Supplemental Figure S15: Marginal means of systolic blood pressure for each smoking groups in quiet sleep, both study sites



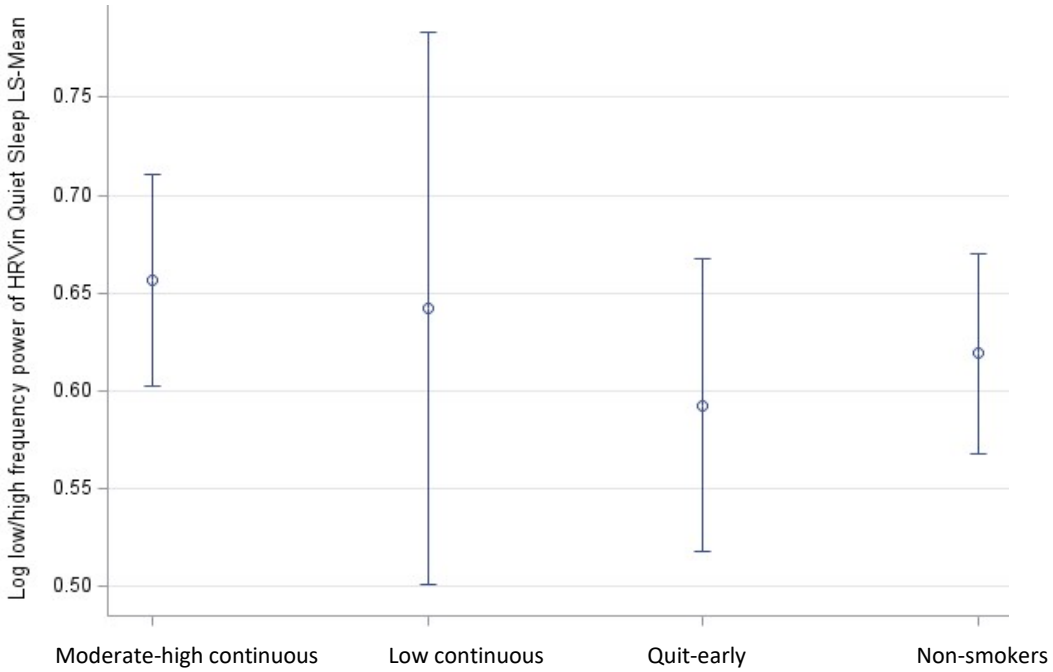
Supplemental Figure S16: Marginal means of diastolic blood pressure for each smoking groups in quiet sleep, both study sites



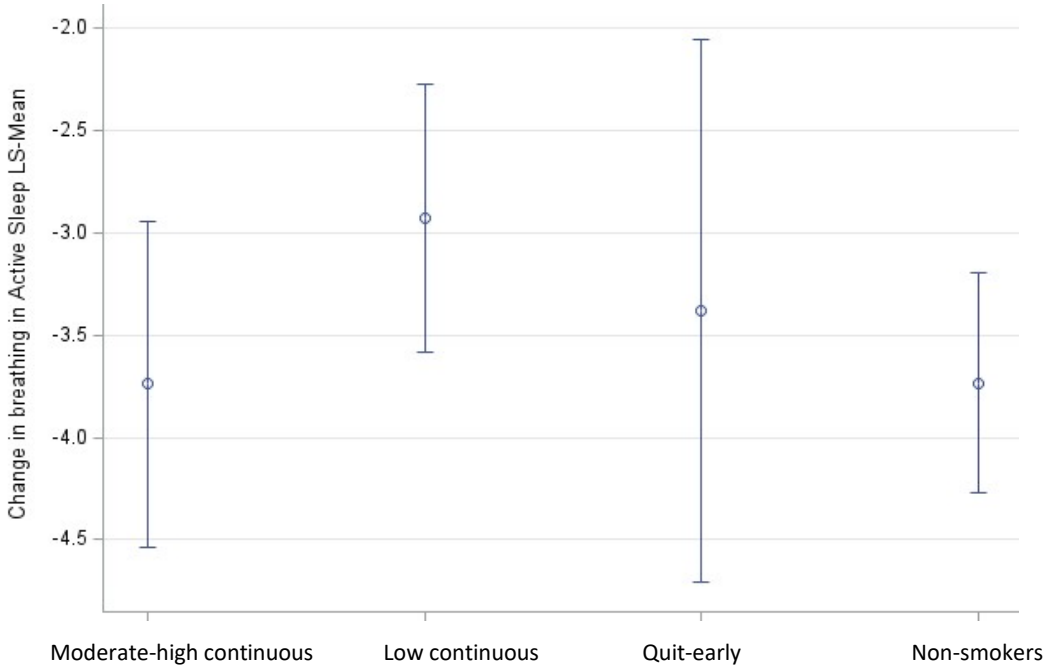
Supplemental Figure S17: Marginal means log low frequency power of HRV for each smoking groups in quiet sleep, both study sites



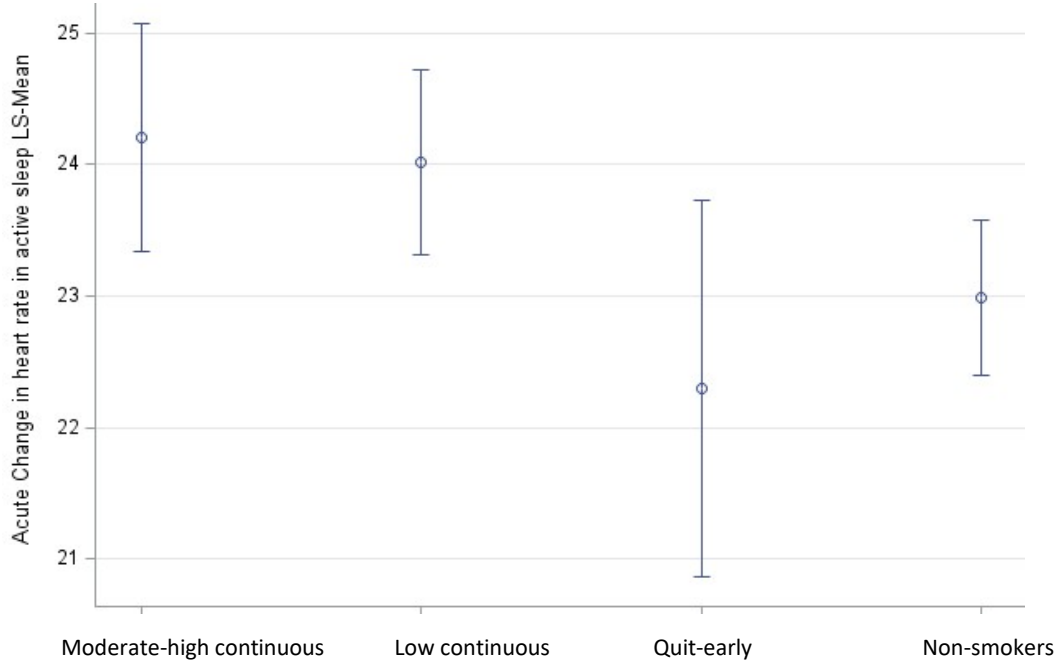
Supplemental Figure S18: Marginal means log high frequency power of HRV for each smoking groups in quiet sleep, both study sites



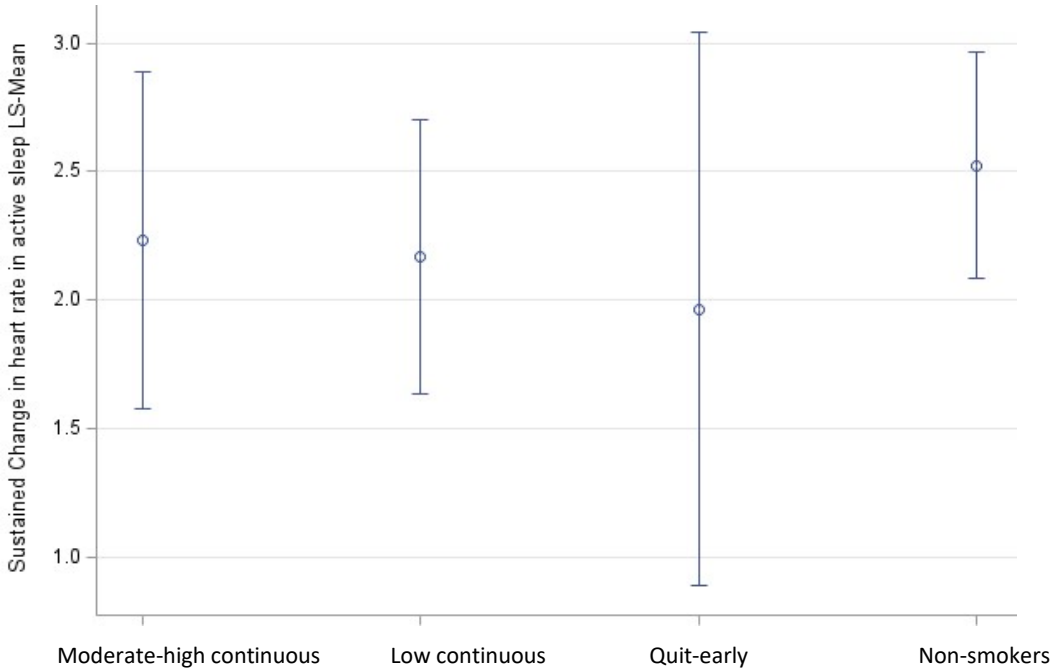
Supplemental Figure S19: Marginal means of ratio of low-lo-high frequency power of HRV for each smoking groups in quiet sleep, both study si



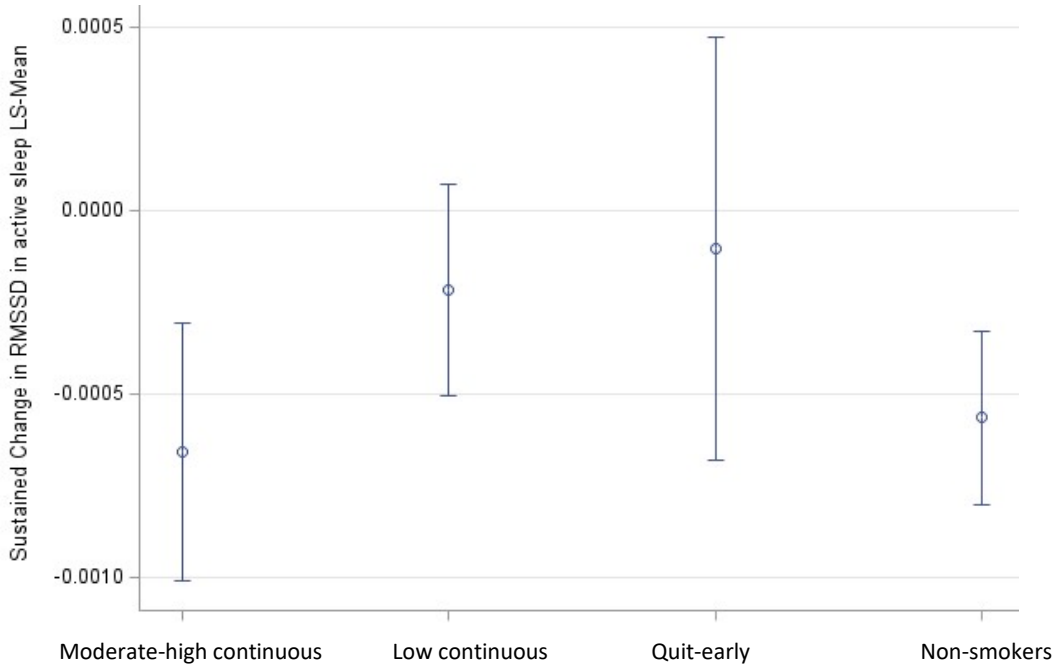
Supplemental Figure S20: Marginal means of change in breathing rate after tilt for each smoking groups in active sleep, both study sites



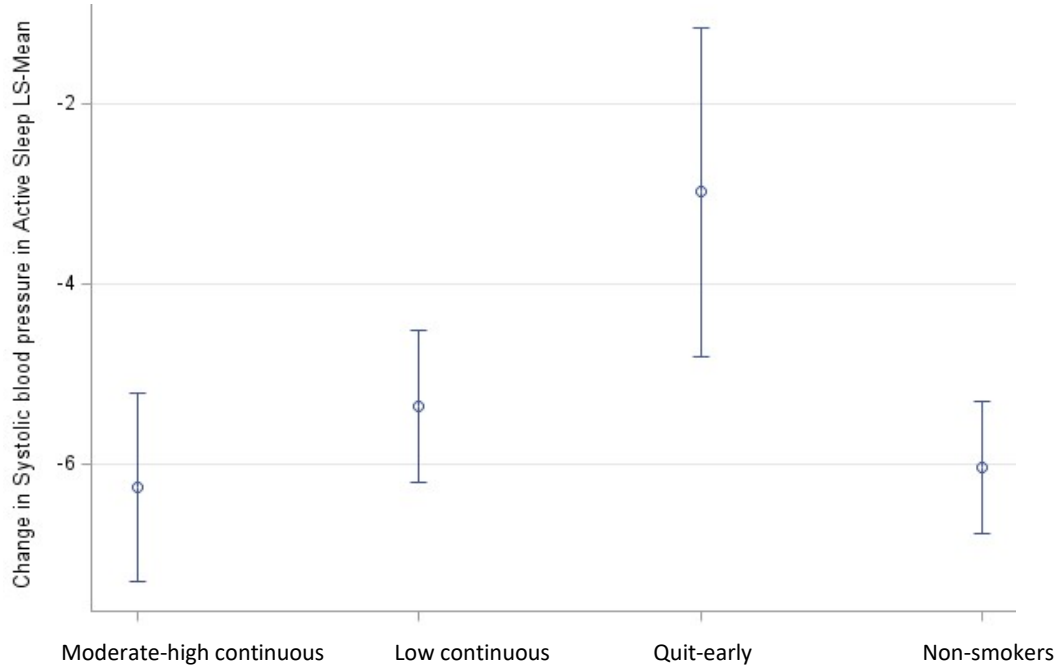
Supplemental Figure S21: Marginal means of acute change in heart rate after tilt for each smoking groups in active sleep, both study sites



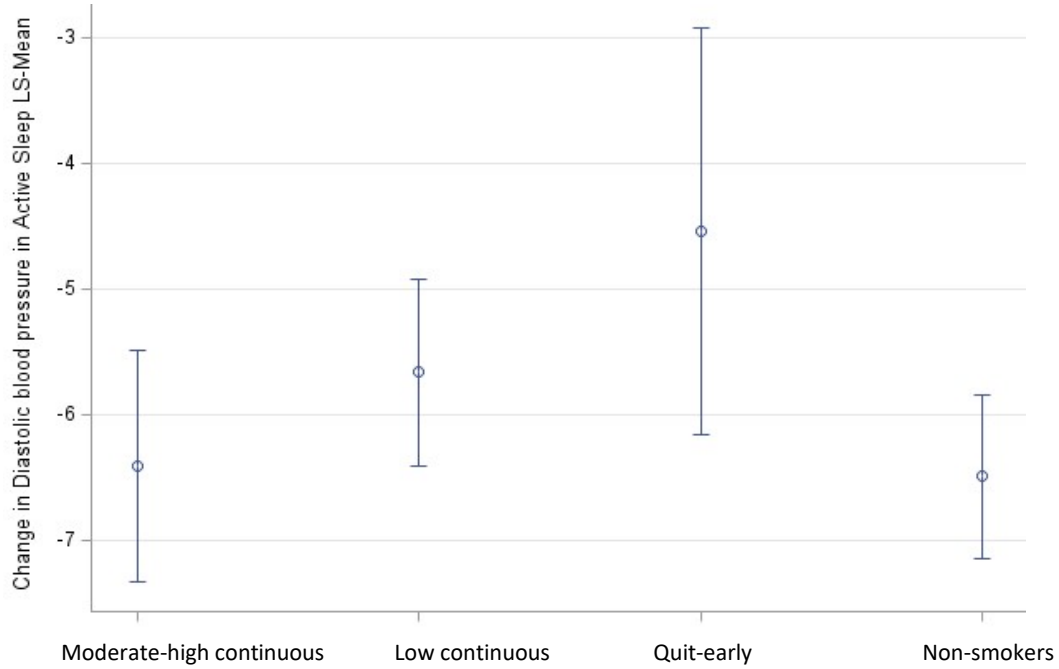
Supplemental Figure S22: Marginal means of sustained change in hear rate after tilt for each smoking groups in active sleep, both study sites



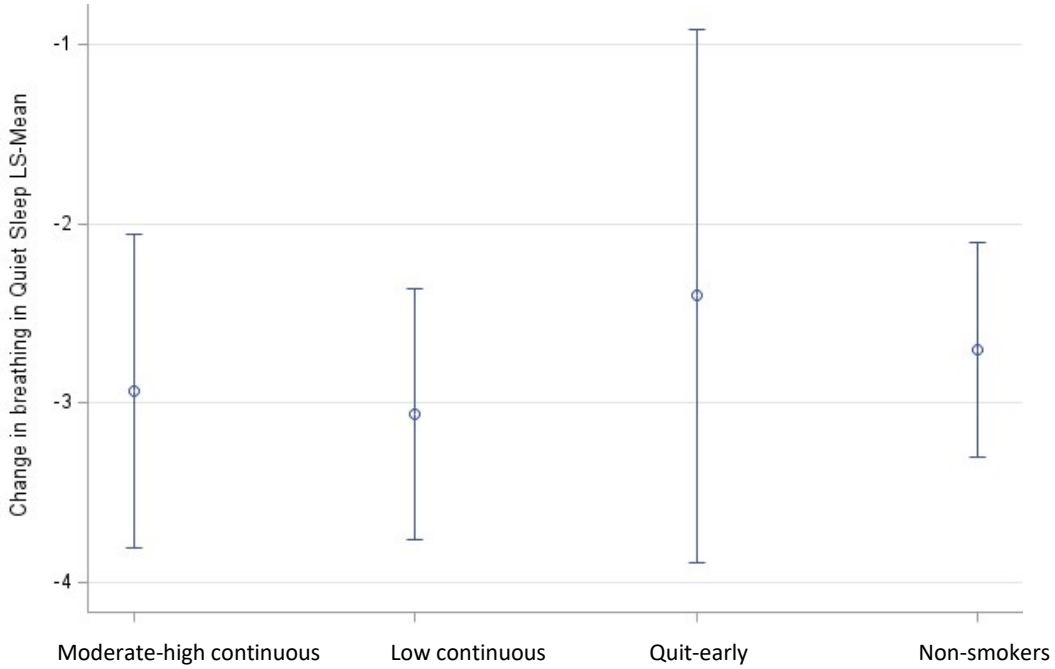
Supplemental Figure S23: Marginal means of sustained change in RMSSD after tilt for each smoking groups in active sleep, both study sites



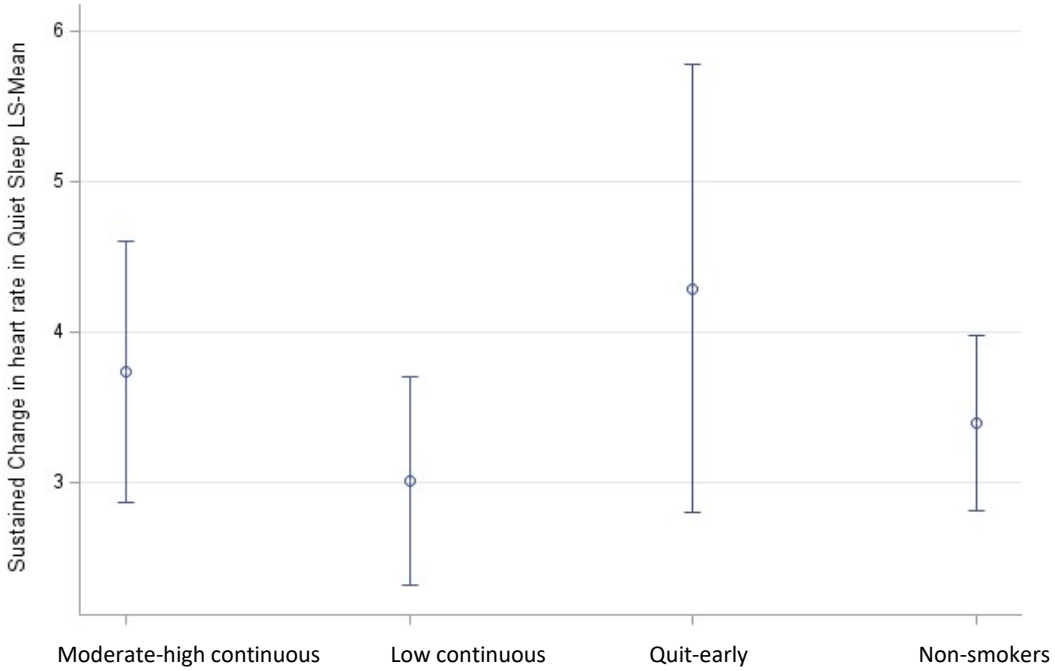
Supplemental Figure S24: Marginal means of change in systolic blood pressure after tilt for each smoking groups in active sleep, both study site



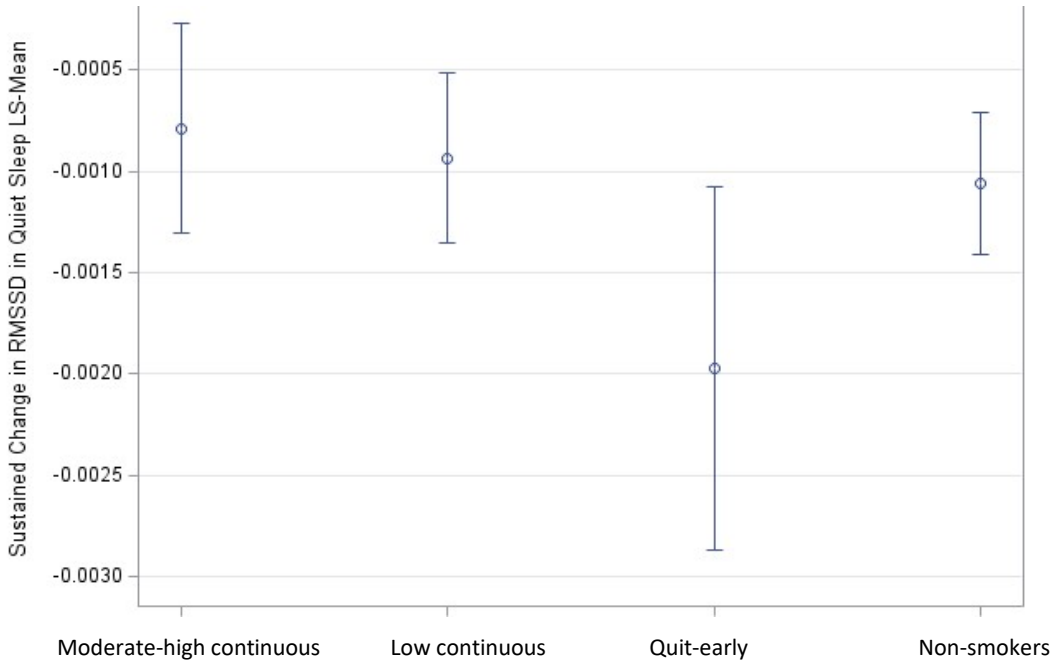
Supplemental Figure S25: Marginal means of change in diastolic blood pressure after tilt for each smoking groups in active sleep, both study sit



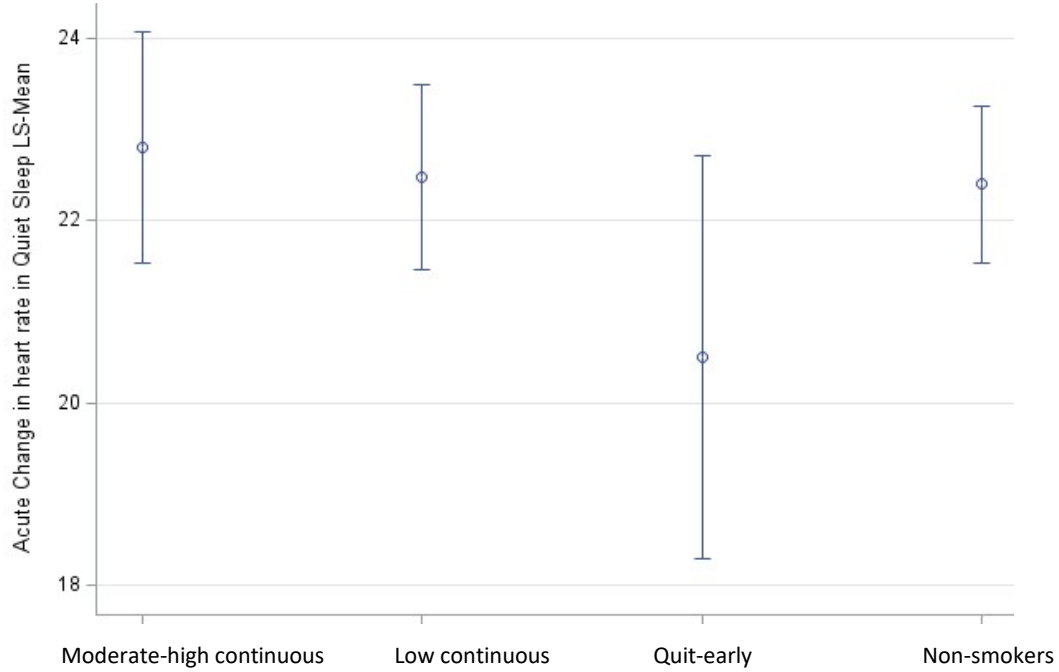
Supplemental Figure S26: Marginal means of change in breathing rate after tilt for each smoking groups in quiet sleep, both study sites



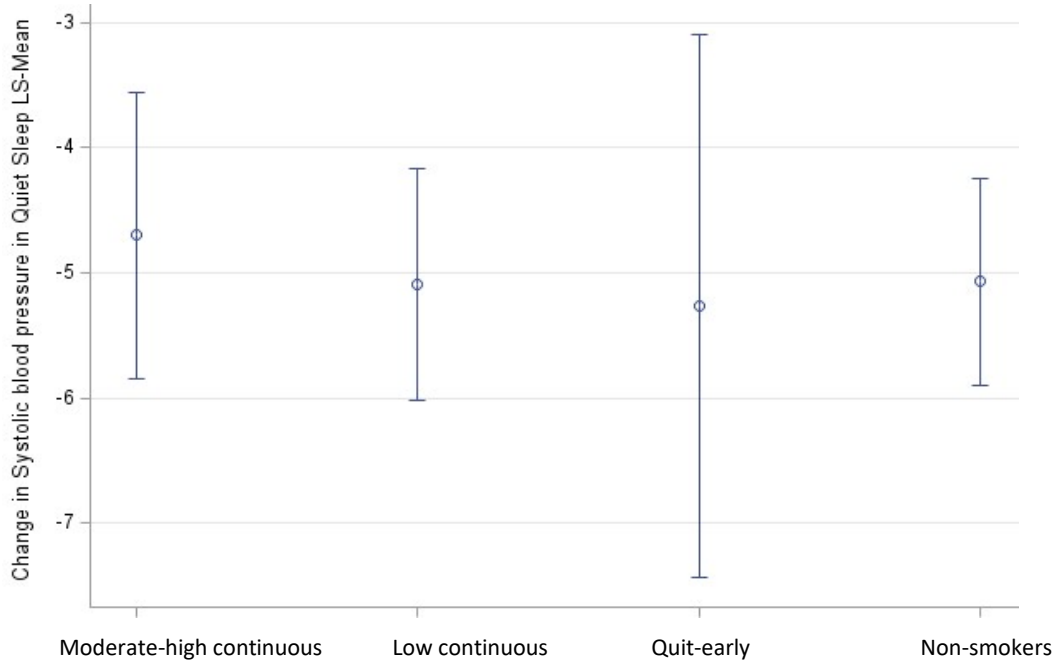
Supplemental Figure S27: Marginal means of sustained change in heart rate after tilt for each smoking groups in quiet sleep, both study sites



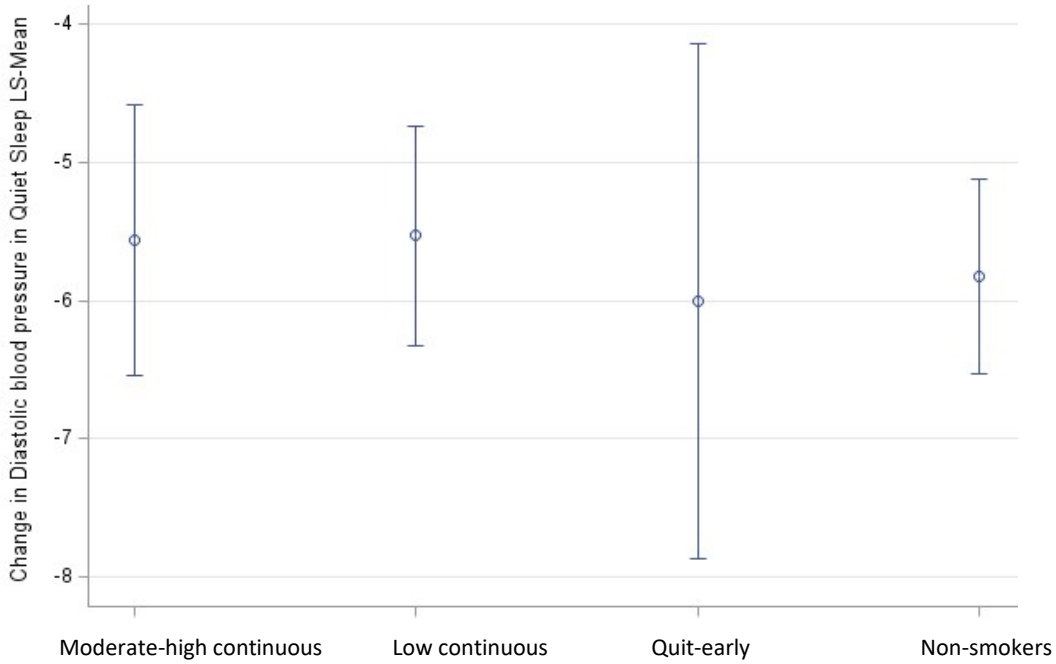
Supplemental Figure S28: Marginal means of sustained change in RMSSD after tilt for each smoking groups in quiet sleep, both study sites



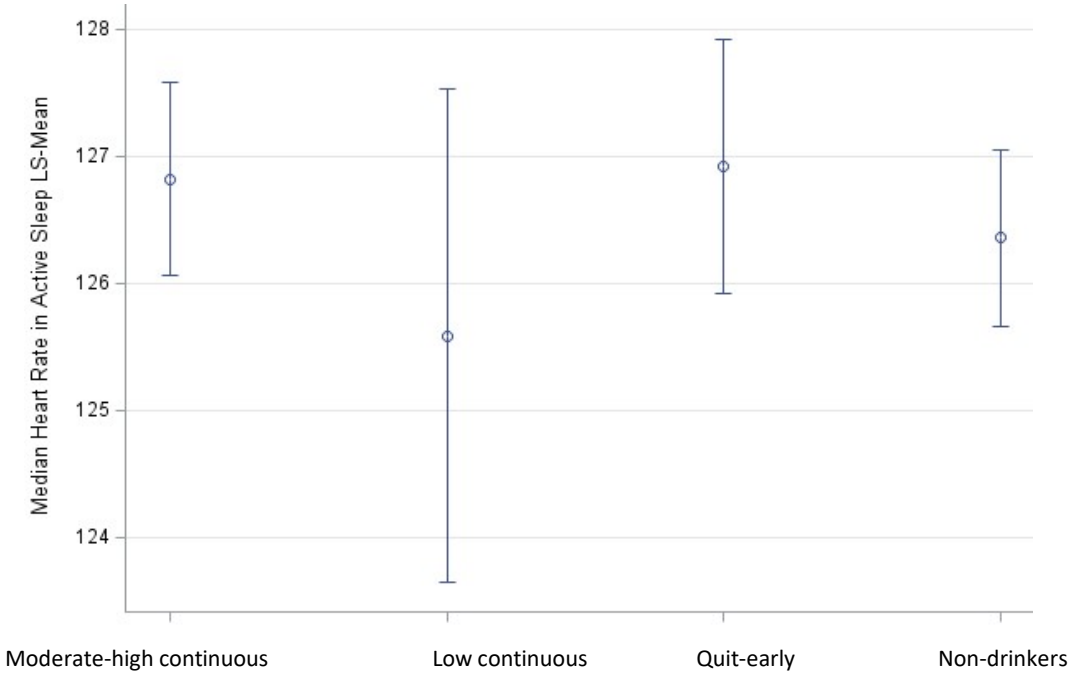
Supplemental Figure S29: Marginal means of acute change in heart rate after tilt for each smoking groups in quiet sleep, both study sites



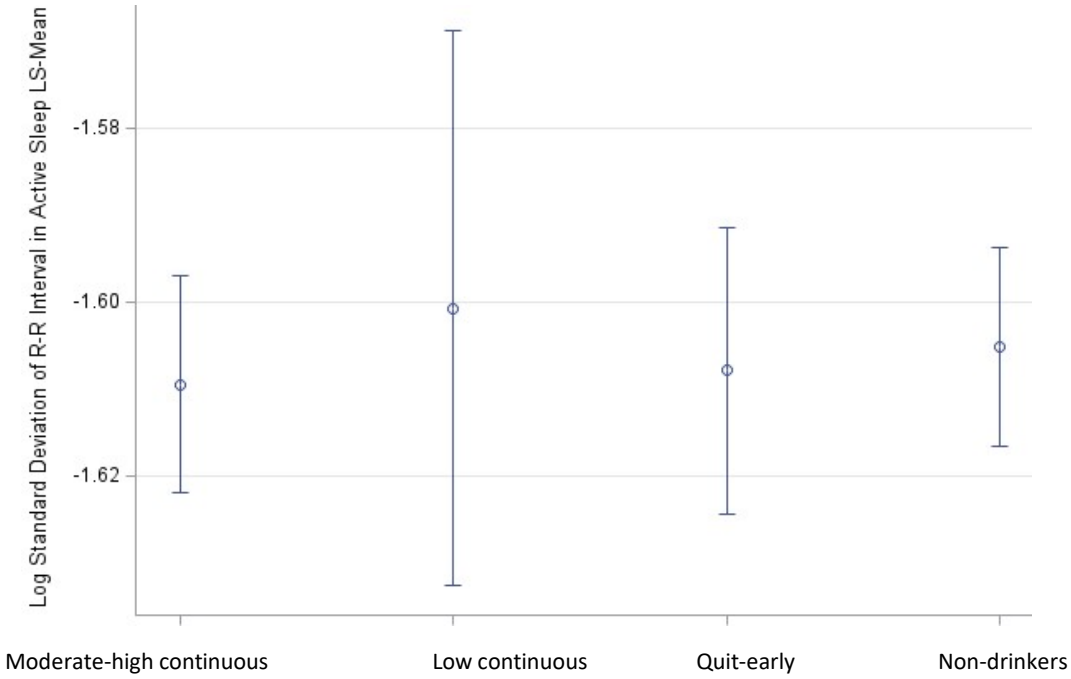
Supplemental Figure S30: Marginal means of change in systolic blood pressure after tilt for each smoking groups in quiet sleep, both study sites



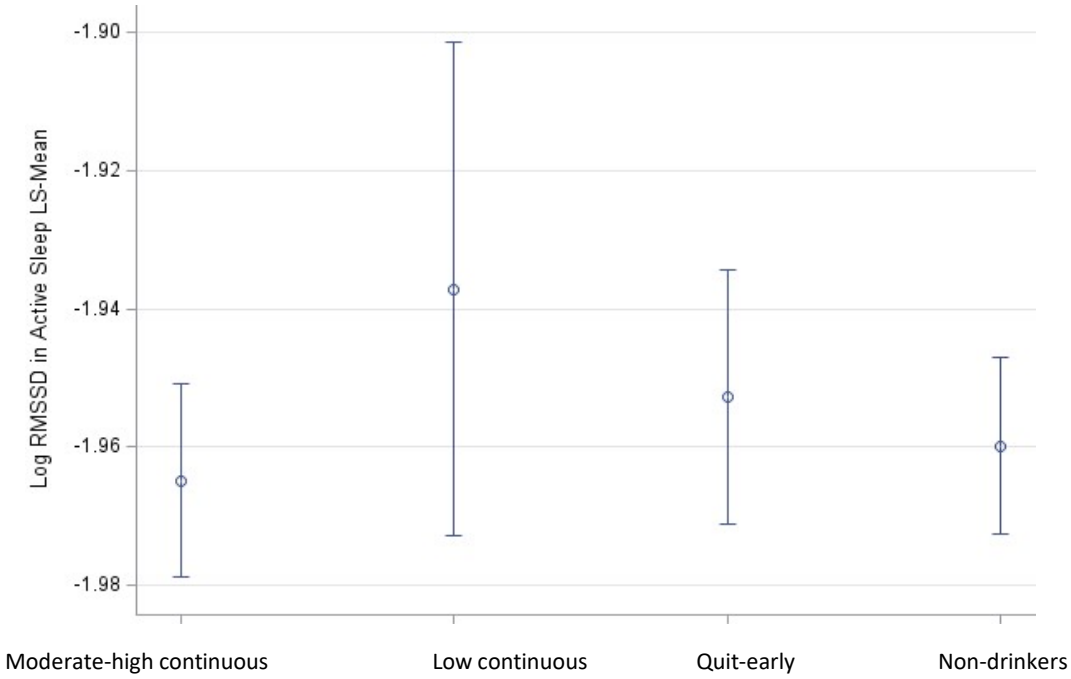
Supplemental Figure S31: Marginal means of change in diastolic blood pressure after tilt for each smoking groups in quiet sleep, both study site



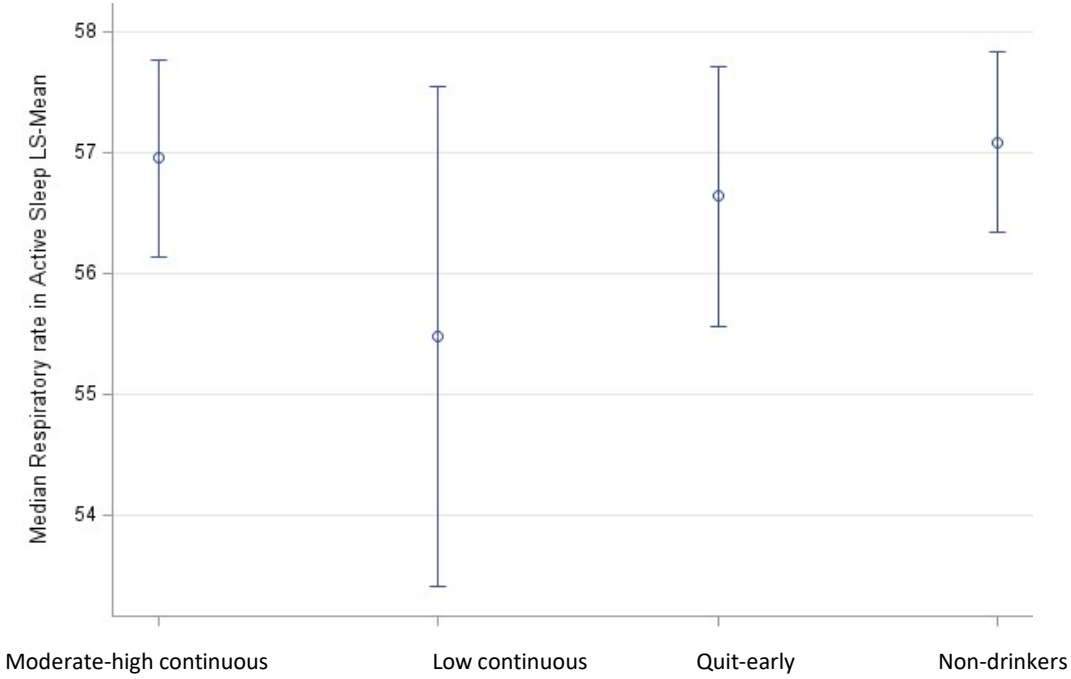
Supplemental Figure S32: Marginal means of median heart rate for each drinking groups in active sleep, both study sites



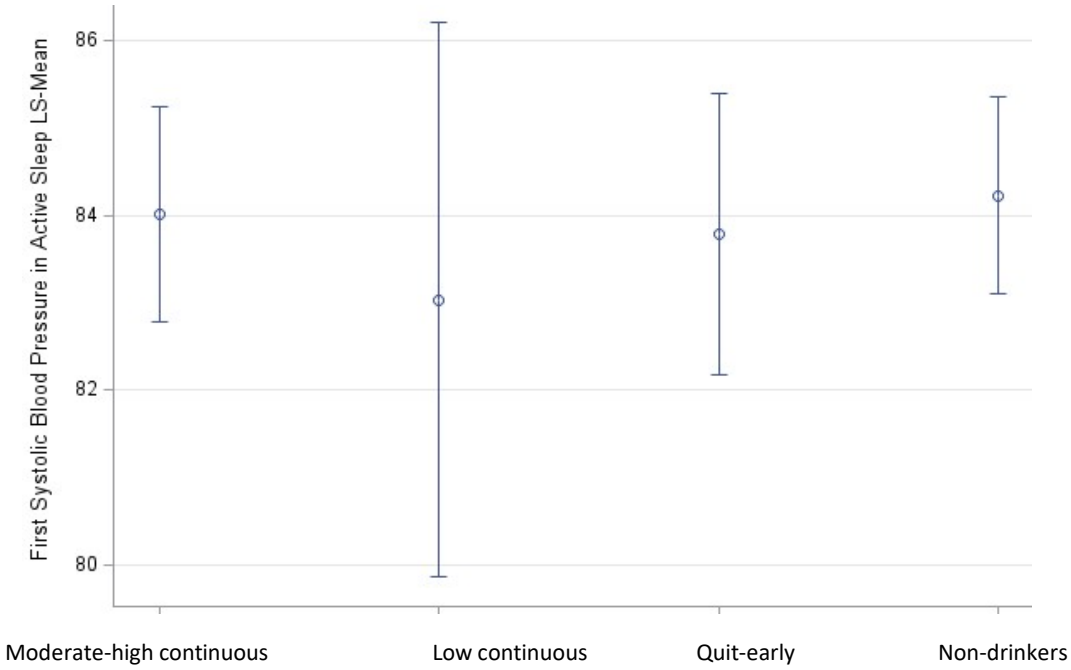
Supplemental Figure S33: Marginal means $\log_{10}$SD-RRi for each drinking groups in active sleep, both study sites



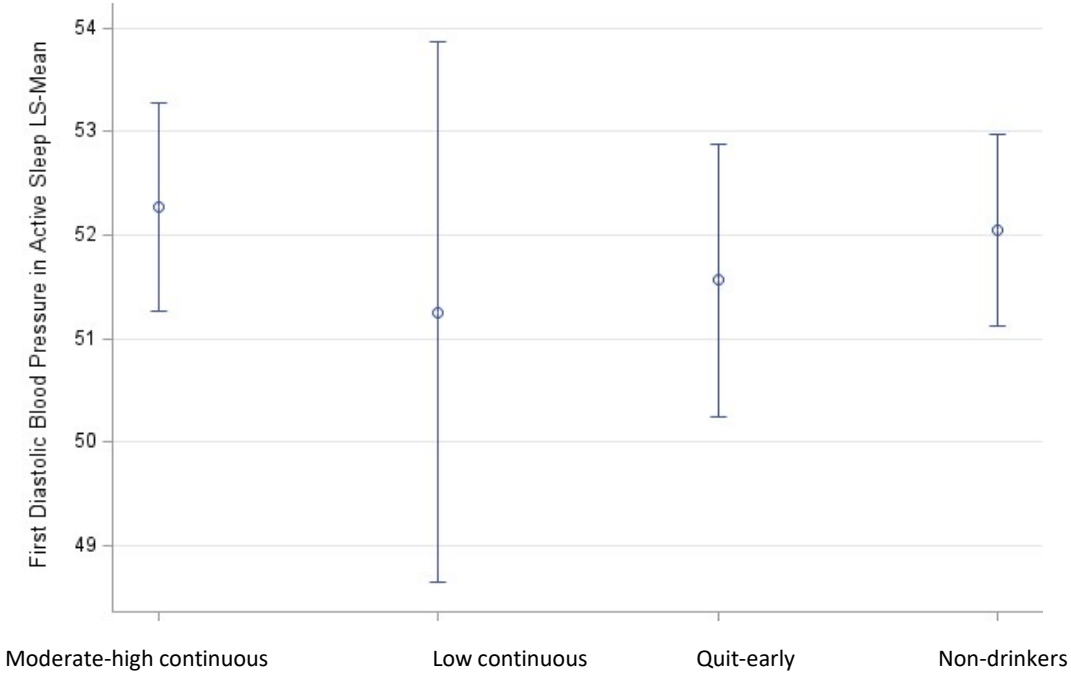
Supplemental Figure S34: Marginal means of Log RMSSD for each drinking groups in active sleep, both study sites



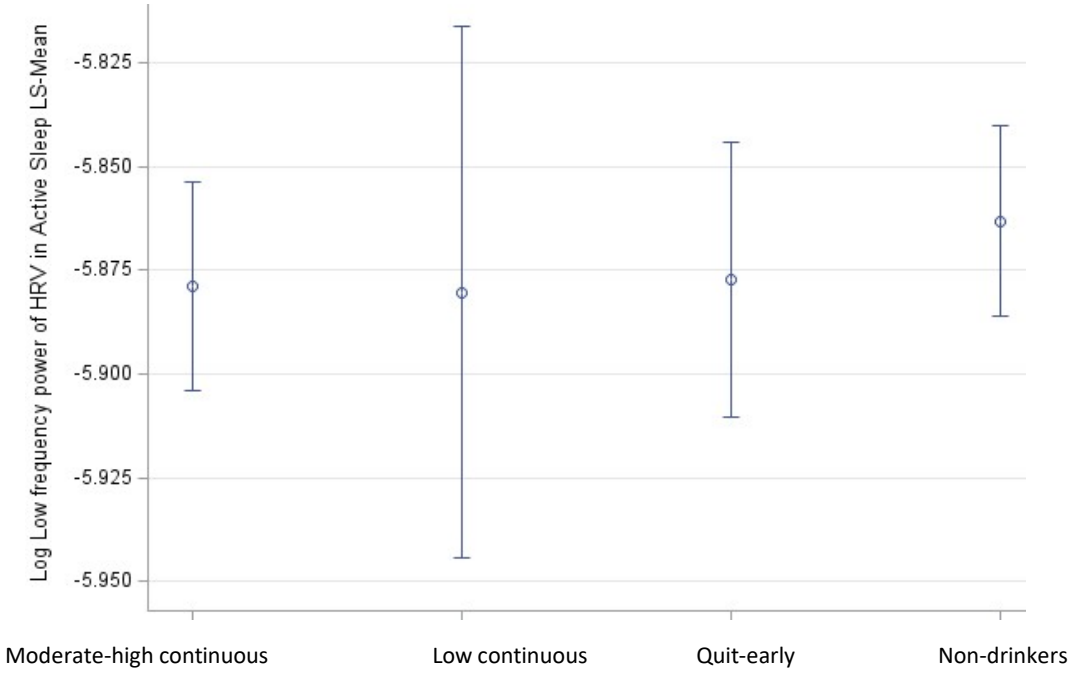
Supplemental Figure S35: Marginal means of median respiratory rate for each drinking groups in active sleep, both study sites



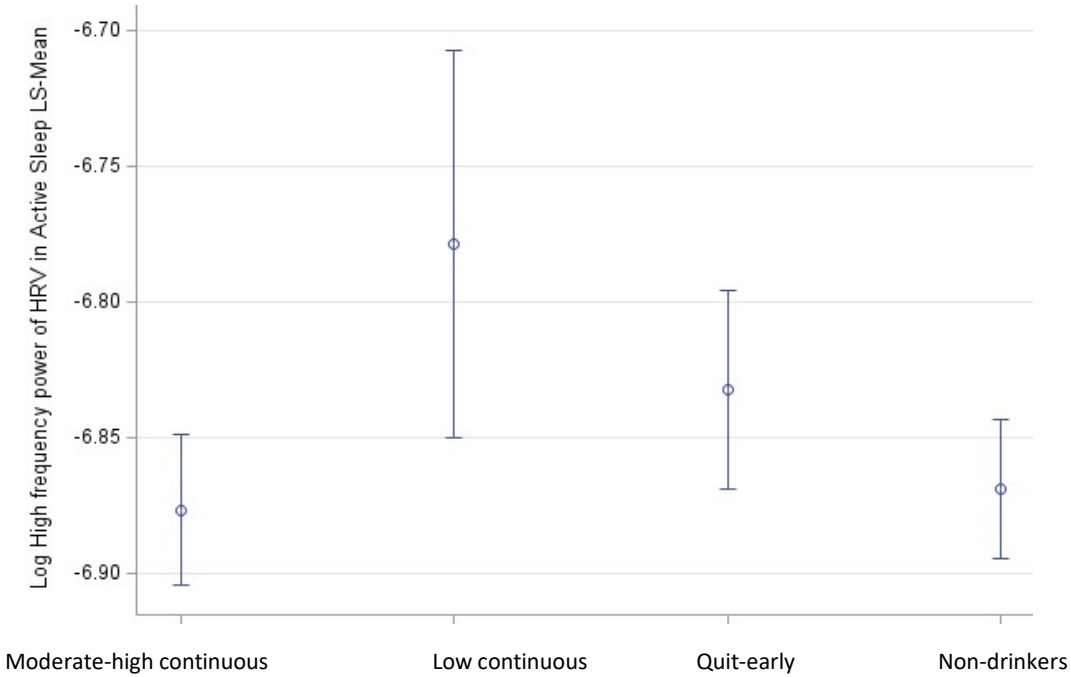
Supplemental Figure S36: Marginal means of systolic blood pressure for each drinking groups in active sleep, both study sites



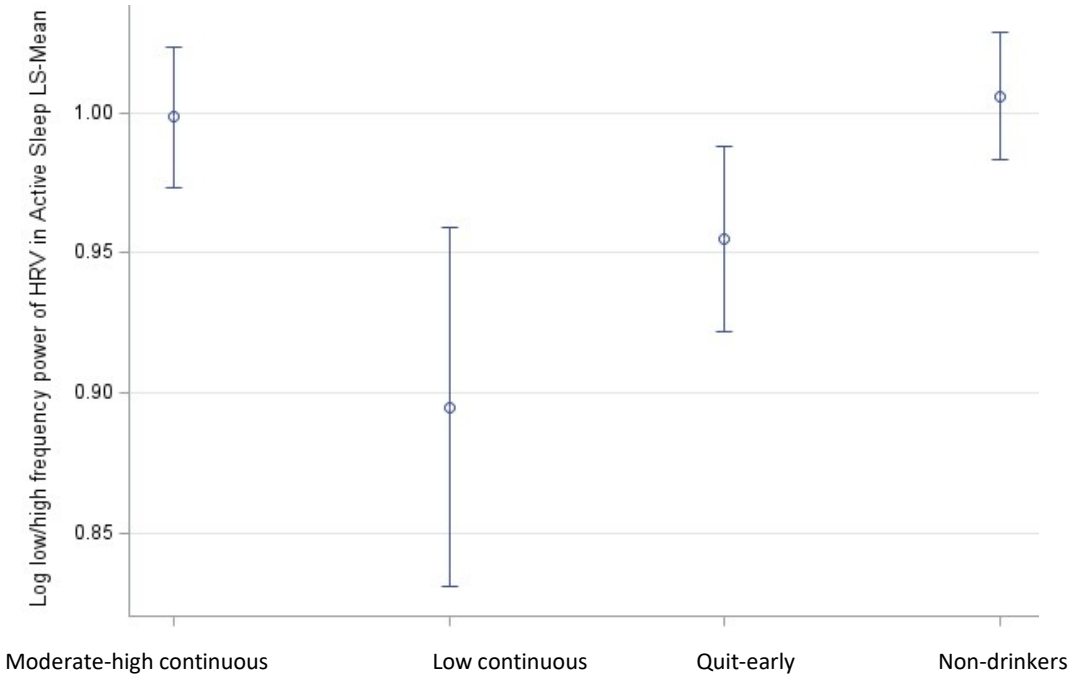
Supplemental Figure S37: Marginal means of diastolic blood pressure for each drinking groups in active sleep, both study sites



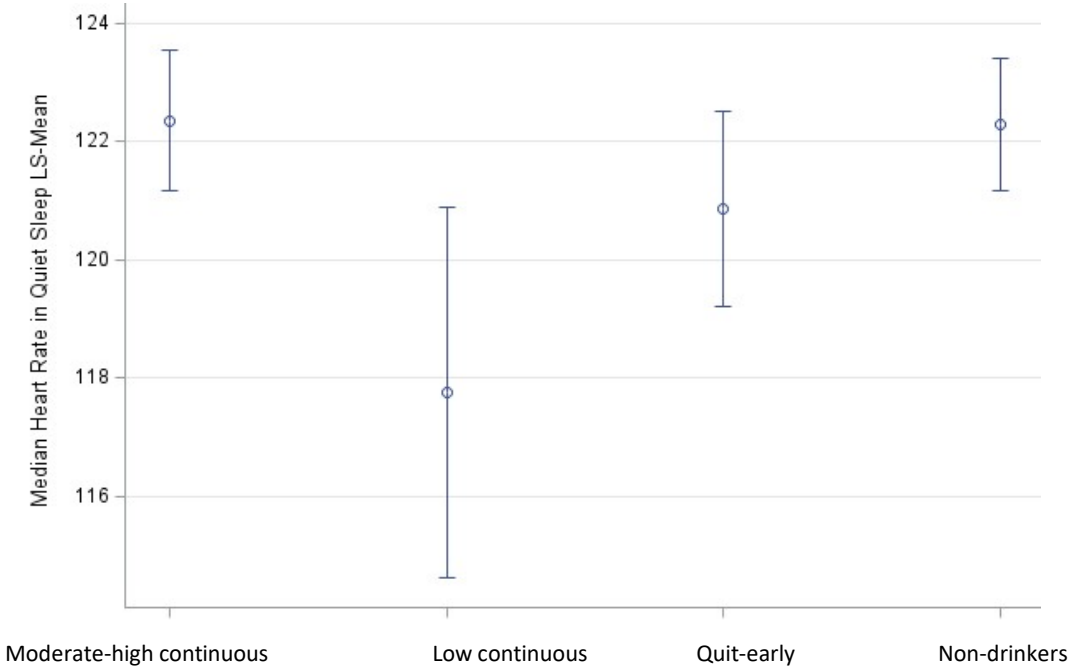
Supplemental Figure S38: Marginal means log low frequency power of HRV for each drinking groups in active sleep, both study sites



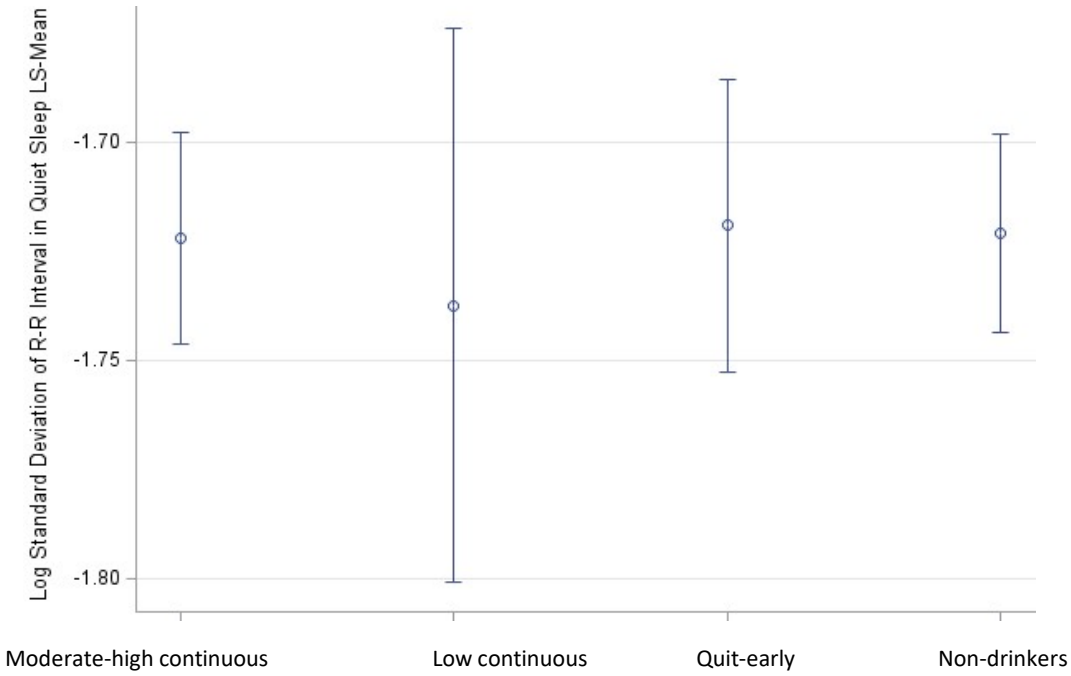
Supplemental Figure S39: Marginal means log high frequency power of HRV for each drinking groups in active sleep, both study sites



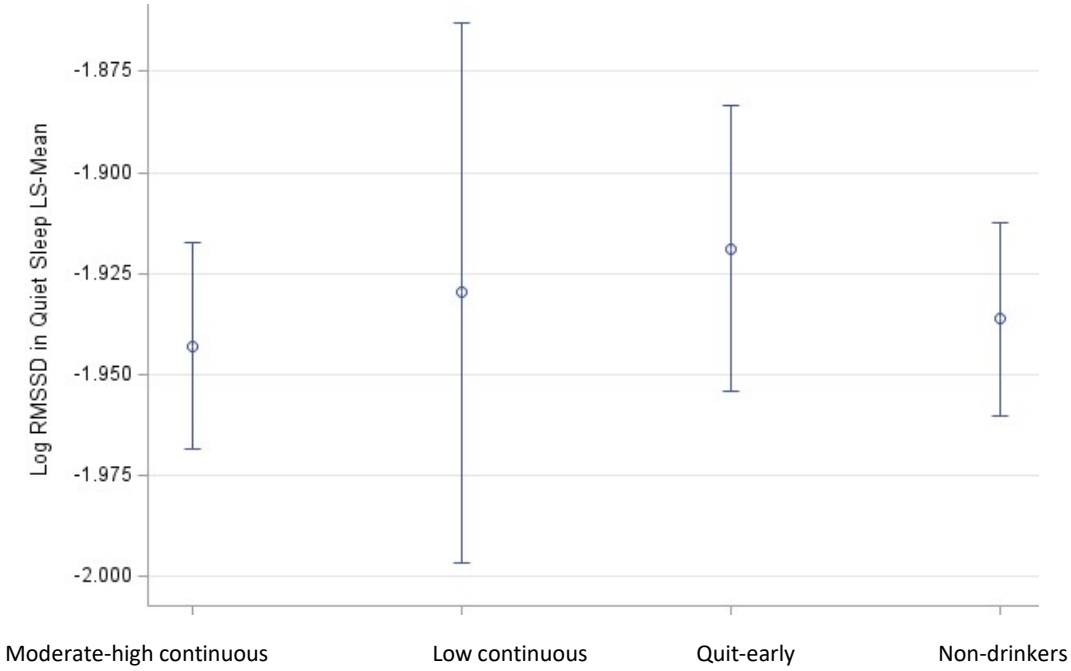
Supplemental Figure S40: Marginal means of ratio of low to high frequency power of HRV for each drinking groups in active sleep, both study sites



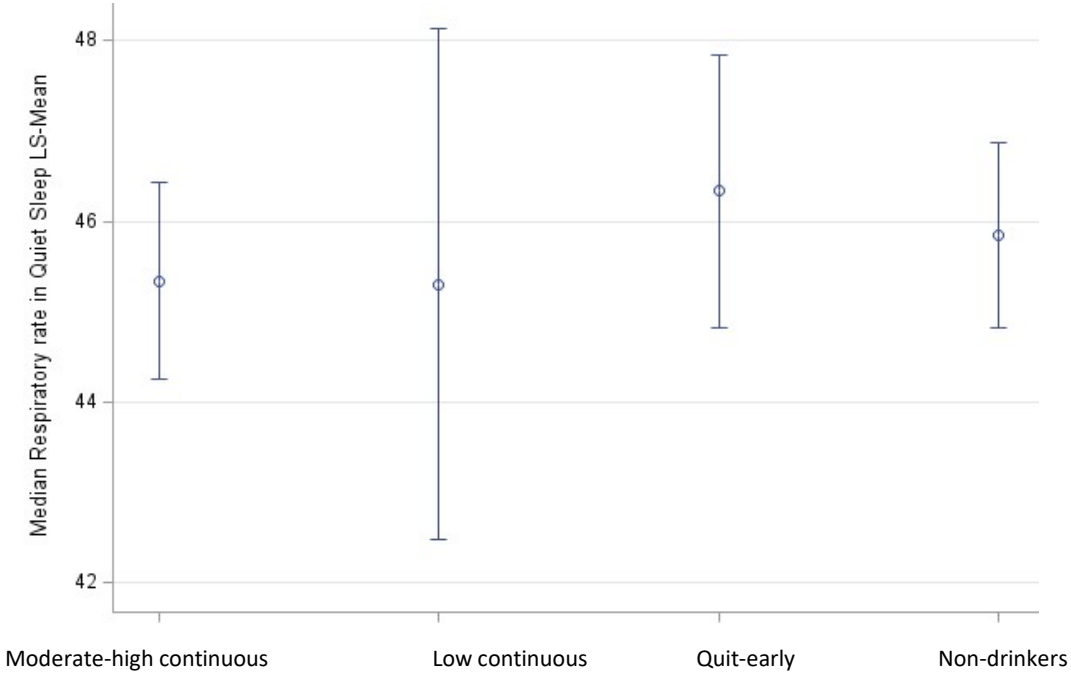
Supplemental Figure S41: Marginal means of median heart rate for each drinking groups in quiet sleep, both study site



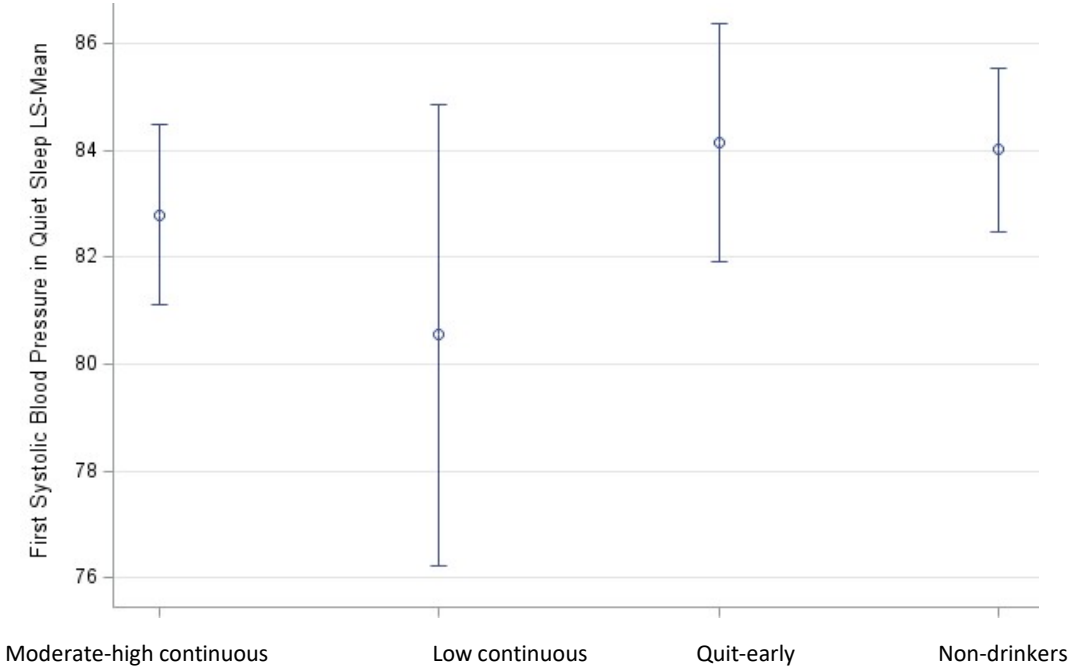
Supplemental Figure S42: Marginal means $\log_{10}$SD-RRi for each drinking groups in quiet sleep, both study sites



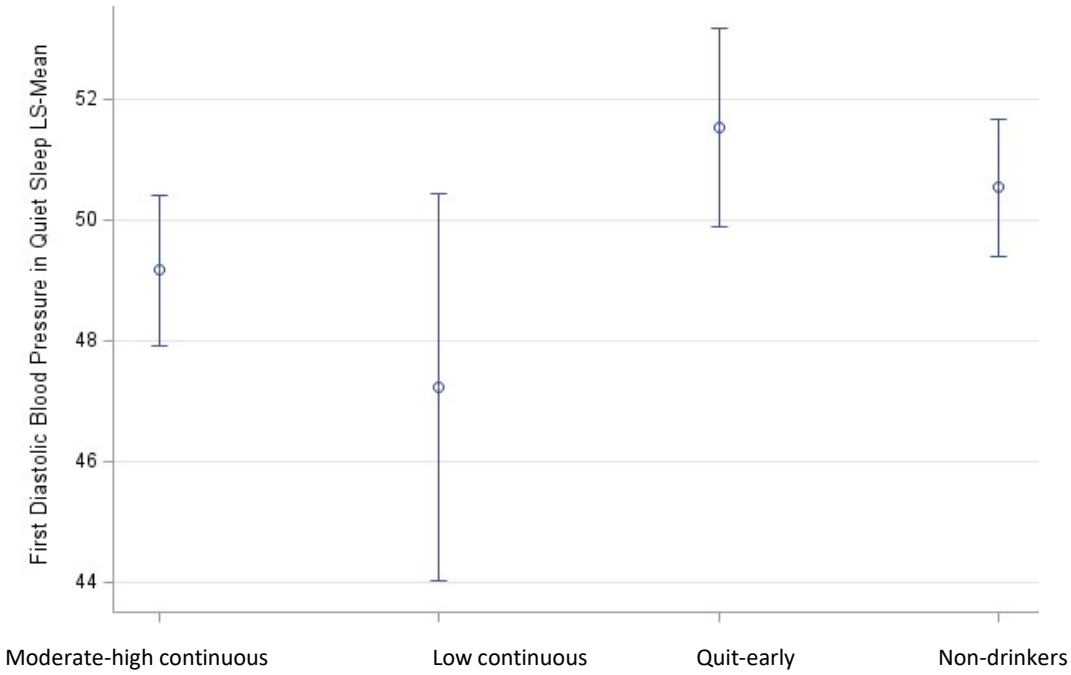
Supplemental Figure S43: Marginal means of Log RMSSD for each drinking groups in quiet sleep, both study sites



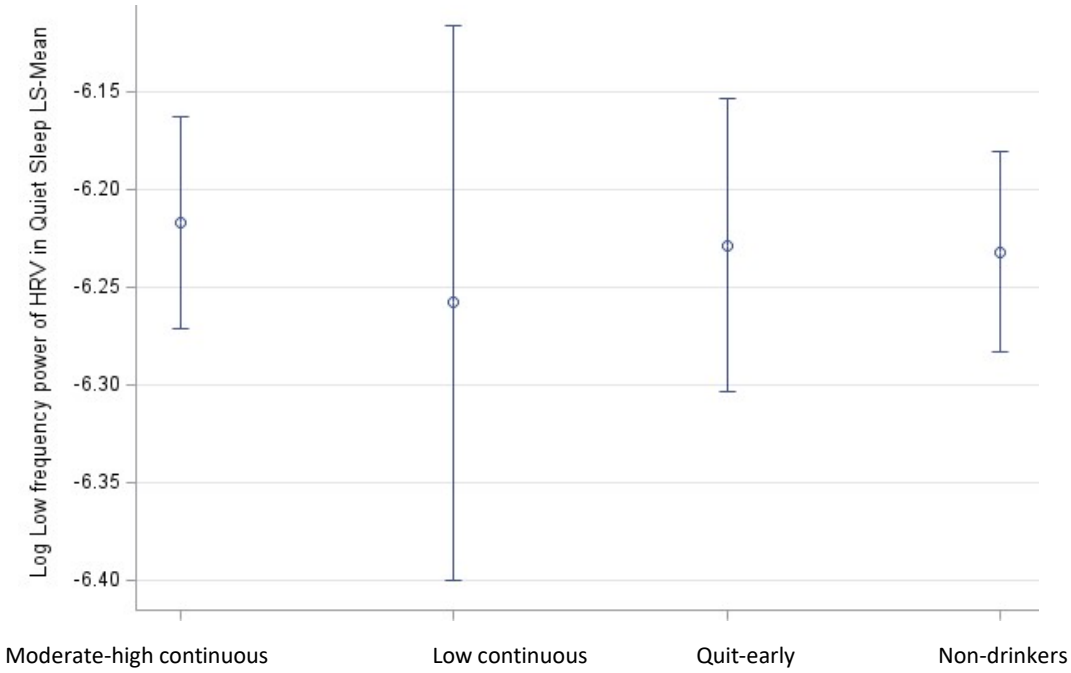
Supplemental Figure S44: Marginal means of median respiratory rate for each drinking groups in quiet sleep, both study sites



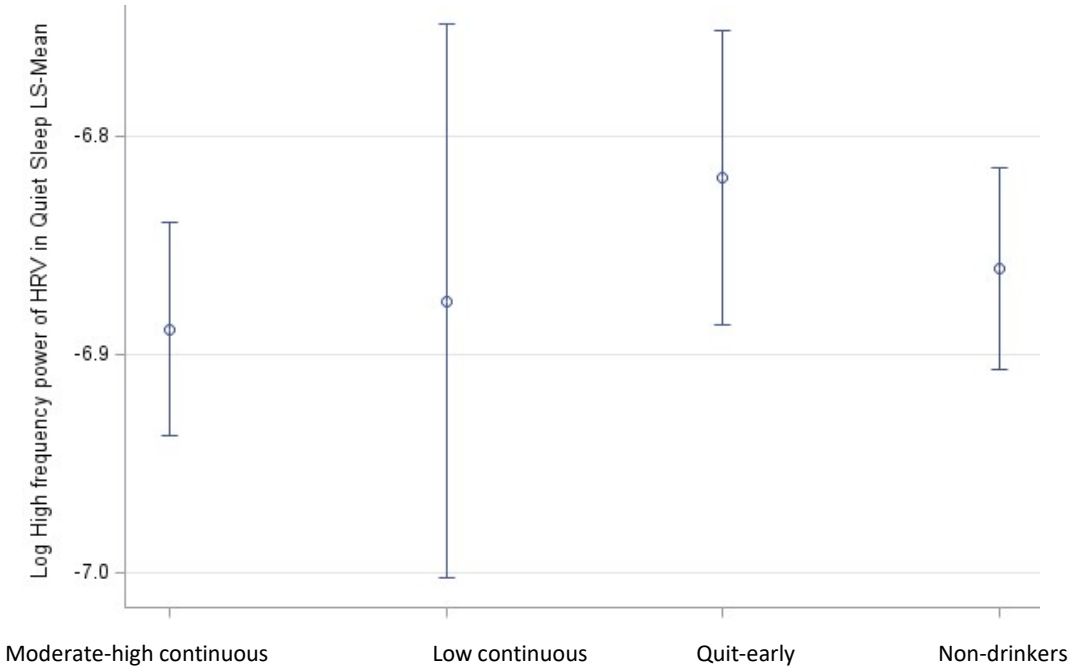
Supplemental Figure S45: Marginal means of systolic blood pressure for each drinking groups in quiet sleep, both study sites



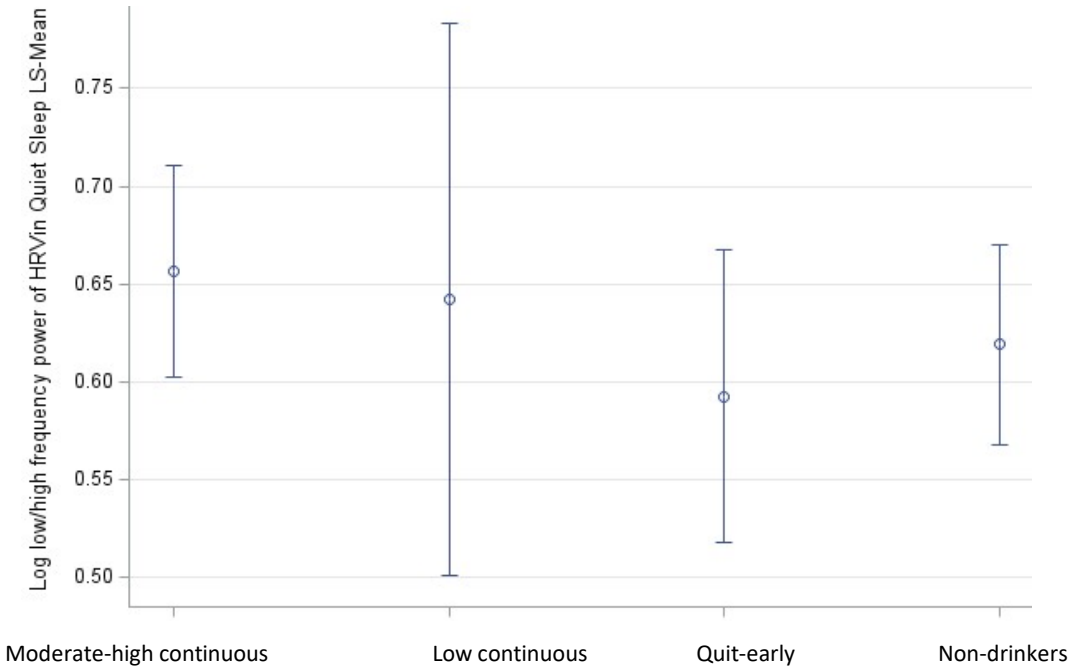
Supplemental Figure S46: Marginal means of diastolic blood pressure for each drinking groups in quiet sleep, both study sites



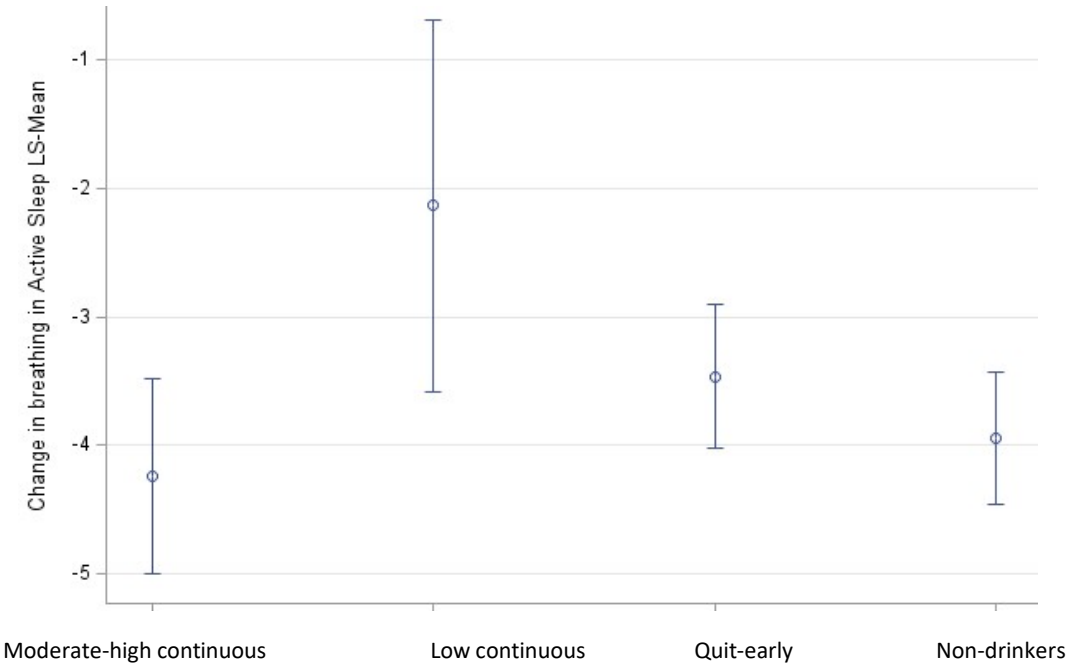
Supplemental Figure S47: Marginal means log low frequency power of HRV for each drinking groups in quiet sleep, both study sites



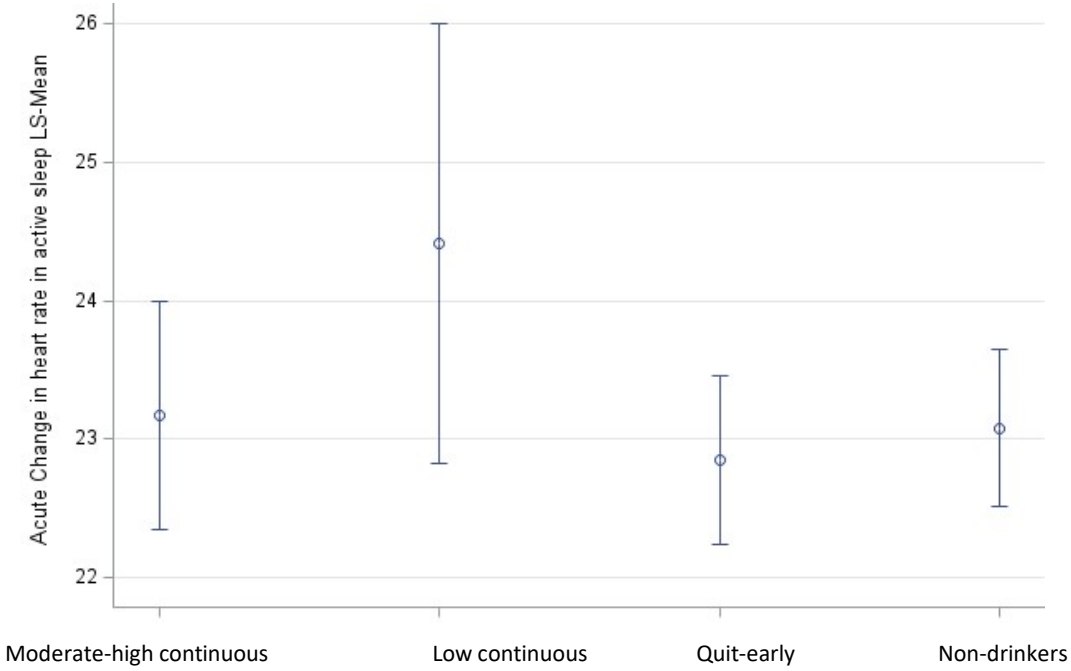
Supplemental Figure S48: Marginal means log high frequency power of HRV for each drinking groups in quiet sleep, both study sites



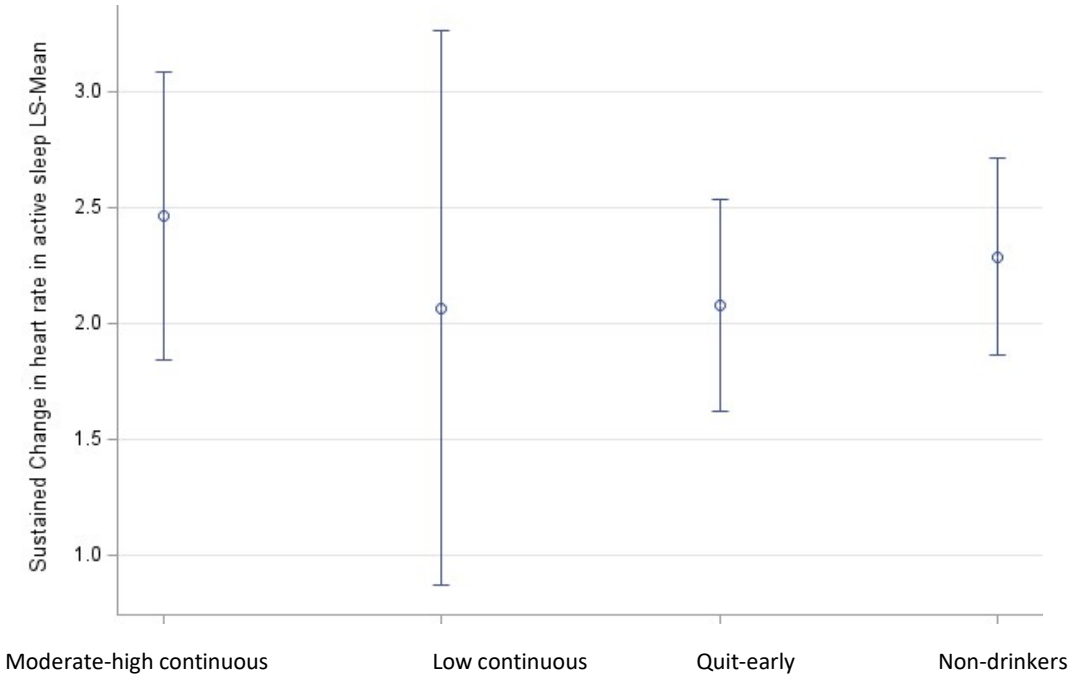
Supplemental Figure S49: Marginal means of ratio of low-lo-high frequency power of HRV for each drinking groups in quiet sleep, both study sites



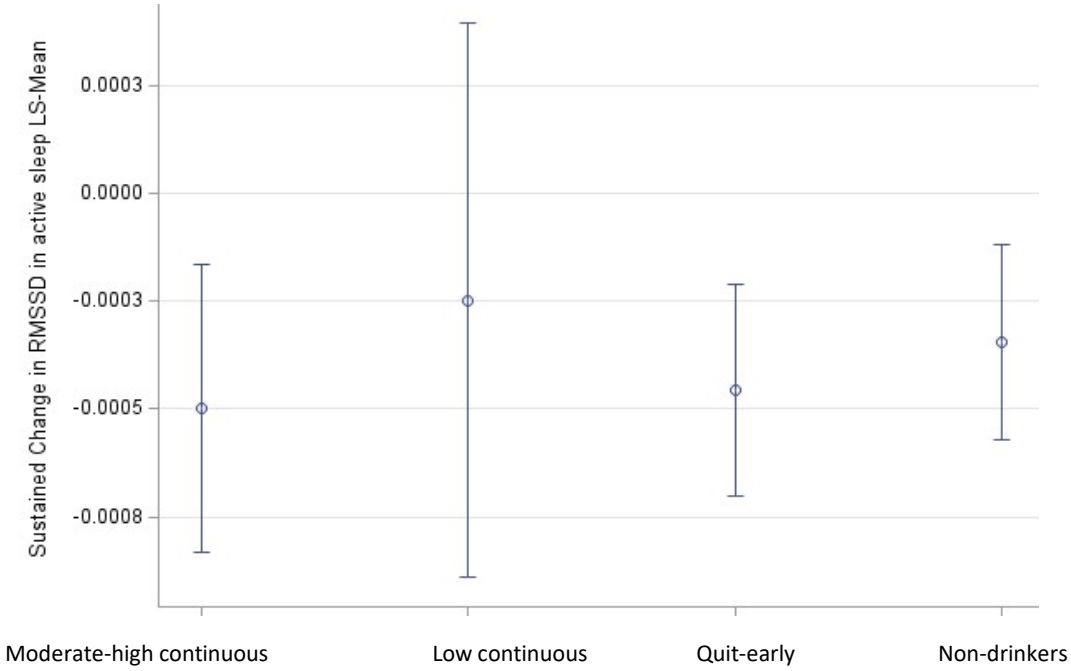
Supplemental Figure S50: Marginal means of change in breathing rate after tilt for each drinking groups in active sleep, both study sites



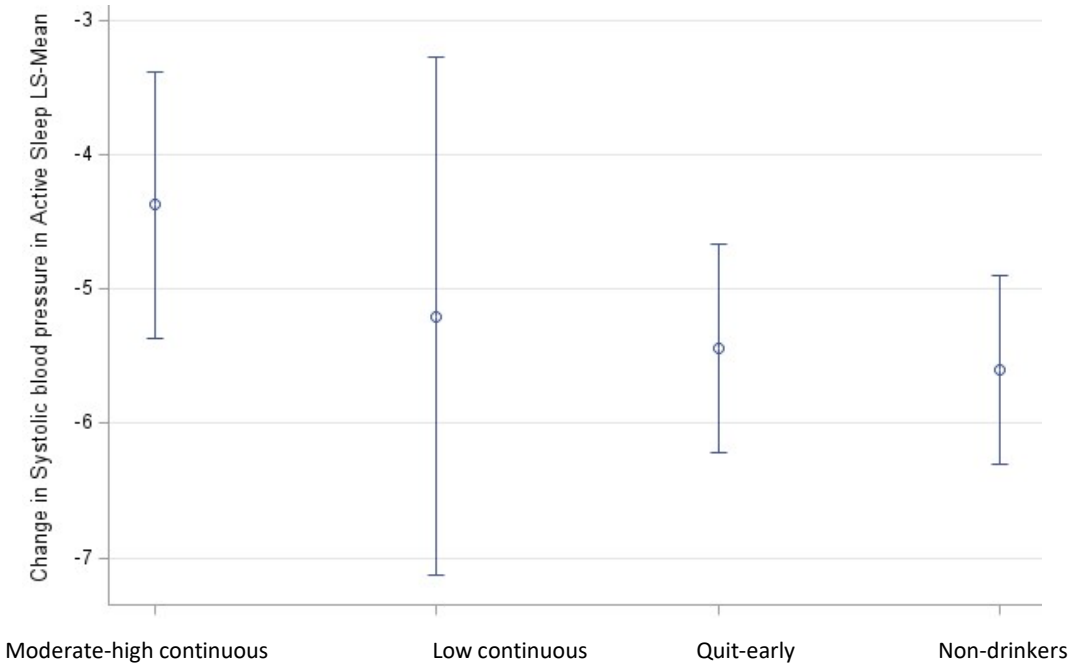
Supplemental Figure S51: Marginal means of acute change in heart rate after tilt for each drinking groups in active sleep, both study sites



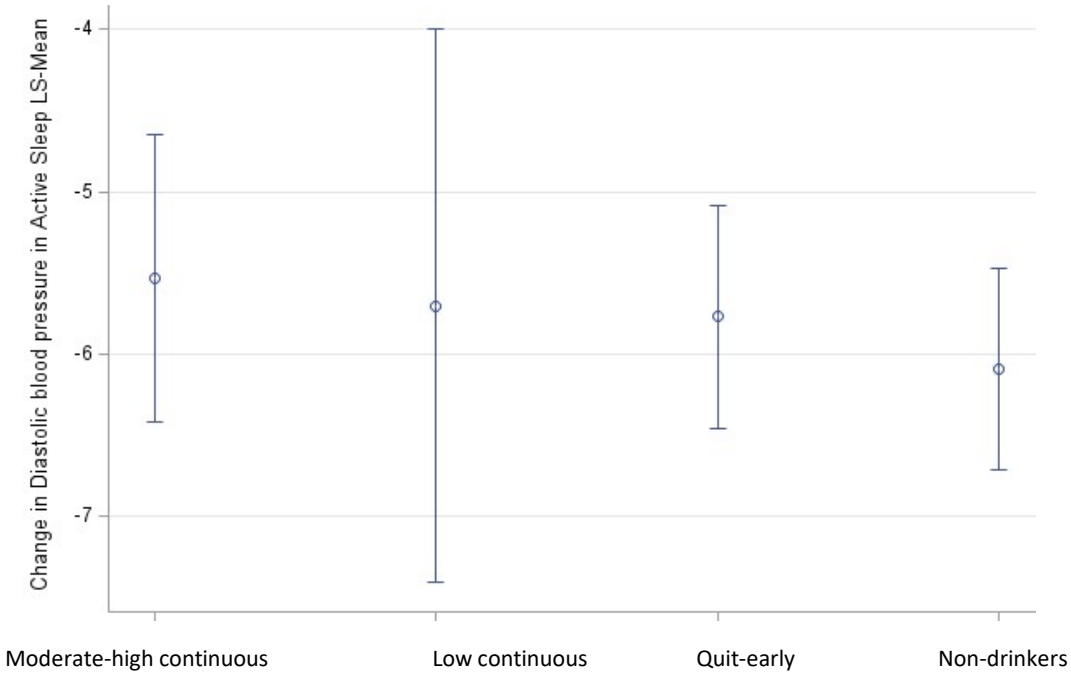
Supplemental Figure S52: Marginal means of sustained change in hear rate after tilt for each drinking groups in active sleep, both study sites



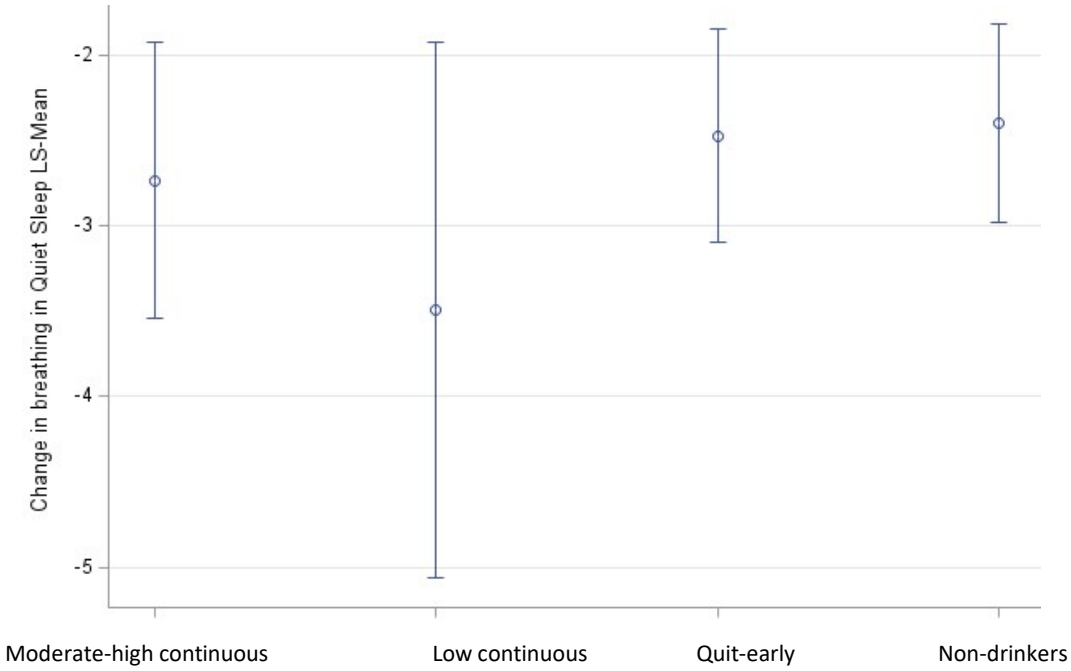
Supplemental Figure S53: Marginal means of sustained change in RMSSD after tilt for each drinking groups in active sleep, both study sites



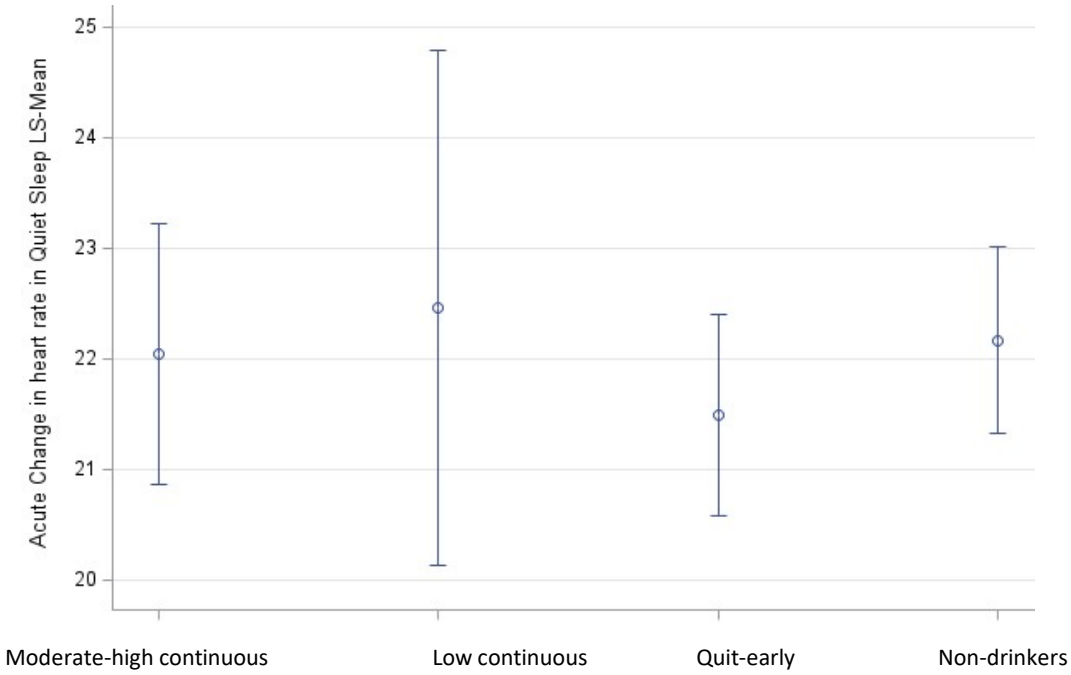
Supplemental Figure S54: Marginal means of change in systolic blood pressure after tilt for each drinking groups in active sleep, both study sites



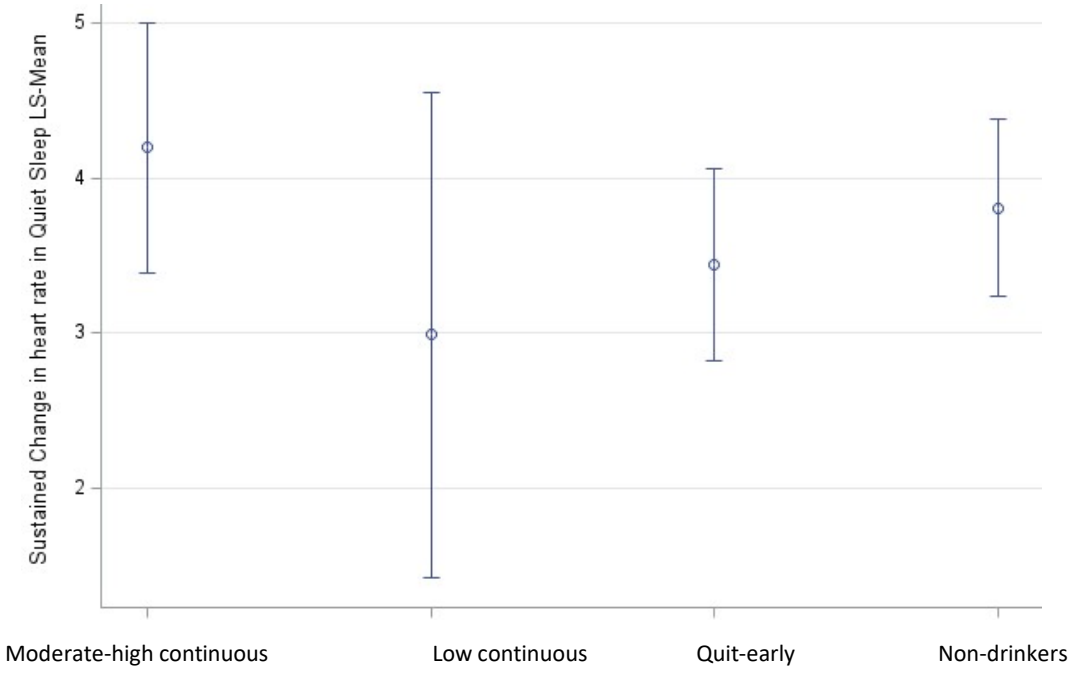
Supplemental Figure S55: Marginal means of change in diastolic blood pressure after tilt for each drinking groups in active sleep, both study sites



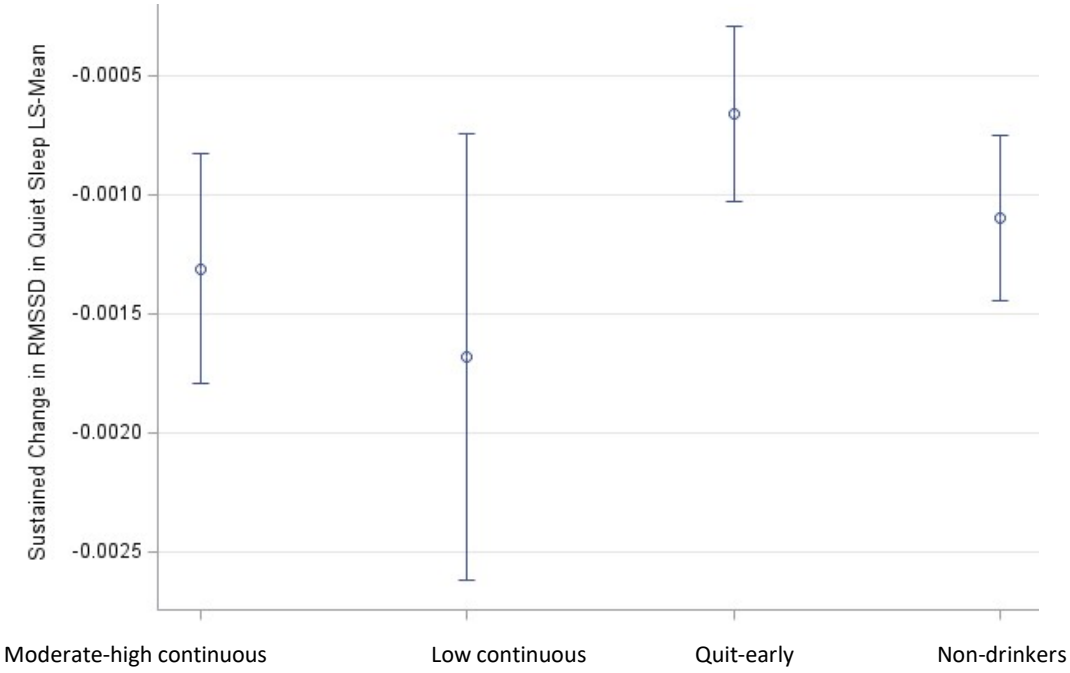
Supplemental Figure S56: Marginal means of change in breathing rate after tilt for each drinking groups in quiet sleep, both study sites



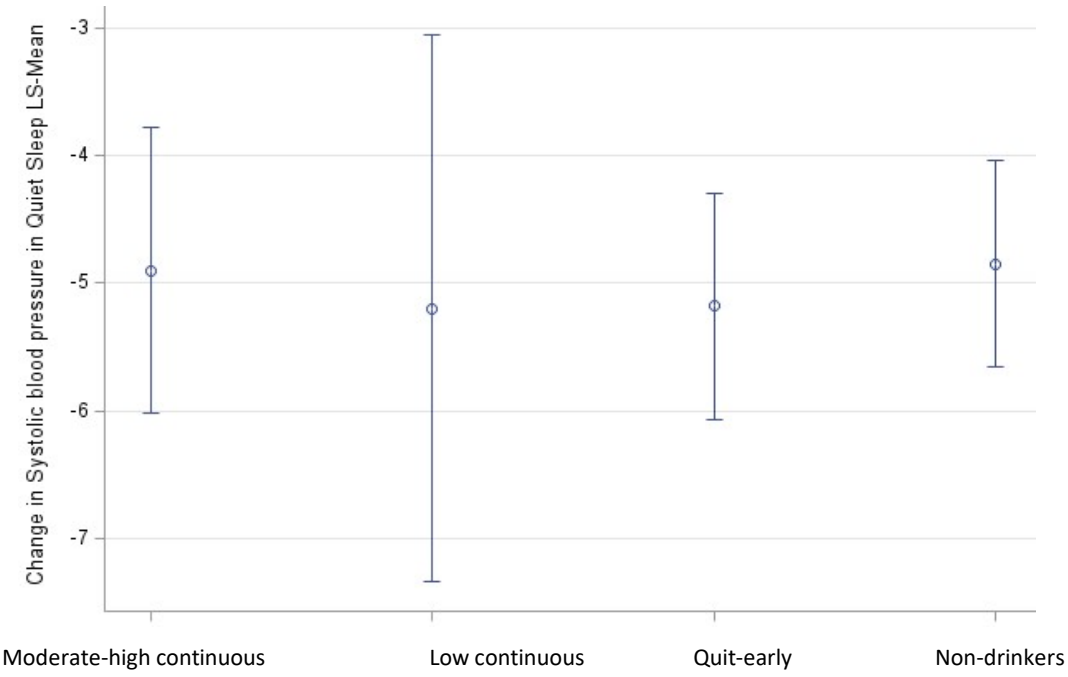
Supplemental Figure S57: Marginal means of acute change in heart rate after tilt for each drinking groups in quiet sleep, both study sites



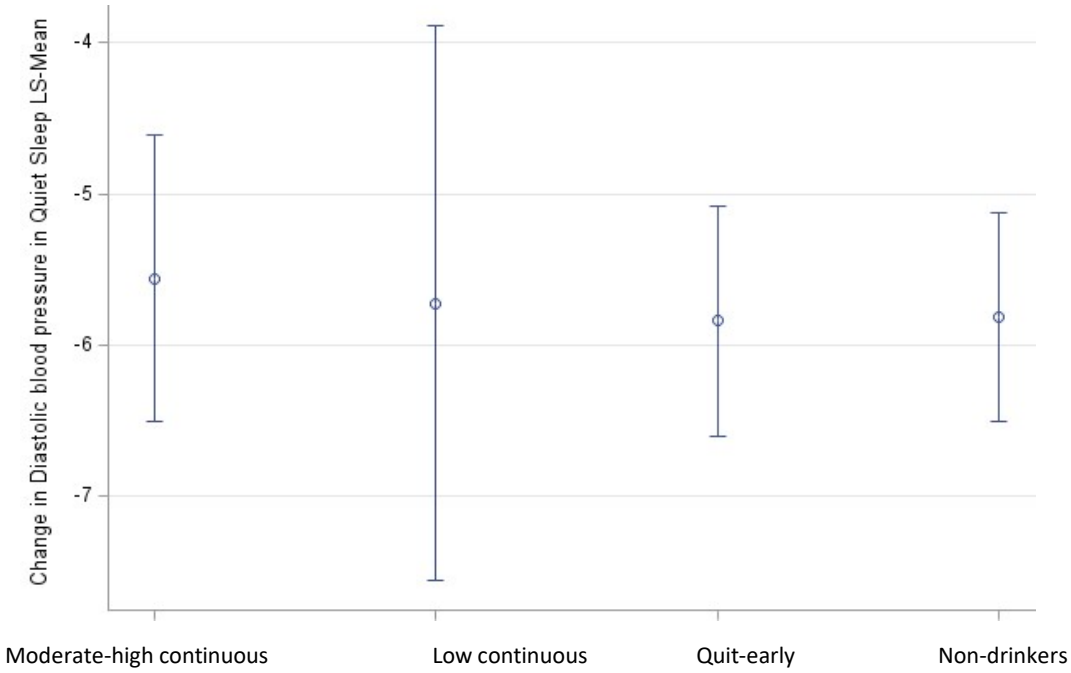
Supplemental Figure S58: Marginal means of sustained change in heart rate after tilt for each drinking groups in quiet sleep, both study sites



Supplemental Figure S59: Marginal means of sustained change in RMSSD after tilt for each drinking groups in quiet sleep, both study sites



Supplemental Figure S60: Marginal means of change in systolic blood pressure after tilt for each drinking groups in quiet sleep, both study sites



Supplemental Figure S61: Marginal means of change in diastolic blood pressure after tilt for each drinking groups in quiet sleep, both study sites