Supplemental Material

Table S1. Baseline characteristics by inclusion in analytic sample: The Study of Women's Health Across the Nation (SWAN).

	Included (N=3083)	Excluded (N=219)
Age, median (Q1-Q3)	46.0 (44.0 - 48.0)	46.0 (44.0 - 48.0)
Race/Ethnicity, % (n)		
Black	28.4 (875)	26.9 (59)
White	47.5 (1464)	39.7 (87)
Chinese	7.8 (242)	3.7 (8)
Hispanic	7.4 (227)	26.9 (59)
Japanese	8.9 (275)	2.7 (6)
Education, % (n)		
High school or less	23.8 (727)	42.8 (92)
Vocational/some college	32.5 (993)	27.0 (58)
College or higher	43.7 (1336)	30.2 (65)
Financial strain, % (n)		
Somewhat/very hard	38.6 (1182)	60.5 (130)
Not hard	61.4 (1883)	39.5 (85)
Menopause stage, % (n)		

	Included (N=3083)	Excluded (N=219)
Early perimenopause	45.7 (1402)	46.7 (99)
Premenopause	54.1 (1658)	52.8 (112)
Unknown	0.2 (5)	0.5 (1)
BMI, median (Q1-Q3)	26.5 (22.8 - 32.0)	28.6 (24.5 - 33.6)
SBP (mmHg), median (Q1-Q3)	115.0 (106.0 - 127.0)	119.0 (111.0 - 130.0)
DBP (mmHg), median (Q1-Q3)	74.0 (69.0 - 81.0)	80.0 (71.0 - 84.0)
LDL-C cholesterol (mg/dl), median (Q1-Q3)	114.0 (94.0 - 135.0)	119.0 (99.0 - 136.5)
HDL-C (mg/dl), median (Q1-Q3)	54.0 (46.0 - 64.0)	50.0 (42.0 - 58.0)
Triglycerides (mg/dl), median (Q1-Q3)	90.0 (67.0 - 129.0)	106.0 (75.0 - 156.0)
HOMA-IR, median (Q1-Q3)	1.8 (1.3 - 3.0)	2.5 (1.5-4.5)
Smoking status, % (n)		
Past/never	83.3 (2568)	69.4 (152)
Current	16.7 (513)	30.6 (67)
Physical activity score, median (Q1-Q3)	7.6 (6.4 - 8.9)	7.3 (5.8 - 8.8)
Medication use		
BP lowering, % (n)	14.2 (439)	14.6 (32)

	Included (N=3083)	Excluded (N=219)
Lipid lowering, % (n)	1.0 (31)	1.4 (3)
Anti-diabetics, % (n)	2.7 (84)	6.8 (15)
Estradiol (pg/mL), median (Q1-Q3)	54.8 (32.8 - 88.2)	62.7 (34.5 - 96.3)

VMS = vasomotor symptoms; BMI = body mass index; BP = blood pressure; SBP = systolic blood pressure; DBP = diastolic blood pressure; LDL-C = low density lipoprotein cholesterol; HDL-C = high density lipoprotein cholesterol; HOMA-IR = homeostatic model assessment insulin resistance

Table S2. Relation between baseline VMS and adjudicated nonfatal CVD events in SWAN (N=3083).

	Model 1 HR (95% CI) P value	Model 2 HR (95% CI) P value
Frequency of VMS, prior two weeks		
1-5 days	1.94 (1.12-3.36) 0.02	1.64 (0.93-2.88) 0.087
≥6 days	2.58 (1.33-5.00) 0.01	2.25 (1.12-4.51) 0.02

Relative to no VMS, prior two weeks

Model 1: Adjusted for site, baseline age, race/ethnicity

Model 2: Adjusted for model 1 covariates + baseline education, financial strain, menopause stage, SBP, BMI, LDL-C, triglycerides, HOMA-IR, medication use (BP-lowering, lipid-lowering, anti-diabetic, hormone therapy), smoking, physical activity

Table S3. Relation between VMS over the study and adjudicated nonfatal CVD events in SWAN (N=3083).

	Model 1 HR (95% CI) P value	Model 2 HR (95% CI) P value
Persistent frequent VMS (>33% of attended visits with frequent VMS)*	2.15 (1.30, 3.55) 0.003	1.99 (1.16, 3.40) 0.01

*Relative to ≤33% of attended visits with frequent VMS

Frequent VMS: VMS ≥6 days in the prior two weeks; Missing covariate values imputed based upon mean levels

Model 1: Adjusted for site, baseline age, race/ethnicity, number of attended visits

Model 2: Adjusted for model 1 covariates + baseline education, average financial strain, baseline menopause stage, average systolic blood pressure, average body mass index, average low density lipoprotein cholesterol, average triglycerides, average homeostatic model assessment insulin resistance, average physical activity, proportion of visits smoking, medication use (proportion of visits using blood pressure-lowering, lipid-lowering, anti-diabetic, hormone therapy), number of attended visits

Table S4. Relation between VMS and combined incident fatal and nonfatal CVD events in SWAN, adjusting for endogenous estradiol concentrations (N=3083).

	HR (95% CI) P value
Baseline frequency of VMS, past two weeks*	
1-5 days	1.01 (0.74, 1.37) 0.98
≥6 days	1.48 (1.03-2.14) 0.03
Persistent frequent VMS over the study (>33% of attended visits with frequent VMS)§	1.75 (1.32, 2.33) 0.0001

*Relative to no VMS, prior two weeks, §Relative to ≤33% of attended visits with frequent (≥6 days in the prior two weeks) VMS; baseline VMS and persistent VMS considered in two separate models

Missing covariate values imputed based upon mean levels; For baseline VMS models, covariates derived from baseline; for persistent VMS models, covariates averaged over study (proportion of visits for categorical variables) with the exception of age, menopause stage, and education which were baseline values for both models

Adjusted for site, age, race/ethnicity, education, financial strain, menopause stage, SBP, BMI, LDL-C, triglycerides, HOMA-IR, medication use (BP-lowering, lipid-lowering, anti-diabetic, hormone therapy), smoking, physical activity, endogenous estradiol, cycle day of blood draw (baseline VMS models), and number of attended visits (VMS persistence models)