PUBLISHED MANUSCRIPTS


**Primary Question:** Does the initiation of metformin, a commonly used drug, associate with worse bone mineral density?

**Summary of Findings:** Over four years of follow-up, women who initiated metformin had no important differences in bone mineral density compared with women who did not start metformin.


**Primary Question:** Does the relationship over 2 years between Urinary Incontinence (UI) and Disability, differ by UI type?

**Summary of Findings:** Urinary incontinence has strong association with multiple areas of disability after two years. It is important to address UI earlier in symptom onset. Screening for mixed UI (both Stress and Urge) and UI that occurs more frequently and in larger amounts more specifically may yield better information regarding an individual’s future disability risk.


**Primary Question:** Do obesity and metabolic syndrome have unique effects on cardiovascular risk?

**Summary of Findings:** There are a significant proportion of metabolically healthy obese individuals within SWAN. The findings from this study suggest that there is only a minimal impact of obesity on carotid artery thickness over the effect of metabolic syndrome alone.


**Primary Question:**

1. Are lower volumes of epicardial adipose tissue and paracardial adipose tissue, higher
volume of thoracic perivascular adipose tissue, and better quality of all cardiovascular fat deposits at midlife associated with a higher future cognitive performance?

2. Does the effect of cardiovascular fat on cognitive performance depend on obesity or race/ethnicity?

Summary of Findings:
1. Higher thoracic perivascular adipose tissue volume and radiodensity at midlife were associated with higher future delayed recall and lower future working memory.

2. The effect of cardiovascular fat on cognitive performance did not depend on obesity and race/ethnicity.

[WG#1088]


Primary Question: Using a range of methodologies and extensive consideration of confounders, these studies have shown that frequent and/or persistent VMS are associated with adverse CVD risk factor profiles, poorer underlying peripheral vascular and cerebrovascular health, and elevated risk for clinical CVD events.

[WG#1130]


Primary Question: Can simple to collect variables be used to predict which women during the midlife will have significant declines over the decade from ages 55-65 years in physical health and function

Summary of Findings: Seven variables are moderate predictors of significant declines in two large representative cohorts of women in the midlife. These include baseline health, body mass index, educational attainment, smoking status, osteoarthritis, cardiovascular disease, and depressive symptoms. These variables work well as a risk score and should be considered in clinical settings.

Conclusions and relevance: Seven easy to collect clinical variables were used to create a valid risk score for PCS declines that was replicated in an external cohort of women. The risk score might provide a method for identifying women at high risk for a significant PCS decline in mid-life.

[WG#1058MS2]

7 Shieh A, Karlamangla A, Huang M, Shivappa N, Wirth M, Hebert J, Greendale G. Dietary inflammatory index and fractures in midlife women: Study of Women’s Health Across
Primary Question: Is a more inflammatory diet related to more fractures?

Summary of Findings: A more inflammatory diet is related to more future fractures.


Primary Question: 1) Are LDL subclasses change over the menopause transition independent of aging?
2) Are LDL subclasses during midlife associated with the presence of coronary artery calcification and carotid intima-media thickness?
3) Will these associations vary by the timing of these measures as related to the final menstrual period (FMP)?

Summary of Findings: Women experience significant atherosclerotic increases in LDL subclasses that increases their risk of having greater cIMT levels and higher CAC prevalence. The reported associations were more profound during perimenopause stage.


Primary Question: Does longitudinal exposure to neighborhood socioeconomic vulnerability throughout midlife impact blood pressure levels and their annual progression over time?

Summary of Findings: We used data from the Study of Women’s Health Across the Nation to characterize longitudinal patterns of neighborhood socioeconomic vulnerability and sociodemographic change over time, and to determine their influence on blood pressure levels and their annual progression among women across ten-year follow-up. We identified four unique profiles of neighborhood socioeconomic vulnerability, and found that women living in socioeconomically vulnerable neighborhoods throughout midlife – characterized by lower SES, greater vacant housing, higher population density, and more non-Hispanic Black and Hispanic residents – had significantly higher SBP levels at study start, and experienced the fastest rate of annual SBP growth (at 0.93 mmHg/year) across ten-year follow-up. In our racially, ethnically, and geographically-diverse cohort of 2,738 women transitioning through menopause, neighborhood socioeconomic vulnerability was significantly associated with accelerated increases in systolic blood pressure throughout midlife.

Reeves AN, Elliott MR, Karvonen-Gutierrez C, Harlow SD Selection Bias Masks Racial Differences in Age at Menopause: The Study of Women’s Health Across the Nation JAMA Open Network 2023 Jun 29;dyad085. doi: 10.1093/ije/dyad085. Online ahead of print. PMID: 37382579

Primary Question: Does selection into and out of the SWAN cohort bias estimates of
racial/ethnic differences in the age of final menstrual period (FMP)?

**Summary of Findings:** Overall selection biases cause overestimation of the median age of FMP in Black/Hispanic women, underestimating racial/ethnic disparities. After adjustment, Black women had earlier natural and surgical FMPs (average 1.2 years) versus White women despite control factors. Results are consistent with "weathering" and overuse of reproductive surgeries for Black/Hispanic women – highlighting that selection biases in aging research misinforms understanding of aging in minoritized populations.

[WG#956MS2]

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**Primary Question:** Racial/ethnic disparities in hypertension are well-documented and a pressing public health problem. The contribution of environmental pollutants, including per- and polyfluoroalkyl substances (PFAS), have not been explored even though certain PFAS are higher in Black population and have previously been associated with hypertension incidence. We examined the extent to which racial/ethnic disparities in incident hypertension are explained by racial/ethnic differences in serum PFAS concentrations.

**Summary of Findings:** In this prospective cohort, PFAS were associated with significant and clinically meaningful race/ethnic differences in time to hypertension. A causal mediation analysis revealed that PFOS, and two precursors (EtFOSAA and MeFOSAA) explained around 7-10% of the differences observed in the time to onset of hypertension in Black compared to White participants. Using multipollutant approaches, we found PFAS mixtures could explain 19.1% of the Black-White disparities in hypertension.

[WG#877MS20]

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**Primary Question:** Do women with lower physical function during pre- or perimenopause have higher risk for a cardiovascular event compared to women with better physical function?

**Summary of Findings:** Women with lower physical function during pre- or perimenopause have higher risk of a cardiovascular event as they age. This association appears to be due to higher cardiovascular risk factors among women with lower physical function.

[WG#1019]

**Primary Question:** Are Sleep Disturbances related to fractures as women transition over menopause?

**Summary of Findings:** We found that women with greater sleep disturbances have a higher risk of fracture but this association was explained by shared risk factors.


**Primary Question:** Does having prediabetes increase the risk of bone fractures?

**Summary of Findings:** Having prediabetes increases the risk of future bone fractures in midlife women. This risk is independent of bone mineral density.


**Primary Question:** Do women improve their physical health and function over time, and what are the factors associated with improvement?

**Summary of Findings:** Approximately 15% of women improved their physical health and function over time. Factors associated with improvement include having a higher physical activity score, lower BMI, no sleep disturbances, less financial strain, less medications, and lower baseline physical health and function.


**Primary Question:** This is a methods paper to join together data from two different devices that measure physical activity during waking hours and sleep during night time hours and discusses the issues that arise when merging these data.

**Summary of Findings:** We developed a novel methodology – Method for Activity Sleep Harmonization (MASH) – to combine sleep watch data and activity waist data to create 24-hour sleep-wake cycles. MASH was developed as a two-tiered process that uses available diary data or, if diary data are not available, 1D convolutional neural network (1D CNN)
models are used to create predicted wake intervals. The process then reconciles sleep and activity data disagreement and creates day-level night-day pairs. Most of the reconciling between the sleep and activity data was due to the overlap between sedentary behavior and sleep (e.g., if the participant wore the activity device during sleep which was a protocol deviation).

[WG#1080]


Primary Question: Are sleep timing and regularity of sleep timing associated with psychological health?

Summary of Findings: Unhealthy sleep timing was associated with depressive symptoms. Irregular sleep was associated with depressive symptoms, anxiety symptoms, and worse psychological well-being.

[WG#1063]


Primary Question: In midlife women undergoing the menopause transition, does leisure time physical activity mitigate bone loss?

Summary of Findings: Larger increases in leisure time physical activity from pre-/early perimenopause to late perimenopause/postmenopause were associated with slower bone loss at the hip. More leisure time physical activity over the entire period spanning premenopause to postmenopause was associated with higher postmenopausal bone mineral density at the spine and hip.

[WG#1091]

Primary Question: Are cardio-metabolic and inflammatory variables at baseline predictive of neuropathy in SWAN women at visit 15?

Summary of Findings: We found that baseline metabolic syndrome is a significant predictor of neuropathy even after control for obesity and diabetes. Longitudinal CRP was also strongly predictive even after control for all three metabolic conditions, and mediated the relationship between both obesity and metabolic syndrome with peripheral neuropathy.


Primary Question: What is the time course of sexual functioning among breast cancer survivors following diagnosis compared to women without cancer over an equivalent period of time, and do risk factors for sexual functioning vary between cancer survivors and women without cancer?

Summary of Findings: Except for greater pain with intercourse among breast cancer survivors, negative changes in sexual function during mid-life were similar in those with and without cancer. Both cancer survivors and con-cancer controls showed a decline over time in being sexually active, sexual intercourse frequency, and sexual desire. Characteristics such as depressive symptoms, previously related to sexual functioning among survivors, were similarly related to sexual functioning among women without cancer.


Primary Question: What are the effects of lean mass loss and fat mass gain during the menopause transition on bone density at the end of the menopause transition and fracture in postmenopause?

Summary of Findings: Greater loss of lean during the menopause transition is associated with lower bone density at the hip at the end of the menopause transition, whereas greater gain in fat mass during the menopause transition is associated with greater bone density at the spine and hip. Both greater lean mass loss and fat mass gain during the menopause transition were associated with more fractures in postmenopause.

Primary Question: Are women who have experienced childhood sexual trauma at greater risk for pelvic floor dysfunction as represented by urinary incontinence and/or pelvic pain during intercourse?

Summary of Findings: This analysis identified dyspareunia but not urinary incontinence as a significant midlife consequence of childhood sexual abuse. Clinicians who evaluate and treat pelvic floor dysfunctions should inquire about childhood sexual abuse.


Primary Question: Does exposure to phthalates increase the risk of diabetes over six years in midlife women?

Summary of Findings: Some phthalate metabolites were associated with a higher incidence of diabetes over six years, but the associations were inconsistent across racial/ethnic groups. Whether phthalates cause diabetes requires further investigation.


Primary Question: Are exposures to phthalates associated with hormones including estradiol, testosterone, FSH, SHBG, and AMH, and timing of natural menopause in midlife women?

Summary of Findings: We found that phthalates may affect circulating levels of testosterone in midlife women, especially in postmenopausal women, supporting antiandrogenic properties of phthalates.


Primary Question: Does having a hysterectomy make menopause come earlier?

Summary of Findings: Having a hysterectomy does not bring on menopause earlier than not having a hysterectomy. Women who have hysterectomies would have had a slightly later age at menopause than women who did not have hysterectomies if they hadn’t had the surgery.


Primary Question:
The current study investigated whether pre-pandemic histories of childhood abuse or intimate partner violence (reported roughly 4-12 years prior to the COVID-19 pandemic) were prospectively related to elevated depression, anxiety, interpersonal conflict, and sleep problems during the pandemic among older women.

Summary of Findings:

Wang X, Ding N, Harlow SD, Randolph JF Jr, Mukherjee B, Gold EB, Park SK  Exposure to Heavy Metals and Hormone Levels in Midlife Women: the Study of Women's Health Across the Nation (SWAN)  Environ Pollut Wang X, Ding N, Harlow SD, Randolph JF Jr, Mukherjee B, Gold EB, Park SK. Exposure to heavy metals and hormone levels in midlife women: The Study of Women's Health Across the Nation (SWAN). Environmental Pollution. 2023 Jan 15;317:120740. PMID: 36436662; PMCID: PMC9897061

Primary Question:

Summary of Findings: In this prospective cohort study of 1,355 midlife women representing diverse racial/ethnic groups, a doubling of urinary metal concentration was associated with lower E2 levels by 2.2% (95% CI: -4.0%, -0.3%) for mercury and 3.6% (95% CI: -5.7%, -1.6%) for lead; higher FSH levels by 3.4% (95% CI: 0.9%, 5.9%) for lead; and higher SHBG levels by 3.6% (95% CI: 1.3%, 5.9%) for cadmium. No association was found between metals and testosterone levels.

Kang H, Calafat AM, Karvonen-Gutierrez CA, Park SK  Isomer-specific serum concentrations of perfluorooctane sulfonic acid (PFOS) among U.S. adults: Results from the National Health and Nutrition Examination Survey (NHANES) and the Study of Women's Health Across the Nation Multi-Pollutant Study (SWAN-MPS)  Environmental Science & Technology 2023 Jan 10;57(1):385-394. doi: 10.1021/acs.est.2c04501. Epub 2022 Dec 19. PMID: 36534511 PMCID: PMC10103141

Primary Question: - Does the ratio of concentrations of serum PFOS isomers differ by individual characteristics such as consumption of processed foods or fish/shellfish, drinking tap water, kidney health, or menopausal status? - Does the ratio of concentrations of serum PFOS isomers differ by race/ethnicity?

Summary of Findings: We found that people with frequent fish/shellfish consumption, healthier kidney, and premenopausal status had relatively higher serum concentrations of linear PFOS isomer compared to branched PFOS isomers, while people with white race/ethnicity, frequent processed foods consumption, and drinking tap water had relatively lower serum concentrations of linear PFOS compared to branched PFOS isomers.
Peng MQ, Karvonen-Gutierrez CA, Herman WH, Mukherjee B, Park SK. Phthalate exposure is associated with more rapid body fat gain in midlife women: The Study of Women's Health Across the Nation (SWAN) Multi-Pollutant Study. Environmental Research. 2023 Jan 1;216:114685. PMID: 36341787; PMCID: PMC9870605

**Primary Question:** Does exposure to phthalates cause faster increases in body weight, fat mass, and body fat percentage in women at midlife?

**Summary of Findings:** Exposure to some phthalates was associated with faster gains in body fat in midlife women, especially those who were normal/underweight at baseline.


**Primary Question:** What is the distribution of vaginal microbiota (classified by community state types-CSTs) in a diverse cohort of postmenopausal women? What are the relationships among genitourinary syndrome of menopause symptoms (vaginal dryness, vulvovaginal irritation, sexual pain, dysuria, urinary urgency), CSTs, estrogen, and vaginal atrophy biomarkers (vaginal maturation index and vaginal pH)?

**Summary of Findings:** While close relationships exist among estrogen, the structure of the vaginal microbiota, vaginal atrophy biomarkers (vaginal maturation index and vaginal pH), sexual pain was the only genitourinary syndrome of menopause symptom associated with the structure of vaginal microbiota and vaginal atrophy biomarkers.


**Primary Question:** We explored trajectories of palpitations over time, their risk factors, and their associations with subclinical cardiovascular disease.

**Summary of Findings:** We identified three distinct trajectories of palpitations: high probability of palpitations in the peri- to early postmenopause diminishing in the late postmenopause (15.9% of women), moderate probability of palpitations in the peri- to early postmenopause diminishing in the late postmenopause (34.3%), and sustained low probability of palpitations (49.8%). The high probability group had more financial strain, and a more adverse reproductive and health-related profile at baseline. Palpitations trajectories were not related to atherosclerosis or arterial stiffness.

**Primary Question:** 1) Are lower premenopausal AMH and greater declines in AMH levels over time associated with adverse lipid/lipoprotein profiles in women transitioning through menopause INDEPENDENT OF E2? 2) Are lower levels of AMH overtime associated with adverse changes in lipid profile early in the transition (e.g. during time elapsed between baseline and 1 year before FMP) INDEPENDENT OF E2?

**Summary of Findings:** Lower premenopausal and/or greater declines in E2 over the MT were associated with an atherogenic lipid/lipoprotein profile, while lower premenopausal AMH and/or greater declines in AMH over the MT linked to a greater increase in HDL-C and apo A-1.


**Primary Question:** (1) Our goal was to develop a complex Bayesian joint model for baseline prevalence and longitudinal incidence of MetS components and to use this model to ascertain what factors are associated with prevalence of particular MetS components at baseline, and their incidence, if possible considering the complexity of the problem.  
(2) Since we were able to accomplish (1), our next goal was to ascertain the effect of race/ethnicity on development of MetS modified by menopausal status.  
(3) We also assessed the effect of particular MetS configurations at baseline on the predictive probabilities of particular MetS constellations using a Markov chain approach

**Summary of Findings:** Having central adiposity at baseline, alone or in combination with another MetS component, is the major factor that increases predictive probability of subsequent development of MetS. The predictive probability of development of MetS varies by race/ethnicity and is somewhat modified by menopausal transition stage. Later menopause is protective of developing component MetS.


**Menopause** Christmas M, Janssen I, Joffe H, Upchurch D, Santoro N, Kravitz HM. Menopause hormone therapy and complementary alternative medicine, quality of life, and racial/ethnic differences: the Study of Women's Health Across the Nation (SWAN).
Primary Question: To evaluate if quality of life differed by treatment (hormone therapy and complementary alternative medicine) in a large, diverse cohort of women with menopause-related symptoms.

Summary of Findings:


Primary Question: Is a better Life's Simple 7 (LS7) score and its health behavior components (body mass index, physical activity, smoking and diet) early in midlife associated with better metrics of HDL [higher HDL cholesterol efflux capacity (HDL-CEC), HDL-phospholipids (HDL-PL) and large HDL-particles (HDL-P) concentrations, larger HDL size, and less HDL triglycerides (HDL-Tg),medium and small HDL-P concentrations] later in life? Is a better LS7 score and its health behavior components (body mass index, physical activity, smoking and diet) early in midlife associated with favorable changes of HDL metrics over time?

Summary of Findings: After adjusting for confounders, a higher LS7 at baseline score was associated with higher HDL-PL, total HDL-P, and large HDL-P concentrations, lower HDL-Tg levels and larger overall HDL size later in life.

Ideal BMI was associated with higher HDL-CEC, HDL-PL and large HDL-P levels, larger HDL size and lower HDL-Tg and small HDL-P levels. Ideal physical activity status was associated with higher HDL-PL, total HDL-P, large HDL-P and medium HDL-P concentrations. Ideal smoking status was associated with lower HDL-Tg. Diet was not associated with any of the HDL metrics.

Higher baseline LS7 score was associated with a decrease in HDL size as time progressed. Compared to women with ideal BMI, women in the poor BMI group had larger increases in HDL size over time.


Primary Question: Air pollution has been suggested to be associated with obesity; however, epidemiologic evidence is limited and has largely focused on body mass index (BMI). We examined longitudinal associations of air pollution exposure, including fine particulate matters (PM2.5), nitrogen dioxide (NO2), and ozone (O3) with weight, BMI, waist...
circumference, fat mass, lean mass, and proportion fat mass in midlife women.

**Summary of Findings:** In this prospective cohort study of 1,654 midlife women representing diverse racial/ethnic groups, exposure to air pollution was associated with adverse changes in body composition measures. In particular, PM2.5 and NO2 were positively associated with fat mass and proportion fat mass, and inversely associated with lean mass. In addition, O3 was positively associated with proportion fat mass and inversely associated with lean mass. Associations of PM2.5 and NO2 with body size and composition were modified by physical activity; associations were attenuated among participants with higher physical activity levels.

[WG#1074]


**Primary Question:** Is there a potential for selection into the SWAN cohort to bias estimates of racial/ethnic differences in health?

**Summary of Findings:** Black and Hispanic women had the lowest eligibility rates stemming from high rates of surgical menopause. Their eligibility rates decreased with increasing age at a higher rate than in White women. Higher education was associated with higher odds of eligibility for White women only. Participation was associated with demographic characteristics with little evidence of a “healthy volunteer” bias. Failure to account for selection at study commencement in the SWAN cohort, and similar cohorts of aging, may mis-estimate racial/ethnic disparities in health especially effecting Black and Hispanic women.

[WG#956]


**Primary Question:** Does more insulin resistance lead to faster bone loss?

**Summary of Findings:** The longitudinal associations of insulin resistance with BMD were biphasic, and were more apparent in pre- and postmenopause than in the menopause transition. When insulin resistance is low and when it decreases, insulin resistance appears to be osteoanabolic. When insulin resistance increases, it appears to be osteocatabolic.

[WG#1071]

39 Bromberger JT, Chang Y, Colvin AB, Kravitz HM, Matthews KA.  **Does childhood maltreatment or current stress contribute to increased risk for major depression during the menopause transition?**  *Psychol Med*  Bromberger JT, Chang Y, Colvin AB, Kravitz HM, Matthews KA. Does childhood maltreatment or current stress contribute to increased risk for major depression during the menopause transition? Psychol Med. 2022 Oct;52(13):2570-2577. doi: 10.1017/S0033291720004456. Epub 2020 Dec 10. PMID: 33298219.
Primary Question: Will women who experience various types of stressors, both historical (childhood adversity) or recent/current will be more likely to experience a major depressive episode during the MT (1) than women who do not report such stressors and (2) than during pre- or postmenopause.

Summary of Findings: Among women with lifetime major depression at study entry, compared to pre- or perimenopause, postmenopause poses a greater risk for a major depressive episode for women with childhood emotional abuse or neglect or physical neglect. This is not the case for women without lifetime major depression at study entry.


Primary Question: Is employment status a risk factor for poor physical function in midlife women?

Summary of Findings: Women with lower levels of employment from mid-life to older adulthood were more likely to experience severe impairment in physical function. These associations are not driven by adiposity, physical activity, or health-related variables.


Primary Question: Does C3 or C4 increase around the final menstrual period (FMP)? Are the changes in HDL subclasses over FMP associated with C3/C4 levels?

Summary of Findings: C3 and C4 significantly rise around menopause with C3 showing the steepest rise. Greater decreases in large and increases in small HDL-P concentrations and decreases in the overall size of HDL-P were independently associated with higher levels of C3 and C4 over time.

ahead of print. PMID: 35982358 PMCID: PMC9938082

**Primary Question:** To compare sleep disturbance from 5 years pre- to 5 years post-diagnosis between breast cancer survivors (BCS) and women without cancer over the same period and to identify BCS subgroups exhibiting different sleep trajectories

**Summary of Findings:** No differences were found between breast cancer survivors (BCS) and controls in prevalence of frequent nighttime awakenings either before or after diagnosis. Among BCS, three trajectory groups were identified. Thirty-seven percent of BCS had consistently low prevalence of waking several times per night, 30% had high prevalence and 33% had increasing prevalence which started 2 years pre-diagnosis. Pre-diagnosis vasomotor symptoms, anxiety, depressive symptoms, and smoking differed between the groups.

[WG#869]


**Primary Question:** 1. Are inflammatory biomarkers associated with subsequent incident VMS in women who did not report VMS at baseline? 2. Does the relation of inflammatory biomarkers to incident VMS vary by menopausal status or race/ethnicity?

**Summary of Findings:** Elevations of the inflammatory biomarkers, hs-CRP or IL-6, were not associated either concurrently or with subsequent incident VMS, indicating that inflammation was unlikely to be a risk factor for VMS.

[WG#858]


**Primary Question:** Is there an association between premenopausal anti-Müllerian hormone levels and breast cancer risk?

**Summary of Findings:** Among 1,529 participants included in the analysis, 84 women self-reported an incident breast cancer diagnosis. In a multivariable Cox model adjusted for age, race/ethnicity, smoking, body mass index, and other factors, higher AMH levels were associated with a non-significant increased breast cancer risk.

[WG#895]

45 Ding N, Karvonen-Gutierrez CA, Mukherjee B, Calafat AM, Harlow SD, Park, SK. Per- and Polyfluoroalkyl Substances and Incident Hypertension in Multi-Racial/Ethnic Women: The Study of Women’s Health Across the Nation. *Hypertension*. Ding N, Karvonen-Gutierrez CA, Mukherjee B, Calafat AM, Harlow SD, Park SK. Per- and Polyfluoroalkyl...
Primary Question: Per- and polyfluoroalkyl substances (PFAS) can trigger a combination of pathophysiological responses that may lead to hypertension. However, human evidence to support this hypothesis is scant. We examined the association between PFAS and risks of developing hypertension.

Summary of Findings: We found that women with higher serum concentrations of perfluorooctane sulfonate (PFOS), perfluorooctanoate (PFOA), and 2-(N-ethyl-perfluorooctane sulfonamido) acetate (EtFOSAA) had a higher risk of developing hypertension. No significant associations were observed for perfluorononanoate (PFNA) and perfluorohexane sulfonate (PFHxS).

Primary Question: Is there a clear relationship between specific groups of lipoproteins and subclinical atherosclerosis among perimenopausal women, after taking remaining lipoproteins into consideration? Does this relationship change by women's menopausal status?

Summary of Findings: Carotid intimal medial thickening is positively associated with a cluster of small IDL particles in midlife women, and with a cluster of small and medium LDL particles after menopause.

Primary Question: Exposure to metals may contribute to the development of metabolic syndrome (MetS); however, evidence from midlife women who are at greater risk of cardiometabolic disease is limited. We prospectively examined the associations of 15 urinary metal concentrations with incident MetS in the Study of Women’s Health Across the Nation Multi-Pollutant Study.

Summary of Findings: We found that women with higher urinary concentrations of arsenic, cobalt, and zinc were associated with higher incidence of MetS. Positive associations of urinary arsenic with high blood pressure and impaired fasting glucose, positive associations of urinary cobalt with high blood pressure and abdominal obesity, and positive associations of urinary zinc with high blood pressure and abdominal obesity were observed.
urinary zinc with high blood pressure, impaired fasting glucose, abdominal obesity, and high triglyceride were also observed. A significant association between metal mixture and MetS was also observed using the Environmental Risk Score approach.

Kravitz HM, Colvin AB, Avis NE, Joffe H, Chen Y, Bromberger JT. Risk of high depressive symptoms after the final menstrual period: the Study of Women’s Health Across the Nation (SWAN). Menopause 2022 Jul 1;29(7):805-815. doi: 10.1097/GME.0000000000001988. PMID: 35796553 PMCID: PMC9268212

Primary Question: To examine depressive symptoms during postmenopause and the contribution of depressive symptom trajectories prior to the final menstrual period (FMP) and psychosocial and health factors to postmenopause depressive symptoms.

Summary of Findings: Postmenopause remains a period of increased risk for higher depressive symptoms, especially for women with pre-FMP depressive symptoms. Compared to premenopause, postmenopause was associated with a greater odds of reporting depressive symptoms, but the odds of reporting high depressive symptoms did not differ significantly between postmenopause and early/late perimenopause. Pre-FMP depressive symptom trajectories are highly predictive of postmenopause depressive symptoms independent of health and psychosocial factors, and depressive symptoms tend to be highly consistent over midlife.


Primary Question: Q1. Does the serum level of AMH in a pre- or perimenopausal woman predict her rate of future BMD decline over the next 3 to 4 years? Q2. Is the current level of serum AMH associated with the fraction of peak BMD that will have been lost after a few years, including both ongoing and imminent loss?

Summary of Findings: If a woman will lose more of her peak BMD than the site-specific least significant change (LSC) at either the lumbar spine or femoral neck by the end of the next 2-3 years, then AMH below 100 pg/mL will detect it with sensitivity of 50% in premenopause, 80% in early perimenopause, and 98% in late perimenopause. These findings suggest that AMH measurement can help flag women at the brink of significant bone loss, for early intervention.

Primary Question: Exposure to perfluoroalkyl and polyfluoroalkyl substances (PFAS) has been associated with earlier natural menopause, possibly through depletion of ovarian reserve and disturbance of hormone homeostasis. We aimed to investigate and quantify the degree to which follicle-stimulating hormone (FSH) and estradiol (E2) could mediate the associations between serum PFAS concentrations and incident natural menopause.

Summary of Findings: In this population-based cohort study, we found that the effects of exposure to PFAS on shortening time to incident natural menopause is partially explained through increasing serum concentrations of FSH. No mediation effects were observed for E2.

51 Lee S, Karvonen-Gutierrez C, Mukherjee B, Herman WH, Park SK  
Race-specific associations of urinary phenols and parabens with adipokines in midlife women: The Study of Women's Health Across the Nation (SWAN) 

Primary Question: We examined the cross-sectional associations of urinary phenols and parabens with adipokines. We also evaluated effect modification of these associations by race.

Summary of Findings: Urinary methyl-paraben was associated with lower leptin in all women but this association differed by race. Higher urinary concentrations of methyl-paraben were associated with a lower leptin in white women but with a higher leptin in black women. No significant associations were observed in Asian women.

52 Ylitalo K, Karvonen-Gutierrez C, Sternfeld B, Gabriel K.  
Quantifying Physical Activity Across the Midlife: Does Consideration of Perceived Exertion Matter? 

Primary Question: Changes in heart rate and breathing during physical activity can influence perceptions of exertion. This study compared estimates of physical activity with and without adjustments for perceived exertion.

Summary of Findings: Approximately three-fourths of participants reported any planned exercise activities or sports during the previous year. The most common planned exercise activity for all participants was walking and the most common perceived exertion level was a “moderate” increase in heart rate and breathing during physical activity. For most women, adjusting for perceived exertion did not substantially change estimates of physical activity dose.

Primary Question: Do women who have declines in sexual intercourse frequency over the menopausal transition have a higher risk of developing sexual pain compared to women who have the same or increases in sexual intercourse frequency?

Summary of Findings: Long-term (over 13 years) and short-term (over 2 to 4 years) declines in reported sexual intercourse frequency across the menopausal transition were not associated with an increased risk of developing pain with intercourse. This empirical evidence does not support the “use it or lose it” notion that suggests women are responsible for their sexual pain.


Primary Question: Does excessive weight gain during pregnancy impact the long-term cardiovascular risk profile of the mother? And what proportion of that effect is explained by midlife obesity

Summary of Findings: A history of excessive gestational weight gain was associated with a small but statistically significant increase in atherosclerotic CVD risk score, and a moderate, statistically significant increase in level of the inflammatory marker C-reactive protein across midlife.


Primary Question: Does prediabetes and insulin resistance reduce bone quality?

Summary of Findings: Prediabetes and insulin resistance are associated with reduced bone quality.

**Primary Question:** What genes are associated with variation in AMH levels in women with European Ancestry?

**Summary of Findings:** We identified a variant in the AMH gene and three other loci that may affect the size of the ovarian follicle pool: the previously reported MCM8 locus and three novel signals in or near AMH, TEX41, and CDA7. The strongest signal was a missense variant in the AMH gene (rs10417628).

[WG#997]


**Primary Question:** Is interpersonal violence [childhood abuse, adulthood abuse, intimate partner violence] related to increased risk of subsequent clinical CVD events?

**Summary of Findings:** Childhood abuse, particularly sexual abuse, was associated with increased risk of later CVD in women. IPV was associated with risk for CVD, and these relationships were explained in part by higher SBP among IPV-exposed women.

[WG#764]


**Primary Question:**

**Summary of Findings:**

[WG#994MS3]


**Primary Question:** Are higher volumes of abdominal visceral and cardiovascular (epicardial, paracardial and perivascular aortic) adipose tissue depots at midlife associated with a worse high-density lipoprotein (HDL) metric profile [lower HDL cholesterol efflux capacity (HDL-CEC), lower concentrations of HDL phospholipids (HDL-PL) and large HDL particles (HDL-P), smaller overall HDL size, and increases in levels of HDL triglycerides (HDL-Tg) and small HDL-P]?
Does insulin resistance mediate the observed associations between different adipose tissue depots and HDL metrics?

**Summary of Findings:** After adjusting for potential confounders, higher abdominal visceral adipose tissue volume was associated with lower concentrations of HDL-PL contents, HDL-cholesterol (HDL-C) and large HDL-P subclasses, and smaller overall HDL size. Higher paracardial fat (PAT) volume was associated with lower concentrations of HDL-C and large HDL-P, and smaller overall HDL size. Higher epicardial fat (EAT) volume was associated with more small HDL-P concentrations. Higher perivascular aortic adipose tissue (PVAT) was associated with lower HDL-CEC.

Insulin resistance (IR) partially mediated the associations between adipose tissue depots and HDL metrics as following:
- IR mediated the associations between HDL-CEC, HDL-C, large HDL-P, and HDL size.
- IR also mediated the associations between PAT and HDL-C, large HDL-P and HDL size, and the associations between PVAT and HDL-CEC.

[WG#1014]

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**Primary Question:** Are psychosocial protective factors related to slower progression of CAC over 2.3 years, independently of standard health behaviors and CV health (risk) factors?

**Summary of Findings:** A summary score of positive psychosocial factors was significantly inversely related to CAC progression. This association was stronger in women with presence of coronary calcium at baseline, even after accounting for standard health behaviors and CV health (risk) factors.

[WG#705]

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**Primary Question:** We determined the impact of increasing medication use on health and function in women going through the mid-life.

**Summary of Findings:** There is a moderate correlation between increasing medication use and decreasing physical health and function among women transitioning through the mid-life. These details inform interventions to reduce declines in health and function in older women.

[WG#955]

**Primary Question:** Do patterns of metabolic syndrome during midlife impact physical performance in early old age?

**Summary of Findings:** SWAN women with ≥3 metabolic syndrome (MetS; high-MetS) components compared to those with no MetS components had higher body mass index, pain, financial strain, and lower physical activity and self-reported health at visit 15 (p<0.0001). Compared to Caucasian women, African American and Hispanic women were more likely to be in the high-MetS group and had worse physical functioning along with Chinese women (SPPB, chair stand, stair climb, and gait speed but Hispanic women did not have worse gait speed). After adjustments, high-MetS compared to no MetS demonstrated significantly worse 40-ft walk (β: -0.08; 95% CI: -0.13, -0.03), 4-m gait speed (β: -0.09; 95% CI: -0.15, -0.02), SPPB (β: -0.79; 95% CI: -1.15, -0.44), and chair stands (β:0.69; 95% CI: 0.09, 1.28), though worse stair climb was not significant after adjustments. Excluding women with previous moderate or severe perceived physical function limitations did not change final models.

[WG#1012]


**Primary Question:** How do different types of sleep measures compare to one another when used in the home environment? Does the agreement between measures differ by race/ethnicity?

**Summary of Findings:** Actigraphy and polysomnography produced similar estimates of sleep duration and sleep efficiency. Indices of sleep duration and sleep continuity measured by sleep diaries were consistently different than when measured by actigraphy and polysomnography. Differences in estimates of sleep continuity between sleep diaries and polysomnography were not uniform across race/ethnicity.

[WG#420]

Primary Question: How do SWAN findings help us understanding racial/ethnic health disparities in women's midlife health?

Summary of Findings: This SWAN story documents the presence, magnitude, and longitudinal patterns of racial disparities in selected areas of women’s midlife health (menopause symptoms, sleep, mental health, health-related quality of life, cardio-metabolic health, and physical function) and considers the contextual factors that are likely influencing these disparities.


Primary Question: Do women form distinct groups of SBP, DBP, AND PP over time relative to the FMP?
Do some group of SBP, DBP, AND PP have a piecewise-linear relation with time relative to the FMP suggesting a contribution of the menopause transition?
Do menopause-related factors predict blood pressure trajectory membership or shape?

Summary of Findings: Women were classified into either low, medium, or high trajectory group in each BP measure. The low SBP and PP trajectories (in 36% and 52% of the cohort, respectively) were rising slowly before menopause but showed a significant accelerated rise 1 year after menopause, indicating a menopause contribution. The remaining BP trajectories were rising up until menopause and either continued with the same rise or declined after menopause. A younger menopause age predicted the low SBP and PP trajectories. A greater FSH level predicted a lower, while vasomotor symptoms occurrence predicted a higher SBP and PP levels overtime. Estradiol did not predict trajectory or level of any BP measure.


Primary Question: The present study aimed to identify levels and change in stressful life events across midlife in women and to understand racial/ethnic differences in these experiences. We examine change in total annual number of stressful life events and occurrence of various specific life events.

Summary of Findings: Number of annual life events declined with age and plateaued in later midlife. This pattern was largely consistent across types of life events, though family health and bereavement-related life events increased in later midlife. Compared to White women, Black women experienced more life events, Chinese and Japanese women experienced fewer life events, and Hispanic women experienced fewer life events but experienced increased life events in later midlife.

[WG#963]

Primary Question:
Summary of Findings: Becoming postmenopausal at a younger age is associated with lower postmenopausal bone mineral density, and greater risk of future fracture. [WG#992]


Primary Question: Can women's characteristics measured during their 50's predict declines in older adults?
Summary of Findings: Variables measured at age 55 have a moderate to strong correlation with clinically important declines in physical health and function at age 65. Variables include comorbidities, sociodemographic factors, and lifestyles issues. [WG#1058]


Primary Question: Are age-related declines in bone density, microarchitecture and strength at radius and tibia similar in Black and White postmenopausal women? Do body weight, body composition, physical activity and/or weight change modify age-related skeletal declines?
Summary of Findings: Postmenopausal Black women experience similar rates of skeletal decline as White women. Having low body weight or weight loss increases bone microarchitectural loss in postmenopausal women. [WG#601G]

Endocrinology and Metabolism


Primary Question: Are levels of estradiol (E2) and/or follicle-stimulating hormones (FSH) over the menopause transition associated with an adverse HDL metric profile [lower HDL cholesterol efflux capacity (HDL-CEC), lower concentrations of HDL phospholipids (HDL-PL) and large HDL particles (HDL-P), smaller overall HDL size, and increases in levels of HDL triglycerides (HDL-Tg) and small HDL-P]? Do these associations vary by time since menopause?

Summary of Findings:
Higher levels of estradiol are associated with larger HDL particle size, higher levels of large HDL-P, HDL-CEC and HDL-Tg, but with lower levels of medium HDL-P. The positive association between E2 and HDL-Tg was stronger 2 years after the final menstrual period (FMP) than before. FSH was related to higher total and medium HDL-P, but with smaller HDL particle size, and lower concentrations of large HDL-P, and HDL-CEC per particle. The associations of higher FSH with greater total HDL-P and smaller HDL size were only evident at or after menopause.


Primary Question:
1. What is the time course of vasomotor symptoms (VMS) among women who developed incident breast cancer during follow-up in SWAN before and after their diagnosis and treatment?
2. Are rates of VMS higher in women who developed incident breast cancer during SWAN follow-up than in non-cancer controls from the SWAN cohort?
3. Does treatment with anti-estrogens, endocrine medications, and/or hysterectomy and/or oophorectomy in women who developed incident breast cancer during SWAN follow-up result in greater VMS reporting post-treatment?
4. Do the risk factors for VMS following breast cancer diagnosis differ from those for non-cancer controls?

Summary of Findings: Patterns of prevalent VMS reporting differed significantly between cases and controls, particularly post-diagnosis, the latter only partially explained by tamoxifen use among cases. Incident VMS had small numbers post-diagnosis and a lower rate in cases than in controls pre-diagnosis. Risk factors for VMS largely did not differ between cases and controls.

analysis for individual participant data with a continuous exposure: A case study.  

Primary Question:  
Summary of Findings:  

73  

Primary Question: Prior studies have suggested that poor vision in later life is associated with worse cognitive function. We aim to assess whether there is a similar relationship between vision in mid-life and future cognitive function.  
Summary of Findings: Moderate or worse vision impairment, assessed during mid-life, was associated with lower scores on measures of cognitive function over a 13 year period during which women transitioned from mid-life to later adulthood. Prior studies have suggested a relationship between vision and cognition in older age; this study supports an analogous relationship in mid-life.  

[WG#1027]  

74  

Primary Question: Does change in menopausal status influence change in PSG-assessed sleep across 3 to 4 years? Does the change vary by race/ethnicity?  
Summary of Findings: Among women who were pre- or early-perimenopause at the first sleep assessment, those who transitioned to late perimenopause or postmenopause did not change in sleep duration, wake after sleep onset, NREM and REM delta power, and REM beta power, compared to those who remained pre- or early perimenopause at the second sleep assessment. Women who transitioned did increase in NREM beta power. Findings were adjusted for age, race/ethnicity, site, interval between assessments, and within woman assessment. In addition, for NREM beta power body mass index, depressive symptoms and insomnia yes/no were covariates. Race/ethnicity only moderated the impact of transition group on sleep duration.  

[WG#990]  

75  
Karvonen-Gutierrez CA, Kumar N, Hood MM, Musch DC, Harlow S, Moroi SE Longitudinal association of midlife vision impairment and depressive symptoms: the study of Women’s Health Across the Nation, Michigan site Menopause  

Primary Question: Is midlife vision impairment associated with depressive symptoms?
**Summary of Findings:** Vision impairment was associated with depressive symptoms during the midlife years. There was a significant longitudinal association of mild vision impairment with depressive symptoms among midlife women. Effect size of association of vision impairment and depressive symptoms attenuated but remained significant over time. [WG#921]


**Primary Question:**
1. Are there distinct patterns of changes in menstrual cycle length over the menopausal transition among midlife women?
2. Are patterns of changes in cycle length associated with risk of atherosclerosis after menopause?

**Summary of Findings:**
1. Three distinct patterns of changes in menstrual cycle length over the menopausal transition was identified: stable, late increase, and early increase in cycle length.
2. Compared with women with stable pattern, women with the late increase pattern had lower risk of developing atherosclerosis after menopause.

[WG#899]

77 Park SK, Wang X, Ding N, Karvonen-Gutierrez CA, Calafat AM, Herman WH, Mukherjee B, Harlow SD *Per- and Polyfluoroalkyl Substances (PFAS) and Incident Diabetes in Midlife Women: the Study of Women's Health Across the Nation (SWAN)*

**Primary Question:** Do higher concentrations of serum PFAS increase the risk of developing diabetes?

How many new cases of diabetes in the United States annually could be prevented if serum concentrations of total PFAS were reduced to the background level?

**Summary of Findings:** We found that women with higher serum concentrations of perfluorooctanoate (PFOA), perfluorooctane sulfonate (PFOS), perfluorohexane sulfonate (PFHxS), and 2-(N-methyl-perfluorooctane sulfonamido) acetate (MeFOSAA) had higher risk of developing diabetes. In the United States approximately 370,000 incident diabetes cases each year are attributable to PFAS exposure.

[WG#877MS15]


**Primary Question:** Are different metrics of HDL associated with CAC presence or CAC
density, and does menopausal stage modify the association of HDL metrics with CAC presence and CAC density?

**Summary of Findings:** Only medium HDL-particle (HDL-P) concentrations was independently associated with higher odds of CAC presence; none of the HDL metrics were associated with CAC density. However, menopause status modified the associations between HDL metrics and measures of CAC, where higher small HDL-P and smaller overall HDL size were associated with higher odds of CAC presence in the late perimenopausal stage compared to the pre/early perimenopause stage. Lower large HDL-P and smaller overall HDL size were associated with lower CAC density in the late perimenopausal stage.

[WG#1000]


**Primary Question:**

Does the menopause transition (MT) influence regional fat distribution and waist and hip circumferences?

**Summary of Findings:** The transition from pre- to postmenopause is accompanied by an increase in central fat stores and a decrease in peripheral fat stores. Accelerated gains in visceral, android and gynoid fat mass are associated with the onset of the MT. There are no similar changes in the rates of waist or hip circumference during the MT.

[WG#1017]


**Primary Question:** Environmental exposure to heavy metals may contribute to increased blood pressure, however, evidence from midlife women who are at greater risk of cardio-metabolic disease, is limited. We evaluated the associations of urinary concentrations of arsenic, cadmium, mercury, and lead with longitudinal changes in blood pressure in the Study of Women's Health Across the Nation Multi-Pollutant Study.

**Summary of Findings:** After multivariable adjustment, estimated annualized increases (95%CI) in SBP in the highest and lowest tertiles were 0.93 (0.85, 1.01) mmHg and 0.74 (0.66, 0.82) mmHg for arsenic, 0.82 (0.75, 0.90) mmHg and 0.72 (0.65, 0.80) mmHg for mercury, and 0.86 (0.78, 0.93) mmHg and 0.72 (0.64, 0.79) mmHg for lead, respectively. Similar results were observed for associations of arsenic, mercury, lead with DBP. Urinary cadmium was associated with a greater rate of increase in SBP only among never smokers.

[WG#877MS13]
Primary Question:  Are depressive symptoms (average and change) associated with multiple measures of sleep?

Summary of Findings:  Average depressive symptoms, but not change in depressive symptoms, were associated with a multidimensional measure of sleep. Specifically, higher average depressive symptoms were associated with lower levels of sleep satisfaction and alertness, but no measures of sleep assessed with actigraphy (a research-grade Fitbit).

[WG#922]

82


Primary Question:  Are women who lose bone faster during the menopause transition more likely to fracture?

Summary of Findings:  Women who lose bone faster during the menopause transition are more likely to fracture.

[WG#785]

83


Primary Question:  TBS varies by race/ethnicity.

Summary of Findings:  There was no difference in Trabecular Bone Score (TBS) comparing White and Black women after adjusting for body mass index (BMI) and diabetes status. Japanese women had lower TBS than White women. Our results diverge from established differences in fracture rates by race/ethnicity.

[WG#867]

84


Primary Question:  Do physical activity behavior and physical functioning influence fall risk among older adult women?

Summary of Findings:  Women with low physical activity and poor physical functioning are more likely to fall compared to women with high physical activity and good physical
functioning. Women who experience declining physical functioning over time are more likely to fall, but women who increase physical activity over time are not more likely to fall. Women can be physically active to the extent they are able without increasing fall risk, even among those with physical functioning limitations.

[WG#1029]


**Primary Question:** Do women with a heavy symptom burden at enrollment have an increased risk of having or developing MetS or Diabetes.

**Summary of Findings:** This study found that women in mid-life who experienced multiple high to moderate intensity symptoms across a range of physical and mental health domains, not exclusive to menopausal symptoms, were at higher risk for earlier onset of both type 2 diabetes and MetS than women with a lower symptom burden. Specifically, women in latent symptom classes experiencing a broad range of physical and psychological symptoms at moderate to high intensity, as well as women in the latent class characterized by experience of moderate vasomotor, pain, fatigue, sleep and physical health symptoms that interfere with life but fewer psychological symptoms were at highest risk of earlier onset of MetS and type 2 diabetes.

[WG#806MS2]


**Primary Question:** Perfluoroalkyl and polyfluoroalkyl substances (PFAS) exposure have been associated with obesity and related comorbidities. However, underlying mechanisms are not well understood. Therefore, we determined if serum PFAS concentrations were associated with adipokine profiles in midlife women.

**Summary of Findings:** We found that leptin concentrations and free leptin index (the ratio of leptin to soluble leptin receptor) at a 3-year follow-up were significantly higher in women with higher baseline concentrations of various PFAS compounds. In contrast, PFAS concentrations were not associated with soluble leptin receptor, total adiponectin, or high molecular weight adiponectin.

[WG#877MS11]

Primary Question: Can the accuracy of incontinence sub-type classification be improved by adding a simple self-administered test, called the paper towel test, designed to catch leakage that results from coughing.

Summary of Findings: We conclude that adding a self-administered paper towel test to an epidemiologic study has high participant acceptance (less than 2% declined), and reduces estimation errors in presence and categorization of incontinence.

[PW#916]


Primary Question: To determine the associations of accelerometer-measured sedentary behavior and physical activity with physical performance and examine differences by race/ethnicity

Summary of Findings: Moderate to vigorous intensity physical activity was consistently related to better physical performance. Replacing 10-minutes of sedentary time for an equal amount of moderate to vigorous intensity physical activity was related to improvements on the stair climb, 40 foot walk test, and short physical performance battery. Important race/ethnic differences in the observed associations were noted for the stair climb.

[PW#924]


Primary Question: We aimed to examine associations of serum PFAS concentrations with longitudinal changes in weight, waist circumference (WC), fat mass, and proportion fat in midlife women.

Summary of Findings: PFOS, PFOA, EtFOSAA and MeFOSAA serum concentrations during midlife were positively associated with large body size and body fat in midlife women. Higher PFOS, PFHxS, EtFOSAA and MeFOSAA at baseline were also associated with accelerated increases in measures of adiposity over time. PFAS may be an underappreciated contributing factor to women's obesity risk.

[PW#877MS7]


Primary Question: Is the long-term use of sleep medications associated with improvement...
in sleep disturbances?

**Summary of Findings:** Women who started medications for sleep disturbances had not significant improvement over baseline sleep symptoms and did no better than similar women who did not start sleep medications.

These analyses are limited by their observational nature, but suggest that women who initiated sleep medications rated their sleep disturbances similar after one and two years. The potential benefits of long-term use of sleep medication should be re-examined.

[WG#968MS2]


**Primary Question:** What hormone changes are associated with negative mood and/or VMS?

**Summary of Findings:** Lower PdG excretion and a specific pattern of LH excretion associates with VMS but not negative mood. An oscillatory pattern of LH associating with VMS is consistent with episodic pituitary fatigue leading to increased kisspeptin secretion. These results suggest that increased kisspeptin may be the final step in altering vasomotor tone.

[WG#903]


**Primary Question:** Epidemiologic studies on associations between metals and adipokines have been limited and results are mixed. We examined the associations of 15 urinary metal concentrations with prospectively-assessed serum levels of adipokines including HMW adiponectin, leptin, and soluble leptin receptor (sOB-R).

**Summary of Findings:** In multivariable adjusted adaptive elastic-net models, urinary molybdenum was associated with a 5.54% higher level (95% CI: 1.36%, 9.90%), whereas cadmium was associated with a 4.53% lower level (95% CI: -8.17%, -0.76%) of HMW-adiponectin. Urinary molybdenum was also associated with a 5.95% lower leptin level (95% CI: -10.15%, -1.56%) and a 2.98% (95% CI: 0.69%, 5.32%) higher sOB-R level. Urinary cesium and lead were associated with a 3.58% (95% CI: -6.06%, -1.03%) and a 2.53% (95% CI: -4.80%, -0.21%) lower level of sOB-R, respectively.

[WG#877MS8]

93 Zhao W, Smith JA, Yu M, Crandall CJ, Thurston RC, Hood MM, Ruiz-Narvaez E, Peyser PA, Kardia SLR, Harlow SD **Genetic variants predictive of reproductive aging are associated with vasomotor symptoms in a multiracial/ethnic cohort**
Primary Question: Vasomotor symptoms (VMS), hot flashes and night sweats, are cardinal symptoms of the menopausal transition. Little is known about genetic influences on VMS.

Summary of Findings: The C-allele of rs74827081 in TACR3 was associated with reduced likelihood of frequent VMS in White women. Higher age at menarche PRS (later menarche), was negatively associated with frequent VMS in Black women but positively associated with frequent VMS in Chinese women. With higher PRS for age at menarche, Black women were also less likely to have a persistently high vs persistently low VMS trajectory while White women were less likely to have an FMP onset trajectory (vs. persistently low). Chinese women with higher menopause PRS were more likely to have frequent VMS.


Primary Question: Do the genetic loci that contribute to age at menarche and at menopause also play a role in related sentinel menopausal traits such as duration of the menopausal transition or hormone levels before or after the menopause?

Summary of Findings: Polygenic risk scores associated with onset (menarche) and ending (menopause) of reproductive life are determinants of menopausal timing and hormone levels in multiple ethnic groups


Primary Question: Are African-American women more likely than women from other racial/ethnic backgrounds to experience multiple deaths of friends and/or family members over the course of midlife? Do these deaths have an impact on carotid atherosclerosis that is stronger for African-American women compared to women from other racial/ethnic groups?

Summary of Findings: Consistent with prior research, we found a racial/ethnic disadvantage in the experience of loss—with African-American women much more likely to report three or more upsetting deaths of friends and family members throughout midlife than White, Chinese or Hispanic women. These losses were associated with greater atherosclerosis in the carotid artery for African-American women, but not White, Chinese, or Hispanic women. Our findings in African-American women were not explained by cardiovascular risk factors, including BMI, blood pressure, cholesterol, smoking, or depressive symptoms


**Primary Question:** Are adiponectin and leptin, markers of inflammation derived from fat cells, associated with subclinical cardiovascular disease in women at mid-life?

**Summary of Findings:** Adiponectin, an anti-inflammatory protein, was inversely related to higher levels of atherosclerosis and greater arterial stiffness. Analyses showed that traditional risk factors for heart disease largely accounted for these relationships. Leptin, a pro-inflammatory protein, also was associated with more atherosclerosis in the carotid arteries and these associations remained after taking into account other heart disease risk factors. This study indicates that adiponectin and leptin are important markers of inflammation that are related to risk for heart disease in women.


**Primary Question:** What are the patterns of physical activity and blood lipids across midlife in women? Are physical activity patterns associated with blood lipid patterns across midlife in women?

**Summary of Findings:** The most frequently observed patterns were consistently low physical activity, low or moderate HDL cholesterol, moderately low LDL cholesterol, and consistently low triglycerides. We did not find associations of long-term physical activity patterns with blood lipid patterns across midlife.


**Primary Question:** Social isolation and physical pain are related bidirectionally and as a function of temperament, the social environment, and disease processes, but whether and how these variables cluster in the population are unknown.

**Summary of Findings:** In two cohorts of women, regardless of age and disease status, latent class analysis produced similar sets of social-pain clusters with the same proportion in each cohort having both high social and pain symptomatology; women in this cluster also had elevated mortality.


**Primary Question:** Does increased level of CRP put women at greater risk of bone loss?
Summary of Findings: Within-woman increases in CRP levels predicted increases in the rates of bone loss in the next ~2 years and this association varied by the MT stage.

Each within-woman doubling of CRP was associated with a 0.09% faster yearly decline in femoral neck BMD in MT stages 1 (premenopause and early perimenopause) and 3 (late postmenopause), and 0.10% faster decline in lumbar spine BMD in MT stage 3 only.

[WG#1006]


**Primary Question:** Does presence of cardiovascular risk factors in midlife predict the rate of cognitive decline over midlife?

**Summary of Findings:** We showed that during midlife, women experiences declines in processing speed, working memory and delayed recall. Presence of diabetes, elevated fasting glucose, central obesity as well as a composite index of cardiovascular risk at study baseline were each associated with the midlife rate of change in processing speed. Results suggest that control of cardiovascular risk factors in midlife may prevent cognitive decline in midlife women.

[WG#547]


**Primary Question:** Our main research question was whether the patterns of sleep complaints and sleep duration over a 13-year period would be associated with objective physical function at the end of that 13-year period.

**Summary of Findings:** We found that a consistent pattern of sleep complaints and persistent insufficient sleep duration during midlife were each associated with slower gait speed and, counterintuitively, a lower likelihood of balance problems.

[WG#834]


**Primary Question:** Is the association between excessive pregnancy weight gain and maternal midlife obesity that we have observed in SWAN due to systematic error (statistical bias) in the data collection methods?

**Summary of Findings:** A history of excessive weight gain during pregnancy is associated with an increased risk of maternal midlife obesity, after accounting for bias due to participant drop-out and the use of self-report to measure pregnancy weight.

[WG#961]

Primary Question:
Question 1a: Does VAT increase around the FMP, suggesting a contribution of the menopausal transition?
Question 1b: Do Black women have greater adverse VAT changes around the FMP compared with White women?
Question 2: Do menopause-related changes in VAT increase CAROTID ARTERY ATHEROSCLEROSIS?

Summary of Findings: Women experience accelerated increase in VAT starting 2 years before the FMP, consistent with a menopause-related effect. This menopause-related increase in VAT is associated with greater risk of carotid atherosclerosis.


Primary Question: How do personal and social resources and modifiable behaviors at midlife relate to women’s psychological well-being (PWB) at later life, and does psychological resilience moderate the impact of health problems on PWB?

Summary of Findings: Several modifiable factors at midlife were associated with better PWB in older women: greater physical activity, fewer sleep problems, and less perceived stress. Psychological resilience may moderate the impact of sleep problems.


Primary Question: Do higher amounts of physical activity during middle age slow cognitive aging?

Summary of Findings: We did not find evidence that greater physical activity was related to either better cognitive scores at the beginning of the study, when women were in their 50’s, or less cognitive decline during up to 13 years of follow up.

106 Yi Y, El Khoudary SR, Buchanich JM, Miller RG, Rubinstein D, Matthews K, Orchard TJ, Costacou T. Women with Type 1 diabetes (T1D) experience a shorter reproductive period compared with nondiabetic women: the Pittsburgh Epidemiology of Diabetes Complications (EDC) study and the Study of Women's Health Across the Nation (SWAN). Menopause 2021 Mar 1;28(6):634-641. doi: 10.1097/GME.0000000000001758. PMID: 33651743

Primary Question: Whether the length of reproductive period, age at menarche, and age at
natural menopause differ in women with type 1 diabetes, compared to women without diabetes.

**Summary of Findings:** Women with type 1 diabetes onset before menarche have a shorter reproductive period compared with non-diabetic women, exhibiting delayed menarche and earlier natural menopause.

[WG#1015]


**Primary Question:** To determine whether total sleep time, wake after sleep onset, and sleep fragmentation are associated with cognitive performance, and whether the associations vary by race/ethnicity.

**Summary of Findings:** Wakefulness and physical restlessness during the sleep period are associated with impairment in processing speed among older women. However, when race/ethnicity was examined as a moderator of sleep-cognitive performance, relative to white women, black women had less cognitive resiliency to worse sleep. Sleep-cognitive performance associations in Chinese and Japanese women were not different from white women.

[WG#934]

108 Cortés YI, Brooks M, Barinas-Mitchell E, Matthews KA, Thurston RC, Catov JM  Impact of prior preterm or term small for gestational age birth on maternal blood pressure during the menopause transition in the Study of Women's Health Across the Nation  Menopause 2021 Feb 8;28(3):255-262. doi: 10.1097/GME.0000000000001739. PMID: 33570873

**Primary Question:** Does blood pressure accelerate more rapidly during the menopause transition for women with a history of a preterm birth or term small for gestational age birth compared to women with all term and appropriate for gestational age births?

**Summary of Findings:** This study suggests that women with a history preterm and term SGA delivery have higher BP than women with all term AGA births during the menopause transition, but that rate of change in BP does not differ in these group relative to final menstrual period. Our results highlight that earlier interventions prior to menopause may be necessary among women with a preterm or term SGA delivery to prevent elevated BP in midlife and future CVD.

[WG#836]


**Primary Question:** Are menopausal vasomotor symptoms (VMS) associated with risk of incident cardiovascular disease (CVD) events?

**Summary of Findings:** Women with frequent VMS at baseline or persistently frequent VMS over the course of the study have increased risk for incident CVD / CVD mortality. Findings

**Primary Question:**

**Summary of Findings:**

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**Primary Question:**

Does HDL-C increase reflect a cardio-protective profile of HDL composition and function in women traverse menopause?

**Summary of Findings:** Although HDL-C increased over the MT, measures of HDL composition showed a dramatic adverse changes. While HDL-CEC seemed to increase, HDL-CEC per particle declined. Large HDL-P may be compromised and became less efficient in promoting HDL-CEC during the MT

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Matthews KA, Chen X, Barinas-Mitchell E, Brooks MM, Derby CA, Harlow S, Jackson EA, Thurston RC, El Khoudary SR. *Age at Menopause in Relationship to Lipid Changes and Subclinical Carotid Disease Across 20 Years: Study of Women’s Health Across the Nation*

**Primary Question:** (1) Do women who are older at FMP have less adverse lipid changes around the FMP and thereafter into the postmenopausal years? (2) Do the hypothesized less adverse changes associated with older age at FMP predict less carotid plaque, intima-media thickness, and adventitial diameter measures later in life?
Summary of Findings: Despite the epidemiological literature showing early age at FMP is associated with elevated risk for CVD events and all-cause mortality, we found that later age of FMP had inconsistent associations with lipid changes in mid-life and that the observed changes did not translate into less risk for subclinical carotid disease and in some cases more risk. [WG#949]

114 Lee S, Karvonen-Gutierrez C, Mukherjee B, Herman WH, Harlow SD, Park SK. Urinary concentrations of phenols and parabens and incident diabetes in midlife women: The Study of Women's Health Across the Nation
Primary Question: Although environmental exposure to personal care and product chemicals may play a role in the pathogenesis of diabetes, only a few phenols, most notably bisphenol A, have been studied with limited data. We examined associations between personal care and consumer product chemicals, assessed in urine at two time-points, and incident diabetes in the Study of Women's Health Across the Nation (SWAN), a multi-ethnic prospective cohort of midlife women.
Summary of Findings: We observed consistent inverse associations between parabens and incident diabetes at the Multi-pollutant study (MPS) baseline (1999-2000) and three-year later (2002-2003). Triclocarban with the 3-year exposure later baseline, dichotomized (yes/no) due to low detection rates (<15%), was positively associated with incident diabetes. Positive associations were found for 2,4-dichlorophenol only with the MPS baseline and for bisphenol-A only with the 3-year exposure later baseline. No significant associations were observed for the overall joint effect of phenol and paraben mixture at either time-points. [WG#877MS9]

Primary Question: Does HDL offer less of a protective effect with respect to atherosclerosis in women with lower levels of estradiol compared to women with higher levels? Does increased inflammation explain this difference?
Summary of Findings: SWAN Heart Cohort
The protective cardiovascular association of higher HDL-C levels on AC was modified by estradiol but not CRP concentrations, suggesting a concentration of estradiol level to this association. The pathways through which estradiol might impact this association should be investigated in future studies [WG#945]

Primary Question: What is the prevalence of vision impairment and age-related eye diseases among older women and does it differ by important sociodemographic variables?
Summary of Findings: Although nearly one in 10 Michigan SWAN women were defined as having vision impairment (worse than 20/40 in their better seeing eye) when using their usual correction, the vast majority (75%) of this was able to be corrected. Although there were important disparities in presenting vision impairment by race/ethnicity, economic strain and education, these differences did not persist after optimal correction. Further, despite high burden of ocular conditions, ranging from 3.3% for age-related macular degeneration to 30.2% for hypertensive retinopathy, more than half of women with a given condition were unaware of their diagnosis.

[WG#967]


Primary Question: Summary of Findings: We tried multiple ways of summarizing the social role experience of women over mid-life. Women who had a social role that was “extremely” or “quite a bit” stressful during mid-life had worse carotid intima-media thickness than women who never reported a stressful social role. Rewarding social roles were not related to better cardiovascular disease health.

[WG#850A]


Primary Question: How does the use of medications impact sleep?

Summary of Findings:

[WG#968]


Primary Question: Is multidimensional sleep health longitudinally associated with body mass index and waist-to-hip ratio?

Summary of Findings: There were no substantial changes in body mass index or waist-to-hip ratio from the sleep study to the follow-up assessment. Better sleep health was not longitudinally associated with body mass index or waist-to-hip ratio after accounting for adiposity at the sleep study.

[WG#923]

Primary Question: Is race/ethnicity associated with self-reported receipt of statins among women eligible for statin therapy

Summary of Findings: Women who would benefit from statins (i.e., those with a diagnosis of cardiovascular disease [CVD], diabetes, very high low-density lipoprotein cholesterol (LDL-c) and an elevated risk for CVD events had suboptimal rates of statin us. Less than half of women CVD reported using statins. Black women had lower rates of statin use compared to white participants.

[WG#794]


Primary Question: Do women with a history of nulliparity, hypertensive disorders of pregnancy [HDP], or gestational diabetes mellitus [GDM]) have a higher odds of reporting vasomotor symptoms (VMS) at midlife?

Summary of Findings: Compared to women with no HDP/GDM, women with HDP/GDM had a greater odds of reporting any hot flashes, and nulliparous women had a lower odds of any hot flashes. Similar patterns were observed for frequency of hot flashes, but not independently of socio-demographic factors. Our findings underscore the importance of social and economic disparities in both reproductive outcomes and VMS.

[WG#879]


Primary Question: Summary of Findings:

[WG#1016PUD]


Primary Question: Epidemiologic studies on associations between metals and insulin resistance and β-cell dysfunction have been cross-sectional and focused on individual metals. We assessed the association between exposure to metal mixtures, based on assessment of 15 urinary metals, and longitudinal changes in homeostatic model assessments for insulin resistance (HOMA-IR) and β-cell function (HOMA-β).

Summary of Findings: In multivariable adjusted adaptive elastic-net models, urinary copper, lead, and zinc were associated with higher HOMA-IR at baseline, whereas molybdenum was associated with lower HOMA-IR at baseline. The estimated changes in
baseline HOMA-IR for one standard deviation increase in log-transformed urinary metal concentrations were 1.57% (-1.09%, 4.29%) for copper, 0.70% (-1.59%, 3.05%) for lead, 5.76% (3.05%, 8.55%) for zinc, and -3.25% (-5.45%, -1.00%) for molybdenum, respectively. Urinary zinc was also positively associated with a faster rate of increase in HOMA-IR. Urinary arsenic and zinc were associated with lower baseline HOMA-ß, whereas cobalt was associated with higher baseline HOMA-ß. Arsenic was also associated with a faster rate of decline in HOMA-ß.

[WG#877MS6]


Primary Question: Summary of Findings:


Primary Question: Summary of Findings: We noted important baseline differences in women who did and did not report future sleep disturbances or use of medications for sleep. These include differences in anxiety and pain scores, as well as comorbid conditions. These baseline population differences have been reported in prior studies, but herein we report novel longitudinal data. There was a 3-4 fold rise in medication use for sleep over follow-up; this was observed in all race and ethnicities.

Women who did and did not report sleep disturbances were similar in age, BMI, and socioeconomic backgrounds at baseline (Table 1). However, women reporting sleep disturbances were more likely to have higher anxiety and pain scores and more comorbid conditions. Baseline characteristics were quite similar among women who did and did not use sleep medications during follow-up.

Figure 1a illustrates the 20-year time trends in sleep medication use for women who did and did not report sleep disturbances. In 1997, even among those women who reported sleep disturbances during follow-up, only 2.5% reported use of any sleep medication. This percentage increased to 8% over 20 years. However, the proportion of women reporting sleep medication use who did not report a sleep disturbance remained low, approximately 1-2% over the entire follow-up.

Finally, we examined the rates of medication use among women who reported a sleep
disturbance by race and ethnicity (Figure 1b). There were increases across all races/ethnicities. However, there were substantial racial/ethnic differences in the proportion of women using these medications.

[WG#968MS1]

\textbf{Primary Question:} Can VALENCIA (VAginaL community state typE Nearest Centroid clAssifier), a tool developed to classify vaginal samples into community state types (CSTs) developed from over 13,000 reference vaginal samples from mostly reproductive age women in the U.S. be used for assignment of samples to CSTs from other data sets, including postmenopausal women and women from other regions of the world?

\textbf{Summary of Findings:} VALENCIA provides a much-needed solution for the robust and reproducible assignment of vaginal CSTs, including for postmenopausal women. This will allow unbiased analysis of both small and large vaginal microbiota datasets, comparisons between datasets and meta-analyses that combine multiple datasets.

[WG#977MS2]

\textbf{Primary Question:} How does exposure to coarse particles influence midlife women’s inflammation and coagulation markers?
\textbf{Summary of Findings:} Long-term exposures to coarse particles may increase the risks of thrombosis. This effect was independent from exposures to PM2.5 and other ambient gaseous pollutants.

[WG#935_MS]

\textbf{Primary Question:} Does baseline or early postmenopausal trabecular bone score (TBS) predict fracture?
\textbf{Summary of Findings:} Our results indicate that variation in premenopausal TBS, a plausible estimate of peak TBS, is related to fracture risk, but this association is not independent of BMD. Our data suggest that the in early postmenopause, the risk of fracture associated with TBS is of a similar magnitude to that observed in premenopause, but our power to detect an association in this group is insufficient to warrant a conclusion.

[WG#862]
Primary Question: How much of the impact of race/ethnicity on physical performance is due to differences in financial strain, body size, health conditions, physical activity and perceived stress?

Summary of Findings: This study of racial/ethnic differences in physical performance confirmed that disparities in physical function experienced by older African American and Hispanic women are apparent in mid-life, and that midlife Chinese women also suffer a disparity in physical performance, while Japanese women do not. Some, almost all of the racial/ethnic disparities in physical performance in African Americans and Hispanics can be explained by known socioeconomic, medical, behavioral, or psychosocial factors, but these factors do not account for the disparity in the Chinese.


Primary Question: Can women be grouped into distinct groups based on combinations of trajectories of FSH, frequent VMS, and sleep maintenance problems during the menopausal transition? Do race/ethnicity, body mass index, and depressive symptoms predict group membership?

Summary of Findings: Women can be classified into five distinct groups based on shared patterns of FSH, frequent VMS, and sleep maintenance problems based on trajectories 10 years before and after final menstrual period. Either VMS or sleep maintenance problems can be dominant in the face of high FSH. Race/ethnicity, body mass index, and depressive symptoms at baseline and change in depressive symptoms during the early phase of the transition predict group membership.


Primary Question: What is the relationship between peripheral nerve impairment and recurrent falls (and recurrent fall injuries) among early old age women?

Summary of Findings: Approximately one-quarter of participants had at least 4 peripheral nerve impairment symptoms or monofilament insensitivity. Peripheral nerve impairment may
identify those at high risk for falls, particularly among women during early late life.

[WG#909]

132 Appelhans BM, Lange-Maia BS, Pettee Gabriel K, Karvonen-Gutierrez C, Karavolos K, Dugan SA, Greendale GA, Avery EF, Sternfeld B, Janssen I, Kravitz HM. Body mass index versus bioelectrical impedance analysis for classifying physical function impairment in a racially diverse cohort of midlife women: The Study of Women’s Health Across the Nation (SWAN)


**Primary Question:** Can estimates of body fat and muscle mass derived from bioimpedance measures be used to accurately classify women with and without impairments in physical function?

**Summary of Findings:** Body mass index and percentage body fat do reasonably well for identifying women with impaired physical function. However, different cutpoints should be used for different racial/ethnic groups. Information on muscle mass does not improve the ability to classify women on physical function impairment.

[WG#885]


**Primary Question:** Are HDL and LDL metrics (HDL-C and LDL-C; HDL and LDL particles [HDL-P and LDL-P]; HDL and LDL size) related to vasomotor symptoms (VMS), and does endogenous estradiol affects this association?

**Summary of Findings:** After adjusting for potential confounders (age, site, race/ethnicity, education, menopausal status, physical activity, alcohol use and BMI), severe VMS was associated with smaller HDL size and higher LDL-C, compared to no VMS. Linear trends also showed additional associations between increased VMS and higher total LDL-P and intermediate LDL-P. Additional adjustment for endogenous estradiol attenuated these associations.

[WG#996]

134 Ding N, Harlow SD, Randolph JF, Calafat AM, Mukherjee B, Batterman S, Gold EB, Park SK. Associations between Perfluoroalkyl Substances and Incident Natural Menopause: the Study of Women's Health Across the Nation 1999-2017

J Clin Endocrinol Metab. 2020 Sep 1;105(9):dgaa303. doi: 10.1210/clinem/dgaa303. PMID: 32491182 PMCID: PMC7418447

**Primary Question:** We examined the associations between PFAS exposures and incidence of natural menopause in the multi-racial/ethnic sample of women who were premenopausal at baseline from a prospective cohort, i.e., the Study of Women’s Health Across the Nation (SWAN), with standard approximately annual clinic visits from 1999-2017, and assessed whether the relationship differed by racial/ethnic groups. We next identified subgroups exposed to different patterns of PFAS using the k-means clustering method and evaluated the combined effects of PFAS mixtures on natural menopause.

**Summary of Findings:**

**Primary Question:** Does glomerular filtration rate change over the menopausal transition?

**Summary of Findings:** GFR declines, but no more than would be expected by age. Declines in GFR are associated with declines in FSH and SHBG but not with changes in sex steroids (estradiol, testosterone).


**Primary Question:** Is melatonin, a hormone that controls sleep-wake cycles in humans, also involved in the control of the menstrual cycle?

**Summary of Findings:** We found a rise in aMT6s, a melatonin metabolite that appears in the urine, at the end of the menstrual cycle (just before menses occurs). We believe that melatonin helps to regulate the menstrual cycle. After menopause, the amount of melatonin in the urine declines, suggesting that a drop in melatonin may be partly responsible for some of the symptoms of menopause.


**Primary Question:** The primary objectives of this study were to: 1) describe and compare changes in physical activity from pre- to post-diagnosis (or corresponding time period) in breast cancer survivors (BCS) and controls and 2) in BCS only, evaluate pre-diagnosis predictors of at-risk patterns of physical activity change, post-diagnosis (consistently low and decreased physical activity) to more effectively identify BCSs in greatest need of intervention or referral to physical activity programs.

**Summary of Findings:** The main findings of this study suggested that physical activity changes from pre- to post- breast cancer diagnosis were not statistically significantly different from similarly aged controls. While the majority (54.9%) of BCSs maintained sports/exercise physical activity levels post-diagnosis, 26.8% and 18.3% of BCSs increased and decreased physical activity post-diagnosis, respectively. Pre-diagnosis sleep problems and overweight/obesity status predicted decreased or consistently low physical activity post-diagnosis. Stage of breast cancer diagnosis and treatment were not statistically significant predictors of physical activity change, post-diagnosis.

[WG#877MS5] [WG#930] [WG#1026] [WG#863]
Primary Question:
Summary of Findings:

Asian populations including both Chinese and Japanese women were found to have higher concentrations of arsenic, cadmium, copper, mercury, molybdenum, lead, thallium, compared with other racial/ethnic groups, independent of sociodemographic, lifestyle, dietary, and geographic characteristics. Intake of seafood and rice was associated with high concentrations of arsenic, cesium, mercury, molybdenum and lead in urine samples. Chinese women had the highest overall exposure compared with other racial/ethnic groups.

Primary Question:
Summary of Findings:

Physical function declined with the development of a new condition, and women who had more chronic conditions had a faster decline in physical function when they developed a new condition.

Primary Question:
Summary of Findings:

Breast cancer survivors had significantly lower HRQL, compared to non-cancer controls, at diagnosis and 1 year post-diagnosis. By 2 years post-diagnosis,
survivors and controls no longer differed significantly. Higher perceived stress prior to diagnosis, cigarette smoking, and and having >2 comorbidities were predictors of low HRQL after diagnosis.

[WG#926]


**Primary Question:**

**Summary of Findings:**

[WG#1003PUD]


**Primary Question:** Does midlife aging across 12 years result in change in women’s sleep duration, continuity, and timing as measured by actigraphy?

**Summary of Findings:** Mid-life aging is associated with improved sleep duration and wake after sleep onset, worse latency, and later sleep midpoint as measured by actigraphy; there is no change in self-reported sleep complaints. These results were independent of other changes in women’s lives, including the menopausal transition, stress, and health problems.

[WG#942]


**Primary Question:** When do women experience changes in arterial stiffness relative to the final menstrual period?

**Summary of Findings:** The results of this study showed that women experience increases in central arterial stiffness in the one year period surrounding the FMP. This increase is independent of aging, mid-life CVD risk factors, estradiol, and FSH.

[WG#896]


**Primary Question:**

**Summary of Findings:** An accelerated decline in perceptual (processing) speed, but not memory, may occur in women with metabolic syndrome at midlife. These changes in perceptual speed persisted after adjustment for sociodemographic factors (including site-race/ethnicity and education effects on time), and time-varying lifestyle, mood and
Importantly, practice effects in cognitive testing substantially affected the models of perceptual speed up to 2 follow up cognitive assessments (or up to a mean 3.8±2.1 years after cognitive baseline).

In sum, our results indicate that metabolic syndrome accelerated 10-year decline in perceptual (processing) speed by an additional 6.4 years of aging, and persisted after adjustment for sociodemographic, lifestyle, mood and menopause factors.

[WG#759]


Primary Question: How well does a single measurement antimullerian hormone (AMH) predict the time to a woman’s final menstrual period (menopause)?

Summary of Findings: A single AMH level was able to help a woman know that she could become menopausal within as little as one year, depending on her age.

[WG#454]


Primary Question: Does trabecular bone score (which corresponds to bone strength) decline during the menopause transition?

Summary of Findings: Before the onset of the menopausal transition (MT), TBS was stable in White women with overall sample average BMI and age at final menstrual period (FMP). Decline in TBS began 1.5 years before the FMP, averaging 1.16% per year, a 10-fold change in rate. Two years after the FMP, the rate of TBS decline slowed, but did not stop, averaging 0.89% annually.

[WG#966]


Primary Question: Is faster increase in bone turnover during the menopause transition associated with future fracture?

Summary of Findings: Faster increase in bone turnover during the menopause transition is associated with future fracture.

[WG#946]


**Primary Question:** How much does the self-reported physical activity questionnaire correlate with the accelerometer-measured physical activity in SWAN V? Is this correlation different in different racial or ethnic groups?

**Summary of Findings:** SWAN women are predominantly sedentary, but participate in significant amounts of low-light and high-light physical activity, which may have implications for their future physical health and function. The SWAN physical activity questionnaire had moderate correlation with accelerometry measures, with more frequent statistically significant correlations among white women for the sub-scores.

[WG#911]


**Primary Question:** Are dietary patterns during the midlife associated with measures of subclinical carotid atherosclerosis later in life?

**Summary of Findings:** Among midlife women, the adoption of a diet low in red meat, processed meat, deep-fried products, and sugar-sweetened beverages among midlife women may protect against future atherosclerosis.

[WG#871]


**Primary Question:**

**Summary of Findings:** We identified 4 groups of women who shared a common pattern of sleep maintenance problems throughout the observation period: low pre-surgery prevalence of frequent awakenings (33.5% of women), moderate prevalence (33.0%), increasing prevalence beginning pre-surgery (19.9%), and high prevalence. Frequent awakenings post- surgically in each of the 4 groups were significantly associated with their pre-surgical sleep maintenance problems, and except for one group (which included ~20% of the women) that had a pattern of increasing sleep maintenance problems, did not change during the post-surgery follow-up.

[WG#644A]

Primary Question: 1) Is child maltreatment associated with lower health-related quality of life (HRQoL) and quality-adjusted life years (QALY) and the rate of change in these measures over a 9-year follow-up? 2) Are these associations explained by adulthood psychosocial mediators over time?

Summary of Findings: Any CM was associated with both reduced midlife mental and physical HRQoL over 9 years. Compared to women without CM, women who experienced multiple CM types reported 5 and 4 points lower in MCS and PCS, respectively, and 28 fewer healthy days per year for QALY. But the rate of change over time in these measures was similar between women with and without CM. In longitudinal mediation analyses, low levels of optimism, sleep problems, and low social support each explained >10% of the relationship between multiple CM types and HRQoL and QALY.


Primary Question: Does vascular health measured in late midlife differ by race and ethnicity? Does the effect of traditional risk factors measured from early to late midlife on vascular health differ by race and ethnicity?

Summary of Findings: In late midlife women carotid arterial measures of vascular remodeling and atherosclerosis vary by race/ethnicity. Compared to White women, measures of carotid arterial remodeling (CCA-IMT and IAD) were worse in Black women, similar in Hispanic women, and worse or similar in Chinese women; Yet, carotid plaque, a measure of atherosclerosis, was less prevalent in Black and Hispanic women and of similar prevalence in Chinese women. Despite the racial/ethnic inconsistency between subclinical vascular disease burden and cumulative CVD risk factors assessed across the menopause transition, there was no strong evidence that race or ethnicity consistently moderated the effects of traditional CVD risk factors on individual subclinical vascular disease indices.


Primary Question:

Summary of Findings: Women who reported lack of food access were more likely to report making meals at home (p=0.021) but had less frequent consumption of fresh fruits, fresh vegetables, and lean meats as compared to those that did not report a lack of food access (p=0.04, p=0.001, p=0.048). Being African American (OR: 2.49; 95% CI: 1.20-5.17) and experiencing economic stress (OR: 2.86; 95% CI: 2.53-5.33) were major correlates of reporting lack of food access.

Pavlovic J, Derby C, Crawford S  
**Daily luteal serum and urinary hormone profiles in the menopause transition: Study of Women's Health Across the Nation**  

**Primary Question:** Do blood levels of reproductive hormones match the levels that are seen in urine in midlife women, and is blood peak progesterone lower close to FMP, the same as urine progesterone?  
**Summary of Findings:** Blood and urine hormones are closely related to each other in women in their 50's. Blood progesterone matches urine progesterone but the relationship is weak.  
[WG#957]

**The Effect of Gestational Weight Gain across Reproductive History on Maternal Body Mass Index: The Study of Women's Health Across the Nation.**  
PMID:31794347  PMCID:PMC7045562

**Primary Question:** Our analysis found that each additional pregnancy a woman experienced with excessive gestational weight gain increased the odds of having an obese BMI at midlife, regardless of the total number of births in a woman’s life.  
[WG#410]

Ding N, Harlow SD, Batterman S, Mukherjee B, Park SK  
**Longitudinal trends in perfluoroalkyl and polyfluoroalkyl substances among multiethnic midlife women from 1999 to 2011: The Study of Women’s Health Across the Nation.**  
PMID: 31841808. PMCID: PMC7374929

**Primary Question:** This study examined temporal variations in serum concentrations of per- and polyfluoroalkyl substances (PFAS), a family of synthetic compounds widely used in a variety of industrial applications and consumer products, such as non-stick cookware, carpeting, apparels, food packaging, and firefighting forms, in midlife women. Specifically, we explored how patterns of exposure differ by race/ethnicity and reproductive characteristics.  
**Summary of Findings:** Serum concentrations of legacy compounds (e.g. perfluorooctanoic acid, PFOA, and perfluorooctane sulfonic acid, PFOS) decreased significantly; whereas their replacements (e.g. perfluorononanoic acid, PFNA) increased from 1999-2011. Temporal variations varied significantly by race/ethnicity. For example, Chinese women tended to have consistently higher PFNA concentrations at each follow-up visit, compared to white and black women. Menstruating women also had lower concentrations over time. Parity was associated with lower concentrations at baseline but the differences between nulliparous and parous women narrowed during the follow-up visits.  
[WG#877MS3]

Shieh, A., Epeldegui, M., Karlamangla, A. S., Greendale, G. A  
**Gut permeability, inflammation, and bone density across the menopause transition**  
PMID: 31830000 PMCID: PMC7098720

**Primary Question:** Does gut permeability increase during the menopause transition?  
**Summary of Findings:**
Gut permeability increases during the menopause transition, and higher gut permeability is associated with more inflammation and lower bone mineral density.

[WG#1002]


**Primary Question:** Does reporting of menopausal symptoms vary by season.

**Summary of Findings:** Reporting of hot flashes, night sweats and trouble sleeping varied by season, with peaks in reporting occurring around the time of the summer solstice (longest period of daylight) and troughs occurring around the time of the winter solstice (shortest period of daylight).

[WG#744]


**Primary Question:** Can measuring estradiol or follicle stimulating hormone help identify who will experience loss of bone mineral density by the next year.

**Summary of Findings:** Measuring follicle stimulating hormone can help identify who will experience significant loss of bone mineral density by the next year.

[WG#894]


**Primary Question:**

**Summary of Findings:** Check a marker of bone breakdown after women begin to experience less predictable menstrual bleeding helps predict how fast a woman will lose hip strength during the menopause transition.

[WG#881]


**Primary Question:**

**Summary of Findings:** Greater volume of peri-aortic fat (PVAT) in women at midlife were associated with lower gait speed later in life, independent of overall adiposity, comorbid conditions and other possible confounders.

[WG#882]

**Primary Question:**

**Summary of Findings:**


**Primary Question:**

**Summary of Findings:**


**Primary Question:**

**Summary of Findings:**


**Primary Question:**

**Summary of Findings:**

Overall women’s stair climb time got slower over the follow-up period. We found that higher levels of physical activity were associated with better performance on the stair climb test over time. Also, compared to white women, black women on average had slower stair climb times, which is consistent with some other studies which have shown racial disparities in physical function between white and black women.

Primary Question: Summary of Findings: There is a significant association between perceived discrimination and peripheral neuropathy (Odds ratio = 1.29, 95% CI 1.01, 1.66) and this association is 28.3% (95% CI 17.1, 36.5%) mediated by body mass index.


Primary Question: Summary of Findings:


Primary Question: Summary of Findings: Coffee intake during the midlife in women is associated with a larger CCA-IMT in the future except among women who consumed more than 4 cups of coffee per day. Moderate alcohol intake is associated with a smaller CCA-IMT later in life.


Primary Question: Summary of Findings:


Primary Question: Summary of Findings: There was evidence of an increased risk in fractures among women
initiating blood pressure lowering medications compared to those initiating anti-depressants. This is likely related to an increased risk of falling.

[ WG#887]

Moody DLB, Chang YF, Pantesco EJ, Darden TM, Lewis TT, Brown C, Bromberger JT, Matthews KA  
Everyday Discrimination Prospectively Predicts Blood Pressure across 10 Years in Racially/Ethnically Diverse Midlife Women: Study of Women's Health Across the Nation  
PMID: 30247506; PMCID: PMC6428619.

Primary Question:
Summary of Findings:  
Higher exposure to everyday discrimination at baseline predicted elevated SBP and DBP over the 10-year period in semi-adjusted (including age and time) and fully-adjusted models (also including site, visit, race/ethnicity, education, family history of hypertension, smoking status, medication use, and menopausal and diabetes status). All associations were attenuated upon adjustment for BMI. These associations did not vary by race/ethnicity and models did not predict HTN risk.

[ WG#431]

Residential Exposure to PM2.5 and Ozone and Progression of Subclinical Atherosclerosis Among Women Transitioning Through Menopause: The Study of Women's Health Across the Nation.  
Epub 2019 Feb 7. PMID: 30730252 PMCID: PMC6590715.

Primary Question:
Summary of Findings:  
Among midlife women PM2.5 independently contributed to progression of maximum CIMT, a marker of subclinical atherosclerosis. PM2.5 related to plaque index progression after adjusting for socioeconomic factors, but not after adjusting for other traditional cardiovascular risk factors. There was no association between ozone (O3) and progression of subclinical atherosclerosis biomarkers.

[ WG#819]

Serum Sex Hormones and the Risk of Fracture Across the Menopausal Transition: Study of Women's Health Across the Nation.  
PMID: 30690517 PMCID: PMC6505454

Primary Question:
Summary of Findings:  
We found an inverse association between serum estrogen levels and subsequent fractures: Women whose estradiol level was twice as high as another had a 10% lower risk of fracture

[ WG#849]

Wang X, Mukherjee B, Batterman S, Harlow SD, Park SK  
Urinary metals and metal mixtures in midlife women: The Study of Women’s Health Across the Nation (SWAN)  
Epub 2019 May 15. PMID: 31103473. PMCID: PMC6583796.

Primary Question:
Summary of Findings:  
Asian populations including both Chinese and Japanese women...
were found to have higher concentrations of arsenic, cadmium, copper, mercury, molybdenum, lead, thallium, compared with other racial/ethnic groups, independent of sociodemographic, lifestyle, dietary, and geographic characteristics. Intake of seafood and rice was associated with high concentrations of arsenic, cesium, mercury, molybdenum and lead in urine samples. Chinese women had the highest overall exposure compared with other racial/ethnic groups.


Primary Question:
Summary of Findings: Our study showed that the HSA parameters showed accelerated change around the time of the FMP, i.e., 2 years before to 1 year after the FMP (transmenopausal period). The HSA parameters, bone mineral density (BMD), cross sectional area (CSA) and Section modulus (SM) showed significant decline in the transmenopausal period and over the 10-year period, while outer diameter (OD) and buckling ratio (BR) showed significant increase. In addition, the results reflected the racial/ethnic differences in the hip geometry and its changes over time with Caucasian women suffering largest change both during the transmenopausal period and over 10 years. The rate of change of these parameters could contribute to further understanding of the increased fracture risk with age.


Primary Question:
Summary of Findings: Whites had longer sleep duration than other racial/ethnic groups; less wake after sleep onset (WASO) than Black or Hispanic women, and better sleep quality than Chinese or Japanese women. For WASO differences by White vs Black or Hispanic women, significant mediators included concurrent number of health problems, physical inactivity, proportion of nights reporting vasomotor symptoms, number of life stressors, and financial hardship and increasing number of health problems and life stressors from baseline to sleep study. For perceived sleep quality differences by White vs Chinese or Japanese, significant mediators included positive affect, depressive symptoms, and increasing in depressive symptoms from baseline to the sleep study. For racial/ethnic differences in sleep duration, only concurrent financial hardship served as a significant mediator for Whites vs Hispanics.

Primary Question:
**Summary of Findings:** Constellations over time of cardiometabolic risk components in midlife women depend on race/ethnicity but apparently not stage of menopausal transition. Physical activity is associated with a decreased risk of various common constellations and less dietary caloric intake is associated with recovery from metabolic syndrome over an average of 5 years.

[WG#752]


Primary Question:
**Summary of Findings:**

[WG#786PUD]


Primary Question:
**Summary of Findings:** We identified six latent symptom classes that ranged from highly or moderately symptomatic across all measured symptoms, to moderately symptomatic for a subset of symptoms that might be denominated as vasomotor symptoms, pain, fatigue, and sleep disturbances, to mildly symptomatic across most symptoms measured, to minimally symptomatic. The least symptomatic latent class reported only a few, very mild fatigue, pain and sleep disturbances symptoms. Notably, vasomotor symptoms tended to cluster with symptoms of sleep disturbances and fatigue. Although women did both worsen and improve across the midlife, women tended to track within latent class and menopausal stage did not influence the probability of transition from one latent class to another. Notably fully one-quarter of the women were highly or moderately symptomatic across all measured symptoms in the pre-menopause and the more symptomatic latent classes was strongly associated with worse self-reported health.

[WG#806]


Primary Question:
**Summary of Findings:** Long-term exposure to PM2.5 in early mid-life independently contributes to atherosclerosis as measured by mean of maximum CCA at later mid-life in
multi-ethnic population based cohort of women. However, we did not observe the effect of ozone. And, no association between air pollution and plaque or plaque index was established.


Primary Question:
Summary of Findings: In the average woman, fat and lean mass increased prior to the menopause transition (MT). At the start of the MT, the rate of fat gain doubled and lean mass started to decline; gains and losses, respectively, continued until 2 years after the final menstrual period. Weight climbed linearly during premenopause without acceleration at the beginning of the MT; it stabilized (there was no further increase) after the MT.


Primary Question:
Summary of Findings: The alpha2C del (322-325) genotype was not associated with increased frequency or bother of VMS, hot flashes, or night sweats, in African American women.


Primary Question:
Summary of Findings:


Primary Question:
Summary of Findings: We identified 7 trajectories which we reduced to 5: very low symptoms, consistently low symptoms, increasing symptoms, decreasing symptoms, consistently elevated symptoms. multiple time-invariant and time-varying factors significantly distinguished among the trajectories.

Primary Question: Summary of Findings: Measuring a marker of bone breakdown in the urine when women are having regular or just starting to have irregular menstrual cycles may help identify who will experience loss in bone mineral density over the next several years.

[WG#880]


Primary Question: Summary of Findings: Immediate post-WHI recommendations for ET use were widely adopted. Contrary to current clinical guidelines, however, women with frequent vasomotor symptoms, were less likely post-WHI to use ET.

[WG#890]


Primary Question: Summary of Findings: A healthy lifestyle during midlife is associated with less subclinical atherosclerosis in women later in life. Among the three individual components of the HLS, abstinence from smoking had the strongest association with the measures of subclinical atherosclerosis.

[WG#700]


Primary Question: Summary of Findings:

[WG#960E]


Primary Question: Summary of Findings:

[WG#960D]

Primary Question:
Summary of Findings: Women in the lowest TAT radiodensity tertile were significantly more likely to be White and to have adverse cardiovascular risk factors. Independent of cardiovascular risk factors, women in the middle and high TAT radiodensity tertiles were less likely to have CAC. Although adjusting for BMI attenuated the overall association, women in the middle TAT radiodensity tertile remained at significantly lower odds of CAC when compared to women in the low radiodensity tertile.


Primary Question:
Summary of Findings:


Primary Question:
Summary of Findings:


Primary Question:
Summary of Findings:


Primary Question:
Summary of Findings:

Primary Question:  
Summary of Findings:  


Primary Question:  
Summary of Findings:  Childhood maltreatment was a robust risk factor for reduced midlife mental and physical HRQoL in women. The association between CM and HRQoL MCS was partially explained by the proximal adulthood psychosocial mediators: depressive symptoms, very upsetting life events, or low social support.


Primary Question:  
Summary of Findings:  


Primary Question:  
Summary of Findings:  


Primary Question:  
Summary of Findings:  


**Primary Question:**

**Summary of Findings:**


**Primary Question:**

**Summary of Findings:** In this pooled study that included 21,312 midlife women from eight observational studies, we observed a prospective bi-directional relationship between VMS and depressed mood. Baseline sleep difficulties largely affected the relationship between VMS and subsequent depressed mood over three years, but it had little impact on the relationship between depressed mood and subsequent VMS.


**Primary Question:**

**Summary of Findings:** Depressive symptoms measured at the start of the study were associated with 1 of the 2 hormones we assessed – i.e., with adiponectin but not with leptin. Women who reported more depressive symptoms at baseline had lower levels of adiponectin, an anti-inflammatory hormone, both at baseline and at subsequent follow-up visits, compared to women with few or no depressive symptoms at baseline. However, we did not find a greater decline in concentrations of adiponectin over time for women with more depressive symptoms – that is, depression did not accelerate the rate of change in adiponectin over the 5-year study period. The study findings indicate depression is associated with a “dampening” of adiponectin levels in middle-aged women, which may help explain how depression affects risk for heart disease and diabetes in women as they age.


**Primary Question:**

**Summary of Findings:**

Primary Question:
Summary of Findings: With aging, physical health scores declined and mental health scores improved. Increasing physical activity, lowering BMI, not smoking, and improving sleep are modifiable factors at mid-age that are associated with better HRQL.


Primary Question:
Summary of Findings: All women in the cohort had an increase in their morphologic indices of subclinical atherosclerosis assessed by carotid artery inner lining thickness and coronary artery calcium from baseline to follow-up, but the increase was similar in the three groups. The physiologic marker of subclinical atherosclerosis, assessed by aortic stiffness, increased in the transition group alone with no significant change in the premenopausal or postmenopausal women. There was no correlation between these indices during the follow-up period. Changes in aortic stiffness were more sensitive measures of perimenopausal vascular aging than morphological indices of subclinical atherosclerosis in women undergoing the menopausal transition.


Primary Question:
Summary of Findings: Vaginal dryness increases from 19.4% among all women at baseline (ages 42-53 years) to 47.0% of women sexually active, and 25.3% of women not sexually active at visit 13 (ages 57-69 years). Advancing menopause, surgical menopause (hysterectomy and removal of ovaries), anxiety and marital status were associated with new reports of vaginal dryness, regardless of sexual activity. For women not using hormone therapy, higher levels of estrogen reduced the risk of developing vaginal dryness, while neither testosterone nor DHEAS levels had no effect on this risk. Although vaginal dryness was not associated with subsequent reporting of pain during intercourse, lubricant use in the year before reports of vaginal dryness was associated with a lower chance of reporting of sexual pain.

**Primary Question:**

**Summary of Findings:** Black women had significantly lower volumes of cardiovascular fat compared with White women, independent of individual measures of adiposity. Race modified the associations between adiposity and cardiovascular fat with stronger associations between BMI and paracardial fat in White women compared with Black women, and stronger associations between abdominal visceral fat and epicardial fat in Black women compared with White women.

[WG#755DissertationHypo1]


**Primary Question:**

**Summary of Findings:** Current evidence on the association between body mass index (BMI) and age at menopause remains unclear. We investigated the relationship between BMI and age at menopause using data from 11 prospective studies. A total of 24,196 women who experienced menopause after recruitment was included. Baseline BMI was categorised according to the WHO criteria. Age at menopause, confirmed by natural cessation of menses for C 12 months, was categorised as 45–49, 50–51 (reference category), 52–53, 54–55, and 56 years (late age at menopause). We used multinomial logistic regression models to estimate multivariable relative risk ratios (RRRs) and 95% confidence intervals (CI) for the associations between BMI and age at menopause. The mean (standard deviation) age at menopause was 51.4 (3.3) years, with 2.5% of the women having early and 8.1% late menopause. Compared with those with normal BMI (18.5–24.9 kg/m2), underweight women were at a higher risk of early menopause (RRR 2.15, 95% CI 1.50–3.06), while overweight (1.52, 1.31–1.77) and obese women (1.54, 1.18–2.01) were at increased risk of late menopause. Overweight and obesity were also significantly associated with around 20% increased risk of menopause at ages 52–53 and 54–55 years. We observed no association between underweight and late menopause. The risk of early menopause was higher among obese women albeit not significant (1.23, 0.89–1.71). Underweight women had over twice the risk of experiencing early menopause, while overweight and obese women had over 50% higher risk of experiencing late menopause.

[WG#986PUD]

**Primary Question:**

**Summary of Findings:**

[WG#927]


**Primary Question:**

**Summary of Findings:** Faith could be associated with a different risk of MetS among women of Hispanic vs other ethnicities, suggesting that among women not part of a community of faith, Hispanic ethnicity is risk factor for MetS.

[WG#783]


**Primary Question:**

**Summary of Findings:** Higher baseline grip strength relative to body weight was associated with lower rates of diabetes.

The association between baseline grip strength and diabetes was stronger in White women compared to Blacks.

Rate of change in grip strength was not associated with diabetes incidence.

[WG#813]


**Primary Question:**

**Summary of Findings:** Women’s allostatic load score increased by approximately 2% each year over the course of the study. African American race/ethnicity, low family income, older age, and ability to read and speak only in English were significantly associated with higher allostatic load.

[WG#394]

Hedgeman E, Hasson RE, Karvonen-Gutierrez CA, Herman WH, Harlow SD. **Perceived Stress Across the Midlife: Longitudinal Changes Among a Diverse Sample of Women, The Study of Women's Health Across the Nation (SWAN)** *Women's Midlife Health* 2018 Mar;4(2)
Primary Question:
Summary of Findings: At baseline, Hispanic women, women with less education and women reporting financial hardship were more likely to report high perceived stress levels. After adjustment for sociodemographic factors (age, race / ethnicity, education, financial hardship, site of recruitment), we found that perceived stress decreased over the midlife for most SWAN women, but increased for Hispanic and white women recruited from New Jersey. Changing menopausal status was not a significant predictor of perceived stress after adjustment for these sociodemographic variables.


Primary Question:
Summary of Findings: A4 and E1 decline minimally over the MT, and A4 and E1 are higher in Whites than in African-Americans.


Primary Question:
Summary of Findings: Of the 1339 women reporting urinary incontinence (UI) during follow-up, 814 (61.0%) reported they did not seek treatment for UI. The most frequently reported reasons for not seeking treatment were: UI was not bad enough, the belief that UI is a normal part of aging and that health care providers never asked. Women with more frequent UI were most likely to report beliefs about the cause of UI or motivation barriers as reasons for not seeking treatment regardless of race or ethnicity, socioeconomic status, or education level.


Primary Question:
Summary of Findings: Women who report having had a preterm birth, or multiple adverse pregnancy outcomes, have higher systolic blood pressure at late midlife compared with women who report no adverse pregnancy outcomes.

Black women who report having had a preterm birth have a lower carotid intima-media thickness at late midlife than White women who report having had a preterm birth.

History of adverse pregnancy outcomes was not related to carotid plaque in late midlife.

**Primary Question:**

**Summary of Findings:** Non-steroidal anti-inflammatory drugs (NSAIDs) users had similar bone mineral density trajectory to the reference medication acetaminophen, suggesting they do not differ. Opioid users, however, showed a more pronounced BMD decline in the fifth year of usage, suggesting potential association with decreased BMD if used persistently.

[WG#810]


**Primary Question:**

**Summary of Findings:** A longer duration from menarche to onset of menopause transition (i.e., duration of estrogen exposure) was significantly associated with a lower risk of depression during the menopausal transition and postmenopause

Longer duration of oral contraceptive use was associated with a lower risk of depression while number of pregnancies and breastfeeding were not significantly associated with depression risk during the menopausal transition and postmenopause

[WG#614]


**Primary Question:**

**Summary of Findings:** Across midlife, five patterns of physical activity appeared including: (1) low physical activity, overtime (26.2% of SWAN participants), (2) middle or moderate physical activity, overtime (23.9%), (3) decreasing physical activity, overtime (22.4%), (4) high physical activity, overtime (14.1%), and (5) increasing physical activity, overtime (13.4%). When compared to the low physical activity, overtime group, physical performance improved by 3.5-9.8%. Differences in physical performance were also noted when the other patterns of physical activity were compared to the increasing physical activity group.

[WG#831]


**Primary Question:**

**Summary of Findings:** We observed overall high prevalence rates of herbal CAM use in
both Hispanic and Non-Hispanic White women. Hispanic women in particular used more types of herbal remedies, and were less likely to report their use to physicians. Use of herbal remedies was higher among women who reported trouble paying for basics and among those without health insurance.

[WG#760]


Primary Question: Summary of Findings: Both long- and short-term exposures to ambient gas pollutants increase the potential of forming blood clots, and thus contribute to the greater risk of CVD in midlife women.

[WG#841]

223 Colvin A, Richardson GA, Cyranowski JM, Youk A, Bromberger JT. The Role of Family History of Depression and the Menopausal Transition in the Development of Major Depression in Midlife Women: Study of Women's Health Across the Nation Mental Health Study (SWAN MHS) Depression and Anxiety 2017 Sep;34(9):826-835. doi: 10.1002/da.22651

Primary Question: Summary of Findings: Family history of depression predicts major depression in midlife women independent of the menopausal transition and changes in psychosocial and health profiles. Furthermore, the menopausal transition was associated with major depression only among women without a family history of depression

[WG#632B]


Primary Question: Summary of Findings: We found (1) 4 distinct sleep trajectories for waking several times across the MT in both naturally and surgically menopausal groups, (2) except for one subgroup with an increasing trajectory, this sleep problems tended to remain stable from pre-FMP/pre-surgery to post-FMP/post-surgery, and (3) trouble falling asleep, early morning awakening, and frequent VMS were strongly associated with problems waking several times that persist through post-menopause.

[WG#644]

Across the Nation  J Clin Endocrinol Metab  July 2017, 102(7):2218-2229, PMID: 28368525,
Primary Question:
Summary of Findings:  Cycle length and hormone levels remain relatively well preserved among ELA cycles, although the proportion of ELA cycles becomes lower as the FMP approaches. In non-ELA cycles, much more heterogeneity in hormones and cycle lengths is observed.

Primary Question:
Summary of Findings:  Bone size at baseline (i.e., external size of the femoral neck) was negatively correlated with the amount of change in bone mineral content and bone area over a 14-year period but there was no correlation of baseline bone size and change in bone mineral density. This data suggests that longitudinal changes in bone mineral density are associated with different morphologic changes in different women. In some women (those with narrower bones), there are greater increases in bone area with time but in other women (those with wider bones), there are greater losses in bone mineral content.

Primary Question:
Summary of Findings:  The manuscript describes new Debiased Sparse Partial Correlation (DSPH) methodology and new data visualization tools for modeling metabolomics data. The new tools were used to analyze several data sets including targeted and untargeted metabolomics data from SWAN and to demonstrate the applications of new methodology.

Primary Question:
Summary of Findings:  Black women had more plate-like trabecular morphology and higher axial alignment of trabeculae, whereas white women had more rod-like trabeculae. These differences may contribute to the improved bone strength and lower fracture risk observed in black women.

**Primary Question:**

**Summary of Findings:** We did not find that midlife women at perimenopause experience more eating disorder symptoms than women in premenopause. However, we did observe a significant correlation between the appetite hormone leptin and self-reported binge eating.


**Primary Question:**

**Summary of Findings:** Independent of age, obesity, smoking status, education and study site, women with lower premenopausal E2 levels and a slower rate of FSH change during the early transition had higher risk of developing diabetes in midlife as they transitioned through the menopause. The rate of change in E2 during the menopausal transition and baseline FSH levels and change in FSH in the later menopausal transition do not seem to be associated with diabetes risk.


**Primary Question:**

**Summary of Findings:** Less educated women and African-American women were the highest consumers of energy-dense beverages. Greater consumption of energy-dense beverages was associated with higher odds of developing metabolic syndrome and accumulating additional metabolic syndrome components over time. These associations were primarily driven by risk for hypertension and impaired fasting glucose.


**Primary Question:**

**Summary of Findings:** Decline in sexual function became apparent 20 months prior to FMP and continued to decline more than one year after the FMP, but at a slower rate. Women who had a hysterectomy did not show decline in sexual function prior to hysterectomy, but scores declined afterwards.
Support Vector Machines for Automated Snoring Detection: Proof-of-Concept

**Primary Question:**

**Summary of Findings:** Episodes of snoring during sleep can be reliably identified using a computer algorithm. The computer algorithm performs comparably to human visual scorers in the detection of snoring events during sleep.

Effect of Race and Ethnicity on Antihypertensive Medication Utilization among Women in the United States: The Study of Women's Health Across the Nation (SWAN)

**Primary Question:**

**Summary of Findings:** Use of antihypertension medications increased over time particularly among White and Black women. The most commonly used class of antihypertensive medication was angiotensin converting enzyme inhibitors or angiotensin receptor blockers. Black women were more likely to report use of calcium channel blockers compared to White women. Current guidelines support the use of thiazide diuretics as first line antihypertensive class for most adults; despite increases in thiazide use over time, this class was not the most commonly used antihypertensive medication class.

The Effect of a Healthy Lifestyle on Future Physical Functioning in Midlife Women

**Primary Question:**

**Summary of Findings:** A composite score representing the average values of as many as three repeated measures of diet, physical activity and smoking behavior was associated with faster walking speed, better ability to rise from a seated position, and overall better physical functioning. Most of the association was due to physical activity with smoking behavior and diet playing on insignificant roles.

Duration of the menopausal transition is longer in women with young age at onset: the multiethnic Study of Women's Health Across the Nation

**Primary Question:**

**Summary of Findings:**
Primary Question:
Summary of Findings: Women with an earlier age at onset of menopausal transition had a longer duration of the menopausal transition. Smokers were younger at the onset of the menopausal transition and had a shorter duration of the menopausal transition. African-American race were associated with younger onset but longer duration of the MT.


Primary Question:
Summary of Findings: At the time of the first vision exam, the prevalence of distant visual impairment was 19.3% and of near visual impairment was 39.5% among women in the Michigan site of the Study of Women’s Health Across the Nation. Distant visual impairment was predictive of poorer forward reach and timed stair climb up to 10 years later whereas near visual impairment was only predictive of poorer forward reach. Stratified analyses revealed that the association of near visual impairment and forward reach was present only among black women.


Primary Question:
Summary of Findings: Bodily pain (on a scale of 0-100) increased at a rate of 0.49 points per year during the late reproductive years and menopause transition (10 years before to 0.4 years after the final menstrual period). During early postmenopause (0.4 to 5 years after the final menstrual period), pain decreased at an average rate of 0.82 points per year and plateaued in late postmenopause. Although statistically significant, these changes are unlikely to represent clinically meaningful differences.


Primary Question:
Summary of Findings: The performance of WHtR to screen for cardiometabolic conditions was fair/good among all 5 race/ethnic groups. In race/ethnicity stratified analyses, the boundary values for waist-to-height ratio to screen for cardiometabolic outcomes suggest the need for higher WHtR boundary values in non-Asian minority women compared to Asian women, and range from 0.45 to 0.55. The likelihood of overall high cardiometabolic risk decreases by 0.24 if woman’s WHtR<0.45
(sensitivity 86%, specificity 55%, negative predictive value 55%); whereas the likelihood of overall high cardiometabolic risk increases 6.6-fold if woman’s WHtR>0.55 (sensitivity 53%, specificity 91%, positive predictive value 54%).

Midlife transition is a vulnerable period in women’s lives for progression of abdominal adiposity and related cardiometabolic conditions. A simple public health message: “Keep your waist to less than half of your height”1 applies to mid-life women of all ethnicities to alert about preventable cardiometabolic risk.

[WG#97]


Primary Question:

Summary of Findings: Although cross-sectional studies suggest that human cognitive aging starts in midlife, few longitudinal studies have documented within-individual declines in cognitive performance. Using annually repeated measures of cognitive performance, we showed that cognitive aging in women does indeed occur in midlife, with substantial longitudinal declines in cognitive processing speed and verbal memory.

[WG#697]


Primary Question:

Summary of Findings: We demonstrated that greater volumes of epicardial fat volumes are significantly associated with presence and extent of coronary calcification, independent of age, race, menopausal status and traditional CVD risk factors. Additionally, we reported that the associations between paracardial fat volumes and CAC measures are significantly modified by women’s menopausal status and E2 levels independent of age, race, obesity and other CVD risk factors; while similar effect modifications were not found for epicardial fat volumes as related to CAC measures. Taken together, the current findings suggest PAT as a potential menopause-specific CVD risk factor.

[WG#761]


Primary Question:

Summary of Findings: After taking into account age, race/ethnicity, geographic location, body weight, smoking and recent alcohol use, women exposed to higher and lower levels of apparent temperature over the past week or month had higher levels of some blood markers
of inflammation, blood clotting, and lipid markers than women exposed to lower levels of apparent temperature.


**Primary Question:**

**Summary of Findings:** Our findings suggest that declines in HDL-C and increases in LDL-C around the FMP are associated with subsequent adventitial diameter and carotid plaque scores, respectively, in the postmenopausal years. Furthermore, these associations were independent of age, site, race, educational attainment, number of years after the menopause at the time of the carotid scan, baseline systolic blood pressure and BMI, or medications for hypertension or diabetes. Adjustments for baseline HDL-C or LDL-C and for changes in HDL-C or LDL-C prior to and after the one year interval did reduce the effect sizes somewhat but the associations by and large remained. Taken together, the findings suggest that changes in HDL-C and LDL-C around the FMP do provide unique predictive information.


**Primary Question:**

**Summary of Findings:** This study refutes prior reports of an association between Diminished Ovarian Reserve and CGG trinucleotide repeats of 35-54 CGG length, which would be considered high normal and intermediate in the current FMR1 clinical laboratory reference range. This study confirms an association between Diminished Ovarian Reserve and a very low number of repeats (most notably <20 CGG) in Caucasians, which was reported by one large NY fertility clinic; These repeat lengths would be considered low normal in the current FMR1 clinical laboratory reference ranges.


**Primary Question:**

**Summary of Findings:** Greater concurrent body mass index and WC were significantly positively related to incident VMS in the early menopause stage and negatively related in the late stage of menopause. Percentage weight change since baseline had a shallow U-shaped association with incident frequent (>6 days in the last two weeks) VMS in the early stage and shallow inverse U-shape in the late stage.

**Primary Question:**
**Summary of Findings:** Here, we develop a novel statistical model that generalizes standard mixed models for longitudinal data that include flexible mean functions as well as combined compound symmetry (CS) and autoregressive (AR) covariance structures. Our model generalizes these types of covariance structure by using Bayesian nonparametric methods. The methodology is illustrated using data on Follicle Stimulating Hormone (FSH) profiles in women who are experiencing the menopausal transition. While our main goal was to accommodate different kinds of potential correlations in the data, we also focus on the estimation of a variety of covariance structures and make comparisons with other methods that have been used in the literature. We observe that models that fail to incorporate CS or AR structure can result in very poor estimation of a of a covariance or correlation matrix.


**Primary Question:**
**Summary of Findings:** Women with VMS may be more likely to develop HTN compared to women without VMS. Further research related to VMS including frequency of symptoms is warranted.


**Primary Question:**
**Summary of Findings:** 91 (31%) women had Persistent/recurrent clinical depression, 27 (9%) had one episode of MDD, 35 (12%) experienced minor depression only, 144 (48%) had no depression. Persistent and recurrent depression episodes during midlife are common. Lifetime and recent/current exposures prior to and during the early MT increase risk of a pernicious depression course. In addition to lifetime major or minor depression, upsetting life events and sleep problems posed a greater risk for persistent or recurrent depression than for the other three groups.

Shieh, A, Ishii, S, Greendale GA, Cauley J, Lo JC, Karlamangla AS. Urinary N-telopeptide and Rate of Bone Loss Over the Menopause Transition and Early Postmenopause. *J*
Primary Question:

Summary of Findings: Levels of a marker of bone breakdown in the urine collected during early postmenopause are related to rates of bone loss across and after the menopause transition. This marker of bone breakdown may be useful in identifying women at risk for faster than average bone loss.


Primary Question:

Summary of Findings: Women raised in adverse childhood SES (low-educated and poor parents) were more likely to have/develop metabolic syndrome during midlife than women raised in good childhood SES (high-educated and non-poor parents), regardless of women’s own educational attainment.


Primary Question:

Summary of Findings: Vasomotor symptoms were associated with a 38% reduction in breast cancer risk. Among women who fully transitioned to postmenopause during follow-up, vasomotor symptoms were associated with a 55% reduction in breast cancer risk. Our findings suggest that endogenous sex hormones may play a more limited role in this association than previously hypothesized. Future research is needed to understand the biology underlying this relationship.


Primary Question:

Summary of Findings: Overall, 76% of the women were Caucasian, 22% Japanese, and
other ethnicity (of 300 or more participants) included Hispanic/Latin American (0.2%), Chinese (0.2%), Middle Eastern (0.3%), African/black (0.5%), and Other (1.0%). The median age at baseline was 47 years (Inter-quartile range (IQR): 41-53), and that at the last follow-up was 56 years (IQR: 48-64). Regarding reproductive characteristics, half of the women (49.8%) had their first menstruation (menarche) at 12-13 years of age. The distribution of menopausal status and the prevalence of chronic disease varied considerably among studies. At baseline, most women (57%) were pre- or peri-menopausal, 20% reported a natural menopause (range 0.8-55.6%), and remaining had surgery or were taking hormones. By the end of follow-up, the prevalence of CVD and diabetes were 7.2% (range 0.9-24.6%) and 4.7% (range 1.3-13.2%), respectively.

[WG#754PUD]


Primary Question:
Summary of Findings: Having any exposure to secondhand smoke increases the risk of uterine fibroids in midlife women by approximately 30% compared to having no exposure. In women who never smoked cigarettes, the increased risk of fibroids from secondhand smoke is even greater at nearly 50%.

[WG#799]


Primary Question:
Summary of Findings: Four distinct VMS trajectories were found: early onset and decline after the FMP (early onset, 18.4%), onset near the FMP then decline (late onset, 28.9%), early onset and persistently high (high, 25.5%), and consistently low frequency (low, 27.2%). Relative to women with low levels of VMS across the transition, women with persistently high and early onset VMS had a more adverse psychosocial and health profile and low levels of estradiol, the early onset group was less likely to be obese. The high VMS group was less likely to have a moderate than high rise of FSH. African American women were most likely to be in the late onset or persistently high VMS groups relative to Caucasian women.

[WG#689]

Primary Question:

Summary of Findings: Within a median of 2.14 years of menopause, an improvement in HDL cholesterol efflux capacity and significant alterations in HDL-P subclasses were observed. Whether patterns of these alterations differ in late postmenopause and how they relate to atherogenesis are not known. The reported changes in HDL metrics over menopause call for further evaluation of potential risk on CVD after menopause. [WG#800]


Primary Question:

Summary of Findings: The distribution of this one particular gene (FMR1) does vary by race-ethnicity in women with normal reproductive histories. This report provides unique detail on the distributions for use by researchers and clinicians. [WG#741]


Primary Question:

Summary of Findings: Having a hs-CRP level >3 mg/L was significantly positively associated with premenstrual mood symptoms (adjusted odds ratio (aOR)=1.32, 95% Confidence Interval (CI) 1.062-1.642), abdominal cramps/back pain (aOR=1.413, 95% CI 1.099, 1.817), appetite cravings/weight gain/bloating (aOR=1.407, 95% CI 1.046, 1.893) and breast pain (aOR=1.267, 95% CI 1.030, 1.558). Elevated hs-CRP level was not significantly associated with premenstrual headaches or reporting three or more PMSx. [WG#777]


Primary Question:

Summary of Findings: [WG#804]


Primary Question:

Summary of Findings: Every 100 mg/dL increase in triglyceride levels was associated with
15% increased risk of non-traumatic fracture in midlife women (7% increased risk of non-traumatic fracture for every 50 mg/dL increase in triglyceride level). In diabetic women, the increased risk of non-traumatic fracture was about 50% for every 100 mg/dL increase (23%, every 50 mg/dL increase) in triglyceride level.

[WG#793A]


Primary Question:
Summary of Findings: In non-diabetic, postmenopausal women, the presence of insulin resistance and hyperinsulinemia was associated with smaller bone size, greater volumetric bone mineral density and favorable bone microarchitecture at weight bearing and non-weight bearing skeletal sites. Further, these associations were independent of body weight suggesting that hyperinsulinemia directly effects bone structure independently of obesity.

[WG#601D]


Primary Question:
Summary of Findings: As women transition through menopause, increases in HDL-C levels are independently associated with greater cIMT progression. Thus, the quality of HDL may be altered over the menopausal transition rendering HDL dysfunctional and not providing the expected cardioprotective effect.

[WG#772]


Primary Question:
Summary of Findings:

[WG#710]


Primary Question:
Summary of Findings: We created a bone balance index from markers of bone formation and bone breakdown. We found that this index could predict current bone strength as well as
the direction and magnitude of future change in bone strength.


Primary Question: 
Summary of Findings: Of the four sex hormones studies (E1C, PDG, FSH and LH), only E1C was found to decline more steeply in women with a history of migraine compared to those without. This finding supports the ‘estrogen withdrawal hypothesis’ of migraine pathogenesis. The relatively steeper estrogen decline in women with a history of migraine does not distinguish cycles with and without a headache, suggesting that this rapid luteal E1C decline is more a marker of migraine pathophysiology than mediator of headache.


Primary Question: 
Summary of Findings: High depressive symptoms over five years were common (11% experienced three or more episodes), and coronary calcium was low (54% had no CAC, 25% had scores between 0 and 10, and 21% had CAC ≧10 Agatston score). Women with 3 or more episodes were twice as likely to have significant CAC (≧10 Agatston units) than women with no depressive episodes [OR (95% CI)=2.20 (1.13-4.28), p=0.020] with no difference by race. Women with 1 or 2 episodes did not differ from women with no episodes.


Primary Question: 
Summary of Findings: Some women experience chronic vulvar pain symptoms independent of current estrogen levels, and even while taking hormone replacement. Vulvar atrophy and estrogen deprivation may not be the sole cause of postmenopausal vulvar pain.

**Primary Question:**

**Summary of Findings:**
1. Medication use increases a lot in about 15% of women and very minimally in the rest.
2. Menopause has no effect on the increase in medications observed.
3. Race/ethnicity play significant roles in medication use.

[WG#639]


**Primary Question:**

**Summary of Findings:**
Plasminogen-activator inhibitor 1, which regulates blood clotting, is related to the change in time of calcium in heart arteries in African-American and Caucasian women.

[WG#710C]


**Primary Question:**

**Summary of Findings:**
Substantial limitations in physical functioning predict incident metabolic syndrome. Compared to women who reported no limitations, women who reported some and substantial limitations were more likely to develop hypertension and increased waist circumference. Compared to Caucasian women, African American women were more likely to have elevated fasting glucose, elevated blood pressure, increased waist circumference, and reduced HDL-C, but they were less likely to have elevated triglycerides.

[WG#655]


**Primary Question:**

**Summary of Findings:**
Life satisfaction showed a significant, independent, inverse relationship with IMT, after controlling for important demographic, behavioral, and cardiovascular covariates, such that each 1-point higher life satisfaction score predicted a significant 0.010 mm lower level of mean IMT. In contrast, life engagement was not a significant correlate of IMT, and because reported life events were low in this sample, no
significant association was seen between life events and IMT. Finally, no significant interaction between life satisfaction and race on IMT was observed.

[WG#251]


Primary Question:
Summary of Findings: Women with higher E2 before their FMP, but lower E2 afterwards appeared to have lower risk of atherosclerosis after menopause when compared to women with low E2 before and after their FMP. Women with lower FSH rise over MT had lower IMT than those with a medium or high rise.

[WG#721]


Primary Question:
Summary of Findings: Although perimenopausal women reported perceiving higher levels of stress relative to pre-menopausal women, this increased perception of stress did not translate to significant differences in fibrinogen by stage of the menopausal transition. While perimenopause may represent a sensitive window with respect to the perception of stress, neuroendocrine changes that occur during perimenopause do not appear to exacerbate or interact with such stress, as measured by changes in fibrinogen.

[WG#753]


Primary Question:
Summary of Findings: Higher levels of leptin were associated with poorer mobility physical functioning performance. Higher levels of adiponectin were associated with lower leg strength. Resistin was not associated with any of the physical functioning performance measures.

[WG#684]

Primary Question: Summary of Findings: Women classified as being raised by poor families with parents with little education are likely to have elevated levels of C reactive protein, a generic inflammatory marker, and plasminogen activator inhibitor-1, an inhibitor of fibrinolysis. These relationships are due primarily to women from such families being obese as adults.


Primary Question: Summary of Findings: Cumulative unfair treatment is related to intima media thickness and adventitial diameter. This relationship was moderated by race because unfair treatment was significantly related to higher intima media thickness and adventitial diameter among Caucasian women, and was not significantly related among African American, Hispanic, and Chinese women.


Primary Question: Summary of Findings: After taking into account age, race/ethnicity, geographic location, body weight, smoking and recent alcohol use, women exposed to higher levels of fine particulate matter over the past year had higher levels of some blood markers of inflammation and blood clotting than women exposed to lower levels of pollution. Women who were exposed to higher levels of ozone during the past year had higher levels of a factor associated with blood clotting than women exposed to lower levels. Taking into account menopausal status and other lifestyle and health factors did not change the results.


Primary Question: Summary of Findings: Neither ACE inhibitors nor beta blockers were associated with
improvements in bone mineral density (BMD). Thiazide diuretic use was associated with less annualized loss of BMD compared with non-users, as well as compared with ACE inhibitors and beta blockers. [WG#638E]


Primary Question: Summary of Findings: Day-to-day variability in bedtime and staying up late, past one’s bedtime was associated with greater insulin resistance in mid-life women. Average bedtime was unrelated to metabolic health and no aspect of sleep timing predicted metabolic health five years later. [WG#743]


Primary Question: Summary of Findings: Increased levels of circulating estradiol and testosterone are individually related to increased risk of uterine fibroids. They also act in synergy to increase the risk of fibroids more than each hormone alone. [WG#782]


Primary Question: Summary of Findings: Women with VMS beginning a decade prior to the FMP and declining several years after the FMP had higher mean and maximal IMT than those with consistently low VMS. These associations were not accounted for by demographic factors nor by CVD risk factors. [WG#688]


Primary Question: Summary of Findings: [WG#774]

**Primary Question:**

**Summary of Findings:** No difference was found in the longitudinal intra-abdominal adipose tissue change among black and white midlife women.

[WG#730]


**Primary Question:**

**Summary of Findings:** At baseline, higher BMI was associated with lower intercourse frequency. While overall change in BMI was not associated with changes in sexual functioning over time, during years of greater-than-expected weight gain, sexual desire and intercourse frequency were diminished.

[WG#727]

Hall MH, Casement MD, Troxel WM, Matthews KA, Bromberger J, Kravitz HM, Krafty RT, Buysse DJ. *Chronic Stress is Prospectively Associated with Sleep in Midlife Women: The SWAN Sleep Study.* Sleep. 2015 Oct 1;38(10):1645-54. PMID: 26039965

**Primary Question:**

**Summary of Findings:** Midlife women who experienced chronic stress over a three- to nine-year period reported more subjective sleep complaints and had more objective difficulty staying asleep compared to women who reported moderate to mild levels of stress. The relationship between chronic stress and sleep was observed even after accounting for the effects of other factors that might disrupt sleep in midlife women including sociodemographics, health characteristics, symptoms of depression and other acute stressful events.

[WG#465]


**Primary Question:**

**Summary of Findings:** Late peri-/postmenopausal women have greater volumes of heart fat depots compared with pre-/early peri-menopausal women independent of age, obesity and other covariates. Endogenous sex hormones are associated with volumes of cardiovascular fat in a pattern suggesting that certain hormones may be more related to a specific location of cardiovascular fat than other hormones. Perhaps cardiovascular fat plays a role in the higher risk of CHD reported in women after menopause.

[WG#762]
Primary Question: Summary of Findings: Higher levels of self-reported pain were associated with more actigraphy-assessed sleep disturbance. In particular, more pain was associated with worse sleep continuity including more nighttime body motion and activity (greater movement and fragmentation index and mean activity score), more time spent awake, and a lower percentage of time in bed spent asleep (lower sleep efficiency), as well as more night-to-night variability in these sleep measures.

[WG#517]


Primary Question: Summary of Findings: We observed that a large number of women developed an episode of major depression during midlife. Women with a first lifetime episode of major depression during midlife were more likely to have higher trait anxiety, at least one lifetime medical condition, and to report low functioning due to physical problems during the study. For women with a history of major depression, being more internally focused or ruminative, having a history of an anxiety disorder, higher recent depression symptoms, and being peri- or post-menopause increased the risk for a major depression episode during the study, while older age decreased the risk. For both groups, having 6 or more close friends at study entry reduced the risk of a major depression episode during midlife.

[WG#637]


Primary Question: Summary of Findings: Higher discrimination and hostility were predictive of higher AL level. Higher perceived stress were predictive of a faster rate of increase in AL. Racial and SES differences were present, with African American race, lower income, and lower education predictive of higher AL. In addition, the results identified several significant pathways through which race and SES indirectly predict level and change of AL over time. [WG#661]

Primary Question:
Summary of Findings: Mid-life women with higher 25(OH)D levels have a lower risk of subsequent non-traumatic fracture. Vitamin D supplementation is warranted in midlife women with 25(OH)D <20 ng/mL.

290
Primary Question:
Summary of Findings: The median total duration (in years) of frequent vasomotor symptoms was 7.4 years. Frequent VMS persisted after the final menstrual period for about 4.5 years. The primary factor related to duration was when a woman began having frequent symptoms; those women who began experiencing symptoms had a longer duration.

291
Primary Question:
Summary of Findings: Our major finding is that, while whole-night correlations between restorative slow wave sleep and nocturnal parasympathetic activity were strongly and positively correlated in midlife women, the dynamics of this relationship varied within and across Non-REM sleep periods. Additionally, the dynamics of this relationship differed as a function of sleep-disordered breathing and self-reported symptoms of insomnia.

292
Primary Question:
Summary of Findings: Childbirth or breastfeeding is not, or minimally if any, associated with lower bone strength, and is not associated with fracture risk in later life.

293
Primary Question:
Summary of Findings: Persistent pain is related to CVD risk factors, and these effects may occur partly through effects of low physical activity.

[WG#717]

**Primary Question:**
**Summary of Findings:** We found no clear evidence of racial, socioeconomic or education level disparities in treatment seeking for UI or differences in UI change characteristics for which women reported seeking treatment for UI. Rather, duration of UI symptoms, at least weekly UI just before seeking treatment and worsening of UI symptoms over time had the strongest association with UI treatment-seeking behavior.

[WG#709]


**Primary Question:**
**Summary of Findings:** Inflammation results in slower a decline in mammographic density

[WG#528A]


**Primary Question:**
**Summary of Findings:** The current data suggest that poor performance in simple non-invasive objective physical functioning tests, such as walking speed, may be an early indicator of structural changes in vascular health at late midlife.

[WG#692]


**Primary Question:**
**Summary of Findings:** Women who were consistently ovulatory were not significantly better on cardiometabolic metrics, and were worse off in HDL prior to menopause.

[WG#610]

10.1097/GME.0000000000000305. PMID: 25116050 PMCID: PMC4324399

Primary Question:
Summary of Findings: In Japanese women, high isoflavone intake was associated with higher maximum adult bone mass but a greater rate of lumbar spine bone loss during the menopause transition. Isoflavone intake was not related to maximum adult bone mass or menopause-related bone loss in African American, Caucasian or Chinese women.

299

Primary Question:
Summary of Findings: In this cross-sectional analysis of the SWAN cohort, 5% of women were affected by the complex of symptoms of depressed mood, disturbed sleep and sexual problems. Women with poor social support and more stressful life events, as well as women who were surgically menopausal, had the highest risk of having this symptoms complex.

300

Primary Question:
Summary of Findings: Higher physical activity levels were associated with lower levels of depressive symptoms over ten years independent of potential confounders. Our findings suggest that maintaining moderate intensity PA levels during midlife may be protective against depressive symptoms.

301

Primary Question:
Summary of Findings: An annual increase in VAT of about 3.5% was observed independently of age and known cardiovascular risk factors. This change in VAT was significantly related to the change in bioavailable testosterone.

302

Primary Question:
Summary of Findings: Contrary to expectations, greater time spent preparing meals was associated with developing an adverse cardiometabolic profile.

**Primary Question:**

**Summary of Findings:** As women progressed through the MT and increased frequency of long menstrual cycles is seen. Chinese and Japanese women had longer menstrual cycles compared to Caucasian women. Obese women had longer menstrual cycles as compared to non-obese women. These associations remained after adjustment for smoking, education, physical activity, and time.


**Primary Question:**

**Summary of Findings:**


**Primary Question:**

**Summary of Findings:** Women initiating use of a PPI or H2RA did not have higher rates of subsequent bone loss at the spine, total hip, or femoral neck than women not initiating use of these medications. However, in a positive control analysis, we found that women initiating hormone therapy did have improved bone mineral density compared with those who did not.


**Primary Question:**

**Summary of Findings:** Sleep efficiency declined gradually across the menstrual cycle, but the decline became pronounced in Segment 4 which represents the premenstrual period. The association of segment with sleep efficiency or minutes of total sleep time was modified by sociodemographic factors and personal behaviors, including smoking.

Tomey K, Greendale GA, Kravitz HM, Bromberger JT, Burns JW, Dugan SA, de Leon CF.

**Primary Question:**

**Summary of Findings:** Greater pain experiences that interfered with daily functioning were independently associated with poorer cognitive function, and this association was partly mediated by depressive symptoms. Additionally, an independent association between a greater combined pain score and poorer cognitive function was identified, but was mediated by depressive symptoms and had only an indirect effect.  


**Primary Question:**

**Summary of Findings:** Masturbation, sexual desire and arousal were positively associated with T. Masturbation, arousal and orgasm were negatively associated with FSH. Associations were modest. Estradiol was not related to any measured sexual function domain. Pain with intercourse was not associated with any hormone.


**Primary Question:**

**Summary of Findings:**


**Primary Question:**

**Summary of Findings:** Similar percentages of African American and Caucasian women experienced recurrent depressive episodes over the 11-year follow-up period. Predictors of these episodes of depression varied across the two groups.

Primary Question: Two patterns of bleeding are common during the MT, long-light bleeding and episodes of heavy bleeding. 3 out of 4 women experience at least 3 episodes of menses lasting 10+ days, 2 out of 3 women experience at least 3 episodes of 6+ days of spotting, and 1 out of 4 women experience at least 3 episodes of 3+ days of heavy bleeding. [WG#188D]


Primary Question: We found that midlife women with insomnia were less likely to engage in negative sleep behaviors (i.e., smoking, alcohol consumption, caffeine near bedtime, long daytime napping) compared to women without insomnia; specifically, women with insomnia were less likely to consume caffeine near bedtime and take long daytime naps. In contrast, women with sleep-disordered breathing were less likely to be physically active than women without sleep-disordered breathing; however, no other differences were found for these women. [WG#419]


Primary Question: We found that women with higher anxiety symptom scores at a given visit T were more likely to develop an episode of MDD the following year (T+1). This relationship was more likely for recurrent episodes of MDD than for a woman’s first MDD episode. This increased risk for new occurrences of MDD in association with higher anxiety symptom levels did not differ between African-American or Caucasian women. [WG#554]


Primary Question: Family history of depression is a strong predictor of major depression in midlife women generally, but particularly in those with a lifetime history of depression prior to midlife. These results suggest that women with a family history of depression may benefit from closer monitoring of their mood during midlife. [WG#632A]

Thurston R, Chang Y, Derby CA, Bromberger JT, Harlow SD, Janssen I, Matthews KA. Abuse and Subclinical Cardiovascular Disease among Midlife Women: The Study of

Primary Question:
Summary of Findings:  Childhood sexual abuse was associated with higher subclinical cardiovascular disease controlling for traditional cardiovascular risk factors.

[WG#713]


Primary Question:
Summary of Findings:  It appears that other than obesity, abnormalities in glucose and lipid regulation are the strongest indicators of progression from metabolically benign to at-risk overweight/obese phenotype, a state that is unanimously associated with an elevated risk of cardiovascular morbidity and mortality.

During the present obesity epidemic, public health resources need to have a multi-prong approach, to not only focus on obesity prevention and treatment, but also to identify and treat those with glucose dysregulation and dyslipidemia. Of lifestyle modifications, an increase in physical activity may have the most impact in improving cardiometabolic health.

[WG#651]


Primary Question:
Summary of Findings:  We found that long-term exposure to fine particulate air pollution was associated with C-reactive protein. Effects were particularly large for diabetics and smokers. In addition, effects were observed among several subgroups including those with high blood pressure or cholesterol, high BMI, unmarried or post-menopausal.

[WG#618A]


Primary Question:
Summary of Findings:  There are at least three major mechanisms by which obesity influences fracture risk: increased BMD in response to greater skeletal loading, increased impact forces during a fall, and greater absorption of impact forces by soft tissue padding.
The balance between these factors determines the overall fracture risk in an individual.


**Primary Question:**

**Summary of Findings:** Women with high levels of testosterone and a history of irregular menstrual periods do not appear to develop adverse risks factors for heart disease when they go through menopause.


**Primary Question:**

**Summary of Findings:** Women who have been consistently physically highly active have more self-determination and are more confidence in being able to engage in physical activity now. They are also likely to have a physically active friend. These findings confirm the theory needed for an intervention trial.


**Primary Question:**

**Summary of Findings:** There was no main effect of discrimination on CRP and discrimination did not interaction with race. However, the association was conditional upon body mass index such that greater discrimination was associated with higher CRP among non-obese women.

322 Janssen I, Landay AL, Ruppert K, Powell LH. **Moderate Wine Consumption is Associated with Lower Hemostatic and Inflammatory Factor Over 8 Years: The Study of Women's Health Across the Nation (SWAN).** Nutrition and Aging (Amst) 2014 Jun 12;2(2-3):91-99.DOI 10.3233/NUA-130034

**Primary Question:**

**Summary of Findings:** Moderate wine consumers had significantly lower levels of 4 of the 5 markers, i.e. C-reactive protein, fibrinogen, factor VII, and plasminogen activator inhibitor than women who drank no or little wine. These associations were independent of significant effects of healthy lifestyle and overall alcohol consumption and similar across ethnic groups.

323 Jackson KL, Janssen I, Appelhans BM, Kazlauskaite R, Karavolos K, Dugan SA, Avery EA,

**Primary Question:**

**Summary of Findings:** Body Image Dissatisfaction (perceived actual body size greater than perceived ideal body size) and perceived unattractiveness (unattractive vs. attractive) were both associated with high depressive symptoms (CES-D, d 16). No association was found for either body image discordance (actual body size greater than perceived actual body size) or weight satisfaction and high depressive symptoms. These results were found for the overall cohort of women; no difference by race (Caucasian vs African American) was found.


**Primary Question:**

**Summary of Findings:** Lower levels of E2 and SHBG, and higher levels of FAI were associated with a more atherogenic profile of lipoprotein-subclasses. Sex hormones oscillation at midlife may increase women’s risk of coronary heart disease.


**Primary Question:**

**Summary of Findings:** Our results indicated a significant association between any violence reported during follow-up in SWAN participants and changes in weight and waist circumference in both unadjusted and adjusted models. Women who reported violence, compared to women who did not, were significantly more likely to have changes (increases or decreases) in weight and waist circumference after adjusting for age, race/ethnicity, marital status, smoking, study site and follow-up year.


**Primary Question:**

**Summary of Findings:** Higher baseline serum leptin levels were associated with more severe knee joint damage assessed using MRI. Osteophytes, or bony outgrowths at the edge of the knee joint, were most strongly correlated with serum leptin. Leptin levels increased with age. Having more severe knee joint damage (assessed with MRI) was associated with higher leptin levels but the pattern of change was similar over time.

WG#631

WG#747

WG#542

WG#629D
Primary Question:
Summary of Findings: Low education, low income and financial strain, particularly when experienced consistently over 12 years, were associated with a greater atherosclerosis among women free of clinical CVD. These associations persisted controlling for standard CVD risk factors and were broadly similar between racial/ethnic groups [WG#670]

Primary Question:
Summary of Findings: Our findings demonstrate that WHB likely influence subsequent sleep while sleep does not appear to affect subsequent WHB, and that these relationships are strongest in the context of weekly patterns rather than proximal daily associations. [WG#628]

Primary Question:
Summary of Findings: Non-Caucasian women who had at least some education after college had a much lower risk of osteoporosis-related fractures than non-Caucasian women who had high school, or less than high school, education. This was not the case among Caucasian women, and income was not associated with risk of fracture. [WG#663]

Primary Question:
Summary of Findings: Hot flashes that were reported by women but not captured with skin conductance monitors, or “false positive” hot flashes, were more likely to follow increases in physical activity. This was seen especially among women with depressive and anxious symptoms. Physical activity did not otherwise seem to trigger hot flashes. [WG#690]

Primary Question:
Summary of Findings: Waist circumference increases were significantly higher during years of combined unemployment and elevated depressive symptoms (1.03 cm/year), and
significantly lower in years of full-time employment and elevated depressive symptoms (0.24 cm/year), compared to years of full-time employment and non-elevated depressive symptoms (0.51 cm/year). Employment status was unrelated to waist circumference in years without elevated depressive symptoms. The pattern of results did not vary according to initial waist circumference at baseline or ethnicity/race.


Primary Question:
Summary of Findings: Women who reported a history of child abuse and neglect had elevated levels of C-reactive protein in mid-life. The association was due in large part to elevated body mass index.


Primary Question:
Summary of Findings: Women underestimated the number of VMS at the end of the day compared to those prospectively-reported or physiologically-detected during the day, particularly for African-American or more anxious women. Women overestimated the number of VMS they experienced during the night, particularly if they had poorer sleep.


Primary Question:
Summary of Findings: Approximately one quarter of first-generation Hispanic, Chinese, and Japanese immigrant women reported any sleep complaint compared to 37% of those who were US-born. Our analyses showed that first-generation immigrants had lower odds of reporting any sleep complaints compared to US-born women of the same race/ethnic group. This finding was largely explained by language acculturation.


Primary Question:
Summary of Findings: African American women reported the highest percentage of racial discrimination (35%) followed by Chinese (20%), Japanese (11%), Latina (12%), and white women (3%; p<0.001). Racial discrimination was significantly associated with reduced receipt of CBE. Reported discrimination due to “other” reasons such as age or gender was associated with reduced receipt of Pap smear, CBE), and mammography.

[WG#652]

[WG#695]

[WG#680]

[WG#529]

[WG#186]

Primary Question: Summary of Findings: Short sleep and sleep continuity are unrelated to blood pressure and hypertension in this sample. Less short wave sleep is related to change in diastolic blood pressure over time, whereas more arousal (beta power) is related to having hypertension at baseline. [WG#592]


Primary Question: Summary of Findings: Surgical and natural menopause were significantly associated with greater limitation in PF. The greater limitations observed among surgical and postmenopausal women are most likely to be resulted from the changes in endogenous estrogen and androgens accompanying the menopausal transition. [WG#643]


Primary Question: Summary of Findings: Higher CRP, a marker of inflammation, and higher tPA-ag, a hemostatic marker were associated with greater physical functioning limitations. Higher fibrinogen was associated with greater physical functioning limitations in African Americans only. [WG#682]


Primary Question: Summary of Findings: Physical activity in each domain tested (sport, home, active living, and work) was associated with stronger hip bone in adult women. Therefore being physically active may be an important way to prevent hip fracture in the future. [WG#642]

Ylitalo KR, Herman W, Harlow SD. Monofilament Insensitivity and Small and Large

Primary Question:

Summary of Findings:  The prevalence of peripheral neuropathy is substantial but varies according to the method of assessment. Regardless of assessment method, women with neuropathy and diabetes have larger body sizes, higher HbA1c values, and are more likely to be hypertensive.

[WG#548C]


Primary Question:

Summary of Findings:  Caucasians had fatty liver more often than African-Americans and sex hormone binding globulin, a protein that binds to sex hormones, was associated with a decreased odds of having fatty liver, but other sex hormones were not associated with fatty liver.

[WG#657]


Primary Question:

Summary of Findings:  The adrenal cortex may be a primary contributor to circulating sex steroids in most women

[WG#731]


Primary Question:

Summary of Findings:  In the current pilot study complement protein C3 but not C4 was found to be significantly related to menopausal status independent of age, race and BMI. Further, the association between C3 and postmenopausal status were found to be more pronounced among obese women. Both complement proteins C3 and C4 were found to be significantly associated with hemostatic/coagulation markers in women at midlife. Complement protein C3 was independently associated with two important hemostatic markers, PAI-1 and tPA antigen. These markers have significant roles in thrombus development, stabilization and destabilization in lesion areas. C4 was independently associated with thrombus development factors: factor VIIc and fibrinogen.

[WG#693]


Primary Question:
Summary of Findings: Women initiating use of a SSRI or TCA did not have higher rates of subsequent bone loss at the spine, total hip, or femoral neck than women not initiating use of these medications. Results were similar in women with and without evidence of significant depressive symptoms.


Primary Question: Analyses revealed that HRV during sleep differed significantly by race after adjusting for possible confounders. High frequency HRV during non-rapid eye movement (NREM) and rapid eye movement (REM) sleep was higher in African American and Chinese women, compared to Caucasian women (p’s < 0.001). Sympathovagal tone (ratio of low-to-high frequency HRV) during NREM and REM sleep was significantly lower in African American and Chinese women, compared to Caucasian women (p’s < 0.001). Heart rate variability during sleep did not differ between African American and Chinese women.


Primary Question: Structurally advantageous differences in bone microarchitecture and density contribute to greater bone strength in African Americans and may be a key factor that leads to the lower fracture risk observed in African-American women.

Thurston RC, Chang Y, Mancuso P, Matthews KA. Adipokines, adiposity, and vasomotor symptoms during the menopause transition: findings from the Study of Women’s Health Across the Nation. Fertility and Sterility. Fertil Steril. 2013 Sep;100(3):793-800.PMID:23755948

Primary Question: Lower adiponectin, lower HMW adiponectin, and to a lesser extent higher leptin were associated with lower odds of hot flashes early, but not later, in the menopause transition. These adiokines accounted in part, but not fully, for relations between BMI and VMS.


Primary Question: Femoral neck strength relative to load declines significantly during the menopausal transition, with declines commencing one to two years prior to the final menstrual period. The major determinants of rates of decline are race/ethnicity, history of smoking, body mass index and use of sex steroid hormones.

Primary Question:
Summary of Findings: We found transportation-related physical activity and household-related physical activity to be largely unrelated to sleep, regardless of whether recent levels or the historical pattern were considered. In contrast, greater recent levels of recreational physical activity, as well as consistently high levels of recreational physical activity, were associated with better sleep quality, sleep continuity, and sleep depth in this sample of midlife women.

[WG#599]


Primary Question:
Summary of Findings: Physical activity, particularly household physical activity, was associated with better sleep characteristics in our sample of midlife women. These associations were observed primarily among Caucasian and non-obese midlife women.

[WG#676]


Primary Question:
Summary of Findings: Midlife women experience an increase in cardiovascular risk factors following natural menopause and hysterectomy with or without bilateral oophorectomy. These risks do not appear to be increased by surgical menopause.

[WG#619C]


Primary Question:
Summary of Findings: CRP values were associated inversely with composite strength indices, and the lower values of femoral neck composite strength indices with high CRP explained some but not all of the positive association between CRP and fracture risk.

[WG#623]


Primary Question:
Summary of Findings: Higher education, prior use of oral contraceptives, being employed,
not smoking, not having diabetes, having lower baseline weight and less increase in weight over follow-up, better self-rated health and lower follicle stimulating hormone were significantly independently associated with later age at the FMP. We found no significant racial/ethnic differences in age at natural FMP after controlling for multiple sociodemographic, lifestyle and health factors. Our results and those of others suggest that the age at natural FMP reflects a complex inter-relation of factors, many of which are related to better health, which may partially explain the relation of late age at FMP to reduced morbidity and mortality.

[WG#451]


Primary Question:
Summary of Findings: The prevalence of physical functioning limitations is high among mid-life women. Race/ethnicity, obesity, and economic strain are associated with prevalence and onset of physical functioning limitations. Nevertheless, improvement in functioning is common during this life stage.

[WG#653]


Primary Question:
Summary of Findings: There is an orderly progression in which a decline in ovarian function beginning about 2 years before the FMP is followed by an increase in bone resorption and subsequently to accelerated bone loss during the menopause transition. The increase in bone resorption across the transition is inversely associated with BMI. Ethnic differences in the mean NTX increase are attenuated, but not eliminated, by adjustment for BMI. The data suggest that ethnic differences in BMI, and corresponding ethnic differences in bone resorption, account for ethnic differences in peri-menopausal bone loss.

[WG#437]


Primary Question:
Summary of Findings: Women who reported experiencing discrimination and mistreatment on a day-to-day basis over time reported more difficulty sleeping at night and spent more time awake after falling asleep for the night. Experiencing discrimination had a similar impact on sleep for African-American, Caucasian and Chinese women, and did not affect one racial/ethnic group more than the others.

[WG#504]
Classifying Menopausal Stage by Menstrual Calendars and Annual Interviews: Need for Improved Questionnaires: need for improved questionnaires.  
Menopause.  
2013 Jul;20(7):727-35. PMID: 23481122  
Primary Question:  
Summary of Findings:  Poor agreement was found between annual interview/annual FSH measures and menstrual calendars. Overall, the menstrual calendars staged women earlier than annual interview. The annual interview questions fail to capture the late menopausal transition in approximately one out of every three participants (they go from early menopausal transition to FMP).  
[WG#535]  
Karvonen-Gutierrez C, Ylitalo K.  
Prevalence and correlates of disability in a late middle aged population of women.  
Journal of Aging and Health.  
Primary Question:  
Summary of Findings:  The prevalence of moderate to severe global disability among the Michigan SWAN population was 20%. Important correlates of global disability included race/ethnicity, economic strain, depressive symptoms and peripheral neuropathy. Additionally, knee osteoarthritis, obesity and hypertension were associated with the mobility disability domain.  
[WG#685]  
Gibson CJ, Thurston RC, El Khoudary SR, Sutton-Tyrrell K, Matthews KA.  
Body Mass Index Following Natural Menopause and Hysterectomy with and without Bilateral Oopherectomy.  
International Journal of Obesity.  
Primary Question:  
Summary of Findings:  Midlife women experience an increase in body mass index in the years leading up to and following natural menopause and hysterectomy with or without bilateral oophorectomy. Body mass index increases at an accelerated rate in women following hysterectomy with bilateral oophorectomy compared to following natural menopause, suggesting that oophorectomy may contribute to weight gain and risks for obesity and overweight-related diseases in the postmenopause.  
[WG#619B]  
Karvonen-Gutierrez CA, Harlow SD, Mancuso P, Jacobson J, Mendes de Leon CF, Nan B.  
Association of Leptin Levels With Radiographic Knee Osteoarthritis Among a Cohort of Midlife Women  
Arthritis Care Research.  
Primary Question:  
Summary of Findings:  Higher leptin levels were associated with having knee osteoarthritis and with developing knee osteoarthritis over-and-above the impact of higher body size. Leptin levels increased with age similar patterns of change were observed for women with knee OA at the beginning of follow-up, women who developed knee OA during follow-up and women who did not have knee OA during follow-up.  
[WG#629C]  
Lin WT, Beattie M, Chen L, Oktay K, Crawford SL, Gold EB, Cedars M, Rosen M.  
Comparison of age at natural menopause in BRCA1/2 mutation carriers to a non-clinic-based sample of women in northern California.  
Cancer.  
Primary Question:
Summary of Findings: BRCA 1/2 carriers will undergo earlier natural menopause than the general population by 3-4 years. BRCA 1/2 carriers who are current heavy smokers will undergo even earlier menopause.

[KG#612]

Primary Question:
Summary of Findings: Liver fat and SHBG were each associated with insulin concentrations even when measures of fatness were accounted for, and these associations were not diminished when their relationship with insulin was adjusted for each other. This suggests that liver fat and sex hormone binding globulin affect insulin through independent mechanisms.

[KG#609]

Primary Question:
Summary of Findings: Overall women were not more likely to report high anxiety during and after the menopausal transition than premenopause. However, women with low anxiety at study entry were at greater risk when they were perimenopausal or postmenopausal compared to when they were premenopausal. Women with high anxiety at study entry were at similar risk for high anxiety at all stages of the transition. Perimenopause or postmenopause did not increase risk for high anxiety in this group.

[KG#252F]

Primary Question:
Summary of Findings: Physical functioning differed between women with peripheral neuropathy and women without peripheral neuropathy. These differences were maintained or exacerbated over time for a variety of performance-based physical functioning tasks.

[KG#548B]

Primary Question:
Summary of Findings: The relationships between hormone levels and bone loss varied in the various phases of the menopausal transition.

[KG#621]

**Primary Question:**

**Summary of Findings:** We observed significant correlations between DXA- and QCT-derived measures of femoral neck geometry. Good correlations between simple strength indices indicate that the geometry of femoral neck cross-sections is reasonably well characterized by DXA methods. The results indicate that geometry based stress analyses are valid and that simple indices generated from conventional BMD also have value.

[WG#483]


**Primary Question:**

**Summary of Findings:** In our multivariate models, we found no relationship between the consumption level of any phytoestrogen (isoflavones, coumestrol or lignans) and the development of new onset stress or urge UI in midlife women.

[WG#565]


**Primary Question:**

**Summary of Findings:** African-American and Japanese women have more favorable hip geometry and strength than Caucasian and Chinese women. These findings may help explain the observed racial/ethnic differences in fracture rates.

[WG#487]

Greendale GA, Ishii S, Huang M, Karlamangla AS. Predicting the Timeline to the Final Menstrual Period: The Study of Women’s Health Across the Nation. *Journal of Clinical Endocrinology & Metabolism*. 2013;98(4);1483-1491.

**Primary Question:**

**Summary of Findings:** The models with current and one prior (pre-menopausal or early perimenopausal) serum level of E2 and FSH, along with concurrent values of age, menopause transition stage and whether the current serum sample was obtained in the early follicular phase can discern women had crossed selected landmark dates on the timeline to becoming postmenopausal (2 years prior to FMP, 1 year prior to FMP and FMP) and the models’ discrimination abilities were excellent.

[WG#602]


**Primary Question:**

**Summary of Findings:** Testosterone was weakly negatively associated with adiponectin
and soluble leptin receptor, and weakly positively associated with leptin, though the latter association was attenuated after adjustment for fat mass. SHBG associations were in the opposite direction of those listed for testosterone above, were much stronger, and were not attenuated by adjustment for fat mass, HOMA, or waist circumference.

[WG#574]


**Primary Question:**

**Summary of Findings:** No consistent patterns emerged for the relations of any dietary phytoestrogens or fiber to incident VMS. Although some adjusted odds ratios were statistically significant, patterns were not monotonic for intake amounts related to frequency of VMS.

[WG#564]


**Primary Question:**

**Summary of Findings:** Childhood physical abuse is associated with incident metabolic syndrome over the follow-up visits, independent of race, age at baseline, time-dependent menopausal status, cigarette smoking, physical activity, alcohol abuse, childhood socioeconomic status, and adulthood socioeconomic status.

[WG#524]


**Primary Question:**

**Summary of Findings:** On average, Michigan SWAN participants increased in body size between 1996 and 2008. Women with peripheral neuropathy had larger body sizes than women without peripheral neuropathy. Differences in BMI, waist circumference, and weight between neuropathy groups were maintained over time.

[WG#548A]


**Primary Question:**

**Summary of Findings:** Insomnia-like symptoms, short sleep duration, and ratings of poor sleep quality are associated with high aortic calcification scores in African American and Caucasian women. Adjustments for cardiovascular risk factors and depressive symptoms showed that waking up earlier than anticipated and unable to get back to sleep and ratings of poor sleep quality remain associated with high aortic calcification scores. Sleep characteristics were unrelated to high coronary calcification scores.

[WG#293]

**Primary Question:**

**Summary of Findings:** Shorter sleep duration, reflected in sleep actigraphy and diary measures, was associated with higher BMI in cross-sectional analyses, even when controlling for sleep-disordered breathing. However, sleep duration was not prospectively associated with BMI change in unadjusted or fully-adjusted models.

[WG#588]


**Primary Question:**

**Summary of Findings:** During the menopausal transition, and particularly during the late peri-menopause, the carotid artery undergoes an adaptation that is reflected in increases in Adventitial Diameter followed by increases in Intima-media Thickness. These changes may impact the vulnerability of the vessel in the postmenopausal period, suggesting that the peri-menopause stage as a critical time for applying intervention strategies.

[WG#459C]


**Primary Question:**

**Summary of Findings:** BAI shows similar cross-sectional associations with percent body fat (derived from a DXA scan) as BMI, but is slightly less accurate in tracking change in percent body fat.

[WG#604]


**Primary Question:**

**Summary of Findings:** As compared with women with a history of either MDD or anxiety alone, women with a lifetime history of both MDD and anxiety reported a more severe and recurrent psychiatric history, greater levels of depressive and anxiety symptoms, elevated reports of past-year distressing life events, poorer social functioning, and diminished social support. Exploratory analyses indicated that women with a comorbid history were also more likely to report childhood abuse or neglect, as compared with women with a history of either MDD or anxiety alone.

[WG#551]

**379** Tseng LA, El Khoudary SR, Young EA, Farhat GN, Sowers M, Sutton-Tyrrell K, Newman AB.

Primary Question: Summary of Findings: Women with surgical or naturally occurring post-menopause reported greater limitations in physical function than pre-menopausal women, independent of age, only partly explained by higher BMI and depressive symptoms. [WG#501]


Primary Question: Summary of Findings: Independent of SBP, BMI, lipids and other covariates, lower E2 and SHBG, and higher FAI and FSH were associated with increased subclinical atherosclerosis progression in women during the menopausal transition. [WG#459D]


Primary Question: Summary of Findings: Higher levels of the bone resorption marker, NTX, and greater increases in NTX over the menopausal transition are significantly associated with an increase in fracture risk. These associations were independent of BMD, E2, FSH and other potential covariates. Serum osteocalcin, a marker of osteoblast activity, was also associated with fracture risk in unadjusted analyses only. [WG#527]


Primary Question: Summary of Findings: Composite strength indices of femoral neck predict fracture risk in middle-age women going through the menopause transition, and can predict risk of fracture at any body site (not limited to femoral neck) without information regarding the person’s race/ethnicity. [WG#598]


Primary Question: Summary of Findings: We found hot flash reporting to be associated with higher glucose and HOMA, an indicator of insulin resistance. These associations persisted controlling for cardiovascular risk factors and reproductive hormone concentrations. [WG#461E]

**Primary Question:**

**Summary of Findings:** Current waist circumference predicted future SHBG, testosterone, and FSH, but not vice-versa. Estradiol results were distinct from those above, changing direction across the menopause transition. Estradiol and waist circumference were negatively associated in early menopausal transition stages and positively associated in later transition stages. In addition, they appeared to be reciprocal, with current waist circumference associated with future estradiol, and current estradiol associated with future waist circumference. However, associations in the direction of current waist circumference predicting future estradiol levels were of considerably larger magnitude than the reverse. In SWAN, the predominant temporal sequence is that weight gain leads to changes in sex steroids.

[WG#375B]

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**Primary Question:**

**Summary of Findings:** We found that compared to Caucasian women, African American women had lower levels of adiponectin and high molecular weight adiponectin and higher levels of leptin and soluble leptin receptor molecule despite adjusting for fat mass. In addition, compared to Caucasian women, both Chinese and Japanese women also had lower levels of adiponectin and high molecular weight adiponectin after accounting for differences in fat mass. There were no differences in leptin levels.

All race-ethnic differences were more apparent at lower tertiles of fat mass and were attenuated at higher fat mass tertiles.

[WG#577]

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**Primary Question:**

**Summary of Findings:** Results showed that after accounting for other factors, current major depression (within the last year) is associated with a premenstrual like syndrome in midlife. Whereas, past (i.e. lifetime history of) major depression is associated with an increase in heavy bleeding symptoms in midlife independent of known risk factors for heavy bleeding. Neither current nor past major depression is associated with irregular bleeding symptoms in midlife.

[WG#162]

**Primary Question:**

**Summary of Findings:** From premenopause to postmenopause, women on average have increases in iron, and lower premenopausal iron stores and greater increases in iron over the menopause were associated with increases in insulin resistance.

(WG#603)


**Primary Question:**

**Summary of Findings:** During the menopausal transition, the change in the serum levels of both E2 and FSH vary between women and fall into several distinct patterns. We were able to distinguish four unique E2 and three unique FSH changing groups. These differing groups were strongly related to race/ethnicity and BMI but not smoking, physical activity, or demographic variables.

(WG#532)


**Primary Question:**

**Summary of Findings:** During the late perimenopause and postmenopause stages, Asian women with high isoflavone intakes did better on processing speed, but during early perimenopause and postmenopause, high isoflavone Asian consumers performed worse on verbal recall. The highest isoflavone consumers among non-Asians likewise posted lower verbal memory scores during early perimenopause. A verbal memory benefit of higher dietary lignan consumption was apparent only during late perimenopause, when women from all ethnic/racial groups who were in the highest intake group demonstrated did a little bit better on the verbal test. Coumestrol was unrelated to cognitive performance.

(WG#562)


**Primary Question:**

**Summary of Findings:** The relation between VMS and sleep may depend upon the awareness VMS, not simply their occurrence.

(WG#591)

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**Primary Question:**

**Summary of Findings:** We found that excess energy from food is stored as toxic belly fat in mid-life women. When Caucasian women eat more calories they store more fat inside belly than African American women of the same weight. There is no “free lunch” after menopause: women after menopause have more belly fat.

[WG#490]


**Primary Question:**

**Summary of Findings:** There is a correlation between adrenal androgens DHEAS and Adiol as well as the more potent androgens. Changes in adrenal androgen production rate during the menopausal transition may be important than the decline of ovarian function in terms of altering the estrogen/androgen balance.

[WG#255D]


**Primary Question:**

**Summary of Findings:** Among SWAN participants, women with high serum androgens were at a high risk for metabolic and cardiovascular risks factors, independent of body mass and other factors. Women with a history of irregular menstrual periods and high serum androgens have shown evidence of the highest risk for metabolic and cardiovascular risks factors, while those with a history of irregular menstrual periods but normal androgens do not exhibit increased metabolic risk.

[WG#593]


**Primary Question:**

**Summary of Findings:** Sleep disordered breathing and light sleep were both related to the metabolic syndrome in a multi-ethnic sample of midlife women. Women with both types of sleep disturbances were much more likely to have the metabolic syndrome compared to women with no sleep disturbances.

[WG#423]


**Primary Question:**

**Summary of Findings:** The wide range of circulating levels of Adiol and its contribution to total circulating estrogenicity during the MT is consistent with the observed inter-woman
difference in symptoms at this time. Therefore, we conclude that Adiol contributes to circulating estrogenicity when E2 production falls at menopause and may contribute significantly to the endocrine changes experienced by midlife women.


Primary Question: Mood Symptoms After Natural Menopause and Hysterectomy with and without Bilateral Oophorectomy Among Women in Midlife

Summary of Findings: Midlife women experience a decline in depressive and anxiety symptoms in the years following natural menopause and hysterectomy with or without bilateral oophorectomy. Depressive symptoms also decline similarly in the years leading up to natural menopause or surgery. No differences were seen in the trajectory of mood scores between women who experience natural menopause, hysterectomy with ovarian conservation, or hysterectomy with bilateral oophorectomy.


Primary Question: Role Stress, Role Reward, and Mental Health in a Multiethnic Sample of Midlife Women: Results from the Study of Women's Health Across the Nation (SWAN)

Summary of Findings: Reward across roles buffered the negative impact of stress across roles on poor social functioning. High reward experienced in being a Mother or Married decreased the negative effect of high stress in the same roles on at least one aspect of mental health. Compared to Caucasians, minority women (Hispanic and Chinese) were less affected by overall high role stress in their social functioning, and African American Mothers were less likely to report depressive symptoms.


Primary Question: Lifetime History of Depression and Anxiety Disorders as a Predictor of Quality of Life in Midlife Women in the Absence of Current Illness Episodes

Summary of Findings: Midlife women with a previous history of both a depression and an anxiety disorder have the greatest likelihood of experiencing reduced quality-of-life during the menopause transition, even when they are not currently depressed or anxious. While women with depression/anxiety disorder have the greatest likelihood of experiencing reduced quality-of-life during the menopause transition, hot flashes and sleep disturbance during the menopause transition, hot flashes and sleep disturbance do not explain why these women have reduced quality-of-life. Sleep disturbance has a strong effect on reducing quality-of-life, and explains in part why women with prior depression only are also susceptible to experiencing compromised quality-of-life during the menopause transition.

Primary Question:  
Summary of Findings: Unadjusted indices were similar in Caucasian and African-American women but higher in Chinese and Japanese women. After adjusting for age and menopause status, all three minority groups had higher composite strength indices than Caucasian women.  
[WG#488]


Primary Question:  
Summary of Findings: We found hot flash reporting to be associated with adverse changes in inflammatory and hemostatic markers. In the case of two key hemostatic markers, Factor VIIc and TPA-antigen, these associations persisted controlling for cardiovascular risk factors and estradiol concentrations.  
[WG#461D]


Primary Question:  
Summary of Findings: Three out of 10 items on the everyday discrimination scale differ by race/ethnicity: “receiving poorer service in restaurants or stores”, “being treated as if you are dishonest” and “being treated with less courtesy than other people” (all p-values <.001). Findings suggest that the profile of everyday discrimination may differ slightly for women of different racial/ethnic groups, with “public” experiences appearing to have more salience for African-American and Chinese women, and “dishonesty” having more salience for racial/ethnic minority women overall. “Courtesy” appears to have more salience for Hispanic women only compared to African-American women.  
[WG#320]


Primary Question:  
Summary of Findings: There was evidence of significant night-to-night variability, though relatively modest, based on 3 nights of in-home sleep measures when Night 1 included additional instrumentation to assess respiration and limb movement whereas Nights 2 and 3 included a sleep staging montage. When resources are constrained, 2 nights of in-home sleep assessment with an appropriate sample size can provide robust parameter estimates of sleep. In addition to type of instrumentation, personal characteristics likely to increase variability between nights include smoking, obesity and financial strain.  
[WG#441]

**Primary Question:**

**Summary of Findings:** For middle-aged women going through menopause, involvement in rewarding multiple roles decreases the risk of worsening coronary calcium, an early indicator of heart disease development. This increase in risk is similar in magnitude to the increase in risk associated with higher age or higher BMI.

[WG#523]


**Primary Question:**

**Summary of Findings:** For the total cohort, higher prevalence of plaque was associated with higher levels of AC and CAC, and this association was significant for AC. After stratifying by race, clear differences were observed. Among African-Americans, there was no relationship between carotid plaque and AC, and a trend of a negative association between carotid plaque and CAC. In contrast, for Caucasians, there were significant positive relationships between carotid plaque and both AC and CAC. The interaction of carotid plaque by race was significant for predicting both AC and CAC (p=0.03, 0.002).

[WG#401]


**Primary Question:**

**Summary of Findings:** We found that diabetic women have lower femoral neck strength relative to the loads they bear despite having higher bone mineral density, consistent with the documented higher rates of fracture in diabetic women. Insulin resistance appears to play an important role in the reduction in bone strength in diabetics.

[WG#594]


**Primary Question:**

**Summary of Findings:** There is a period of rapid bone loss that starts about one year before the final menstrual period (FMP) and the bone loss is greatest between 1 year before FMP and 2 years after FMP regardless of ethnicity and body mass. The 10-year cumulative BMD loss in Caucasian women is 10.6% at lumbar spine and 9.1% at femoral neck. The amount of 10-year loss is slightly less in African-American women and slightly more in Chinese and Japanese women.

[WG#552]
Huang M, Norris J, Han W, Block T, Gold E, Crawford S, Greendale GA. Development of an Updated Phytoestrogen Database for Use With the SWAN Food Frequency Questionnaire: Intakes and Food Sources in a Community-Based, Multiethnic Cohort Study. Nutrition and Cancer. 2012;64(2):228-244.

**Primary Question:**

**Summary of Findings:** The expanded database included 4 isoflavones, coumestrol and 4 lignans. The new database estimated isoflavone content of 125 food items (41.8%) versus 14 (4.7%) in the 1994 version and computed coumestrol content of 55 food items (18.4%), compared to 1 (0.3%) in the original version. Newly added were lignans; values for 111 FFQ food items (37.1%) were calculated. We also reported the phytonutrient intakes for each racial and language group in the SWAN sample and identified major food sources from which the phytonutrients came.

[GW#553]


**Primary Question:**

**Summary of Findings:** Negative mood and hot flashes are associated when both are measured on a daily basis. Negative mood does not predict next day hot flashes, but hot flashes do predict next day negative mood.

[GW#543]


**Primary Question:**

**Summary of Findings:** In this longitudinal study, moderate wine consumption (1 glass/day) was associated with lower odds of developing the MetS in midlife women, mainly through the beneficial association between wine consumption and HDL cholesterol and triglycerides, consistent with the literature. (Baer 2002, Opie (2007) Our findings of no relationship of wine consumption with glucose levels are similar to results from large cross-sectional studies. (Djousse 2004) Blood pressure was higher only in women who consumed more than 1 glass of wine per day, consistent with findings from intervention studies. (Leighton 2007) The finding that waist circumference was higher in African American women but lower in Caucasian women who drank 1 glass of wine per day may indicate different drinking patterns in the two groups. Therefore, using a rigorous longitudinal design, the current study supports the hypothesis that moderate wine consumption is good for cardiovascular health.

[WG#406C]


**Primary Question:**

**Summary of Findings:** We found that annually measured values and year to year changes in estrogen (estradiol) levels had no significant relation to the development or worsening of urinary incontinence in mid-life women transitioning through menopause.

**Primary Question:**

**Summary of Findings:** Higher levels of CRP were associated with higher levels of aortic pulse wave velocity even after adjustment for confounders. The association between CRP and pulse wave velocity was stronger in women who were later in their menopausal transition than women who were earlier in their transition.


**Primary Question:**

**Summary of Findings:** After controlling for socio-economic factors and other confounders, African-American and Chinese women were significantly less likely to suffer from involuntary childlessness as compared to non-Hispanic Caucasian women. 302 subjects reported a perceived etiology of infertility. An unexpectedly large proportion of these women (24.5%, 74 out of 302) reported etiologies not known to cause infertility, with African-American women having been most likely to report these etiologies as the reason for not becoming pregnant.


**Primary Question:**

**Summary of Findings:** Beta EEG power in NREM and REM sleep was higher in late perimenopausal and post menopausal women than in pre- and early perimenopausal women. Delta power did not differ by menopausal status. Elevated beta EEG power provides an objective measure of disturbed sleep quality in menopausal women and may be related to elevated arousal level during sleep.


**Primary Question:**

**Summary of Findings:** Mothers who did not consistently breastfeed were significantly more likely to retain abdominal fat than mothers who consistently breastfed.

Conroy SM, Butler LM, Harvey D, Gold EB, Sternfeld B, Greendale GA, Habel LA. Metabolic Syndrome and Mammographic Density: The Study of Women's Health Across the

Primary Question:
Summary of Findings: Women with the MetS and/or insulin resistance did not have higher percent MD compared to women without these conditions. Our results do not support the hypothesis that the MetS and/or insulin resistance affect breast cancer risk via a mechanism reflected by percent MD or dense breast tissue area.


Primary Question:
Summary of Findings: We found hot flash reporting to be associated with adverse changes in inflammatory and hemostatic markers. In the case of two key hemostatic markers, Factor VIIc and TPA-antigen, these associations persisted controlling for cardiovascular risk factors and estradiol concentrations.


Primary Question:
Summary of Findings: Larger body size/higher body fat was associated with fewer physiologically monitored hot flashes among the older women in the sample with hot flashes.


Primary Question:
Summary of Findings:


Primary Question:
Summary of Findings:


Primary Question:
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Primary Question: Summary of Findings:
[WG#581]

Primary Question: Summary of Findings:
[WG#580]

Primary Question: Summary of Findings:
[WG#579]

Primary Question: Summary of Findings:
[WG#572]

Primary Question: Summary of Findings:
[WG#586]

Primary Question: Summary of Findings:
[WG#597]

Primary Question: Summary of Findings:

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Primary Question: Summary of Findings: We found limited evidence for associations between EEG sleep measures and nocturnal VMS or symptoms of depression or anxiety. EEG sleep measures were largely not associated with VMS and mood symptoms across all racial/ethnic groups, although having more frequent nocturnal VMS was associated with longer sleep time. In Caucasians, DSR was higher in women with more frequent nocturnal VMS and with higher depressive symptom scores, while REM latency was longer in women with higher depressive and anxiety symptom scores. Chinese women with higher anxiety symptom scores had shorter sleep latency. Significant racial/ethnic effects did not persist in all fully adjusted models and were not consistently in the expected direction. Antidepressant medication use was a significant covariate in adjusted models for DSR, REM latency and sleep latency. Thus, characteristics of sleep determined by EEG measures seem to be largely independent of these symptoms.


Primary Question: Summary of Findings: The risk of a major depressive episode for women during and immediately after the menopausal transition is about two to four times as great as when they
are premenopausal. However, it appears that the increased risk is likely experienced only by a subset of women. Many questions remain about the cause of major depression during this time and the contributions of alterations of the hormonal conditions and other unmeasured factors. [WG#362]


Primary Question:
Summary of Findings: An integrative methodology is developed to characterize the complex patterns of change in highly variable dynamic biological processes. The method permits estimation of the population mean profile, multiple change points and length of time-windows defined by any two change points of interest using a semi-/non-parametric stochastic mixed effect model and a Bayesian Modeling Average (BMA) approach to account for model uncertainty. It also allows estimation of the mean rate of change of sub-processes by fitting piecewise linear mixed effect models. The methodology is applied to characterize the stages of female ovarian aging and the menopausal transition defined by hormone measures of estradiol (E2) and follicle stimulating hormone (FSH) from two large-scale epidemiological studies with community-based longitudinal designs and ethnic diversity. [WG#531B]


Primary Question:
Summary of Findings: SHBG and FAI are associated with arterial calcification. Obesity status influences the role that SHBG and FAI play in calcification of the coronary arteries and aorta of perimenopausal women. In non-obese women, higher SHBG and lower FAI were associated with greater extent of CAC while lower SHBG was associated with greater extent of CAC in obese women. [WG#317]


Primary Question:
Summary of Findings: SBP and waist circumference were most strongly related to PWV progression than were DBP, triglycerides, LDL-C, HDL-C, and glucose in the total sample of SWAN Heart women. SBP was more strongly associated with PWV progression among African Americans than among Caucasians; in addition, DBP, LDL-C, and to a lesser extent,
glucose levels, were all associated with PWV progression among African Americans only. [WG#499]


**Primary Question:**
**Summary of Findings:** For middle-aged women going through menopause, depression increases the risk of worsening coronary calcium, an early indicator of heart disease development. This increase in risk is similar to the increase in risk associated with higher BMI or higher blood pressure. [WG#518]


**Primary Question:**
**Summary of Findings:** Higher reports of discrimination are associated with a greater amount of fat around the internal organs in middle-aged African-American and White women. Reports of discrimination were not associated with other types of fat surrounding the waist. [WG#516]


**Primary Question:**
**Summary of Findings:** After taking known risk factors into account, negative attitudes toward aging and menopause, negative affect, and PMS-like symptoms do not predict elective hysterectomy. However, hot flashes/night sweats in early menopause do predict elective hysterectomy over the menopausal transition. [WG#493]


**Primary Question:**
**Summary of Findings:** The ovaries are not required. [WG#510]


**Primary Question:**
**Summary of Findings:** The study provides evidence that despite higher BMD at baseline, women with DM experience greater annual average rate of hip bone loss and a higher
fracture risk during the menopausal transition.

[Sweans][WG#456]


Primary Question: Summary of Findings: Obesity and CYP19 and 17-â HSD genes variants influenced rates of E2 decline at the FMP leading to subgroups of postmenopausal women with marked differences in E2 levels. This may have implications for differential postmenopausal bone loss or risk for estrogen-sensitive chronic diseases.

[WG#495]


Primary Question: Summary of Findings: Data collected from outside sources can be used to estimate values for missing data at the time of the study visits. Our estimation approach is based on linear interpolation, with the addition of multiply imputed noise terms to account for the fact that data are estimated rather than observed. We show that this approach is unbiased, on average, and that the interpretation of results is affected by the approach used to estimate missing data.

[WG#381A]


Primary Question: Summary of Findings: The protective effect of HDL-c is reduced among postmenopausal women.

[WG#430]


Primary Question: Summary of Findings: Perimenopausal women with menopausal hot flashes had higher levels of Ntx, a marker of bone turnover, than perimenopausal women without menopausal hot flashes.

[WG#457]


Primary Question:
Summary of Findings: Higher levels of abdominal subcutaneous adipose tissue are associated with less favorable cardiometabolic risk factor levels and with a greater burden of subclinical atherosclerosis. However, among African American but not Caucasian women, these adverse associations are attenuated or reversed when in the presence of high levels of abdominal visceral adipose tissue.


Primary Question:
Summary of Findings: Hot flashes were associated with higher intima media thickness. This association was not fully accounted for by cardiovascular risk factors nor estradiol concentrations. This associations were most pronounced among overweight and obese women.


Primary Question:
Summary of Findings: The endocrinologic patterns and timespans associated with the marked hormone changes of late ovarian aging are relatively consistent, regardless of the chronologic age at which the FMP occurs. Moreover, while obesity, race/ethnicity, and smoking were associated with some differences in absolute serum concentrations of reproductive hormones, they were not associated with variation in the overall patterns and timespans of late ovarian aging.


Primary Question:
Summary of Findings: The prevalence of knee OA (K-L scores > 2) changed from 18.1% at the 1996/7 baseline to 62.4% at the 2007/8 follow-up; the prevalence of moderate to severe knee OA (K-L scores of 3-4) changed from 3.7% to 26.7% in the same time period.

Full-thickness cartilage defects were present in 14.6%, 4.6% and 26.3% of medial, lateral, and patellofemoral compartments, respectively. MR-defined synovitis occurred in 24.7% of knees; in 6.2% of knees, synovitis was moderate to marked. Joint effusions were observed in 70% of knees. Complex or macerated meniscal tears were present in 21.8% of knees. Walking and stair climbing times were 30-40% slower in women with large osteophytes, synovitis, macerated meniscal tears, or full-thickness cartilage defects. In middle-aged women, there is a high prevalence of radiographically-defined knee OA corroborated by significant associations with cartilage defects, complex and macerated meniscal tears, osteophytes and synovitis, knee pain, and lower mobility levels.

**Primary Question:**

**Summary of Findings:** Despite published data indicating a similar 3-11 year CVD event rate among obese individuals with healthy cardiometabolic profiles and normal weight individuals, midlife overweight/obese women with healthy cardiometabolic profiles participating in SWAN have an intermediate burden of subclinical cardiovascular disease, with significantly higher subclinical disease levels compared to healthy normal weight women and borderline significantly lower levels of subclinical disease compared to at-risk overweight/obese women.


**Primary Question:**

**Summary of Findings:** There is significant variation in cardiovascular risk status among middle-aged Puerto Rican, Cuban, Dominican, Central American and South American women, not explained by acculturation or socioeconomic indicators. These differences may be important for targeting screening and preventive interventions.


**Primary Question:**

**Summary of Findings:** Puerto Rican women have more depressive symptoms, poorer physical functioning, more sleep problems, and anxiety compared to the other Hispanic subethnicities.


**Primary Question:**

**Summary of Findings:** Indices of sleep disordered breathing are associated with each of the biomarkers of inflammation and coagulation in the full sample. African Americans who are short and/or inefficient sleepers have higher levels of CRP, fibrinogen, and PAI-1 in full multivariate models.
454  Knight JM, Avery EF, Janssen I, Powell LH.  **Cortisol and Depressive Symptoms in a Population-Based Cohort of Midlife Women.** *Psychosomatic Medicine.* 2010;72(9):855-861.

**Primary Question:**

**Summary of Findings:**  Midlife women from a population-based sample with higher CES-D scores have significantly flatter diurnal cortisol slope than those with lower scores, even after adjusting for covariates and possibly contaminating behaviors.

[WG#489]


**Primary Question:**

**Summary of Findings:**  Healthy women with a history of at least 2 episodes of major depression show greater progression across a 2 ½ follow-up period compared to women who have 1 or no episodes. The effect was only obtained in those with any calcification at baseline. Other important predictors of progression were initial calcification, body mass index, and systolic blood pressure.

[WG#434]


**Primary Question:**

**Summary of Findings:**  Reporting of symptoms associated with menopause among Hispanic women differed by county of origin but not acculturation. Central American women appear to be at greatest risk for both Vasomotor Symptoms (VMS) and vaginal dryness.

[WG#429]


**Primary Question:**

**Summary of Findings:**  Higher concurrent depressive symptom scores were significantly related to several performance-based functions including slower timed walk, lower walking velocities and chair rise, as well as lower leg strength, slower 2-lb lift, and slower stair climb after adjusting for relevant covariates. Persistent depressive symptoms were related to slower 2-lb lift, velocity, and sit-to-stand compared to those did not report depressive symptoms at any time point. Those with higher concurrent depressive scores and those reporting depressive symptoms at >3 time points were significantly more likely to have perceived limitations in physical functioning.

[WG#466]

Primary Question: 
Summary of Findings: Women with radiographic evidence of knee osteoarthritis were 22% stronger than women without knee osteoarthritis. Quadriceps strength was also greater in women without cartilaginous defects on the medial tibia, femur, and patella when compared with women with cartilaginous defects in these regions. 

[Troxl#500]

Primary Question: 
Summary of Findings: Women who were married at the time of the sleep study had better sleep quality and better sleep continuity than unmarried women. However, most of these associations were reduced to non-significance when accounting for other known risk factors for sleep disturbance. Analyses of women’s marital histories revealed that women who were consistently married throughout the study follow-up had better sleep quality and continuity than women who were consistently unmarried or those who had lost a partner. These differences generally persisted even after covariate adjustment. Women who gained a partner over the course of the study were similar to the consistently married group for most sleep outcomes. However, they had poorer actigraphy-assessed sleep fragmentation, which may reflect an acclimation period of adjusting to a new relationship. 

[Troxl#462]

Primary Question: 
Summary of Findings: Higher levels of physical activity were associated with lower levels of IAF, the fat that surrounds the organs deep in the abdomen. This fat has been associated with diabetes and heart disease. Motivating white and black women to increase their physical activity during their middle years may lessen intra-abdominal fat which may impact positively on diabetes and cardiovascular risk profiles. 

[Troxl#392]

Primary Question: 
Summary of Findings: Hormones, specifically lower SHBG and higher androgens predict obesity in women transitioning the menopause. Among women undergoing a natural transition, bleeding patterns were not related to obesity. However, women undergoing surgical menopause and women who initiated HT prior to their final period were at increased risk for obesity. 

[Troxl#375A]

462 Bromberger JT, Schott LL, Kravitz HM, Sowers M, Avis NE, Gold EB, Randolph JF, Matthews KA. Longitudinal Change in Reproductive Hormones and Depressive Symptoms

Primary Question:
Summary of Findings: A woman in midlife is more likely to experience high levels of depressive symptoms when peri- or postmenopausal than when premenopausal. Current total testosterone and a smaller decrease in testosterone levels from baseline were associated with high depressive symptoms. Testosterone, menopausal status, and other health and lifestyle factors independently influence depressive symptoms in women during midlife.

[WG#222]


Primary Question:
Summary of Findings: Depressive and anxiety symptoms had a small negative effect on cognitive processing speed in our sample of mid-life women. However, the 4 symptoms studied—depressive, anxiety, sleep disturbance and vasomotor—did not account for the transient absence of SDMT learning observed during the late perimenopause in SWAN.

[WG#433]


Primary Question:
Summary of Findings: Higher levels of physical activity did not increase the observed decline with age in percent mammographic density. Our results do not support percent mammographic density being part of a pathway by which physical activity reduces breast cancer risk.

[WG#418]


Primary Question:
Summary of Findings: Women who were heavy adolescents have fewer children later in life than women who were not heavy.

[WG#388]


Primary Question:
Summary of Findings: At the midlife, there were associated and parallel declines in both cognitive and physical functioning levels and their 4-year changes. These parallel declines were explained, in part, by socioeconomic status and metabolic syndrome status, after
adjusting for menstrual status and race/ethnicity.

[WG#270]


Primary Question:
Summary of Findings: 1. ethnic differences in pre-menopausal bone density and peri-menopausal bone loss are greatly affected by body weight 2. bone density of pre-menopausal and early peri-menopausal women is inversely correlated with blood levels of FSH, not blood levels of estrogen, when these are measured once-yearly on day 2-5 of the menstrual cycle 3. rates of bone loss in middle-aged women correlate with once-yearly measurements of blood FSH, not blood estrogen 4. middle-aged women do not lose significant bone until their menses become less frequent 5. at that time, bone loss is as rapid as during the years immediately after the final menses

[WG#514]


Primary Question:
Summary of Findings: Women with higher levels of bio-available testosterone had more IAF, independent of age and other CVD risk factors, and also independent of physical activity levels. The relation is similar in black and white women. However, when black and white women with the same amount of total fat (or BMI) are compared, black women have significantly less intra-abdominal fat.

[WG#336]


Primary Question:
Summary of Findings: Physical abuse and sexual abuse are associated with obesity and central adiposity at baseline, and most subtypes of abuse/neglect are associated with changes in central adiposity for normal-weight and overweight women. Trait Anger and SHBG (sex hormone binding globulin) mediate cross-sectional relationships.

[WG#458]


Primary Question:
Summary of Findings: We observed lower percent mammographic density among current smokers, those who started to smoke before age 18, and those who smoked 20 or more cigarettes per day, compared to never active smokers. Our data support an antiestrogenic hypothesis for the relation between smoking and breast cancer in pre-/early perimenopausal
women.

[WG#386]


Primary Question:
Summary of Findings:

[WG#478]


Primary Question:
Summary of Findings: The relationships between depressive symptoms and inflammation may be bi-directional. Depressive symptoms were related to subsequent inflammation and vice versa, but no associations were found for coagulation. The relationship between depressive symptoms and inflammation were most apparent in normal or overweight women, rather than obese women.

[WG#414]


Primary Question:
Summary of Findings: Total cholesterol, LDL-cholesterol, and apolipoprotein B increase substantially around the time of the final menstrual period. Other risk factors, including blood pressure, inflammatory and hemostatic factors, glucose and insulin, do not show a unique rise around the final menstrual period. The changes in lipids were similar across ethnic groups.

[WG#325]


Primary Question:
Summary of Findings: The 2007 prevalence of x-ray defined knee osteoarthritis (OAK) was 50% in these 72 women. Upward trajectories of both cartilage oligomeric matrix protein (COMP) and cross-linked telopeptide of type II collagen (CTX-II) were associated with progression of OAK severity and body size. COMP trajectories were associated with pain and stiffness scores, but not functioning. CTX-II trajectories were associated with stiffness scores, but not knee pain or functioning scores. Multiple, biennial measures of COMP or CTX-II taken over a 10-year period are modestly predictive of subsequent OAK and stiffness in the knees.

[WG#443]

**Primary Question:**

**Summary of Findings:** Higher CRP was associated with worse perceived and performance-based physical functioning, including more time spent in double support, slower stair climb, shorter forward reach and slower 2-lb lift in concurrent and prospective analyses. Higher fibrinogen levels were associated with slower chair rise in concurrent analyses and shorter forward reach in concurrent and prospective analyses.

[WG#424]


**Primary Question:**

**Summary of Findings:** Mean GI and GL were consistently lower in Caucasian women than African American, Japanese or Chinese women. Mean GI and GL values were inversely associated with education, income and sports activity, and positively associated with current smoking and consumption of more than 1 drink of alcohol per day. GI was positively associated with consumption of grains and potatoes and inversely associated with consumption of fruits, dairy foods, and sweets.

[WG#348]


**Primary Question:**

**Summary of Findings:** Ninety-eight percent of physicians performing hysterectomies on participants of SWAN are board certified physicians. Nearly all are board certified in Obstetrics and Gynecology via the American Board of Obstetrics and Gynecology. It thus appears that these physicians are appropriately trained to carry out this commonly performed procedure.

[WG#450]


**Primary Question:**

**Summary of Findings:** The menopausal transition appears to decrease the risk of developing urinary incontinence. Instead, aging, weight gain, diabetes, and smoking increase the risk.

[WG#248D]


**Primary Question:**
**Summary of Findings:** Higher levels of hopelessness are associated with greater atherosclerosis in women after taking into account age, race, blood pressure, obesity, smoking and depressive symptoms. In contrast, depressive symptoms are not related to atherosclerosis once the effects of hopelessness are considered. Relations do not differ for African American and white women.

**Primary Question:**

**Summary of Findings:** Hostility was associated with a greater amount of visceral, but not subcutaneous fat in African-American and Caucasian women. Although there were significant racial/ethnic differences in hostility (higher in African-American women), subcutaneous fat (higher in African-American women) and visceral fat (lower in African-American women), the observed associations did not differ by race/ethnicity.

**Primary Question:**

**Summary of Findings:** Fat gain is associated with increased reporting of hot flashes over and above the previous years’ hot flash reporting. Fat gain was not associated with night sweat reporting.

**Primary Question:**

**Summary of Findings:** Women reported a greater impact of physical health on their functioning when they were late perimenopausal or postmenopausal than when they were premenopausal.

**Primary Question:**

**Summary of Findings:** DHEAS declines with age in premenopausal women, but exhibits a transient increase during the late menopause transition. Ovarian status-related patterns were similar in all 5 ethnic groups.

**Primary Question:**

**Summary of Findings:** Genetic variations in the way estrogen is metabolized, and variations in estrogen receptor genes, may be associated with breast density.

[WG#447]


**Primary Question:**

**Summary of Findings:** Daily spiritual experiences were not protective for systolic blood pressure or hypertension among midlife women in SWAN.

[WG#335/63]


**Primary Question:**

**Summary of Findings:** Each focus group session yielded important information about ethnic variations such as terminology, concepts and attitudes toward menopause and symptoms. Using focus groups can provide greater insight into the meaning of cultural or ethnic differences, produce more cross-culturally valid interpretations, and enhance the validity and generalizability of the study data.

[WG#62]


**Primary Question:**

**Summary of Findings:** Changes in blood cholesterol occurred late in the menopause transition, with only small changes during early menopause, with peaks in total cholesterol, LDL cholesterol and triglyceride levels during late perimenopause. These changes were greater than changes due to aging. Increases in total and LDL cholesterol and in triglycerides were smallest among women who were heaviest at baseline.

[WG#176]


**Primary Question:**

**Summary of Findings:** Late perimenopause produced a subtle decrement in measured
cognitive performance, characterized by women not being able to learn as well as they had during pre- and early perimenopause. The disturbance appears to be transient, rebounding in postmenopause. Hormone use may have either beneficial or detrimental effects on cognitive performance, depending on when it is begun.


**Primary Question:**
**Summary of Findings:** Women with more depressive symptoms have significantly more visceral fat than less depressed women, after taking into account important risk factors for central adiposity. Depressive symptoms were not associated with subcutaneous fat.

Avis NE, Brockwell S, Randolph JF Jr, Shen S, Cain VS, Ory M, Greendale GA. **Longitudinal Changes in Sexual Functioning as Women Transition through Menopause: Results from the Study of Women’s Health Across the Nation.** *Menopause.* 2009;16(3):442-452.

**Primary Question:**
**Summary of Findings:** The menopause transition is associated with decreases in women’s sexual desire and increases in pain during sexual intercourse. The menopause transition does not have an impact on the importance of sex, emotional satisfaction or physical pleasure.


**Primary Question:**
**Summary of Findings:** Fibroids was a presenting symptom more frequently in African-American women than Caucasian women, while Caucasian women were more likely to have prolapse compared to African-American women. There were no differences between the groups in levels of estradiol or testosterone hormone levels. African-American women had almost twice the uterine weight as that of Caucasian women.


**Primary Question:**
**Summary of Findings:** In the full sample of women (including women with the metabolic syndrome at baseline), lifetime history / current depression at baseline was associated with significantly greater odds of having the metabolic syndrome over the course of the study. In women who were free of the metabolic syndrome at baseline, lifetime history / current depression at baseline predicted significantly greater risk of developing the metabolic syndrome over the course of the follow-up.

**Primary Question:**

**Summary of Findings:** Classes of anovulatory cycles do not progress predictably to menopause. Ovulatory cycles may recur in women whose previous cycles exhibited loss of estrogen-negative feedback on LH and FSH. Changes in cycle class do not correlate with occurrence of vasomotor symptoms.

[WG#296]


**Primary Question:**

**Summary of Findings:** Even among women who are premenopausal or early in the menopause transition, women hot flashes and/or night sweats have a lower bone density on average than women without hot flashes or night sweats.

[WG#363]


**Primary Question:**

**Summary of Findings:**

[WG#472]


**Primary Question:**

**Summary of Findings:** Body mass index and weight were not associated with dense breast area in this longitudinal study. Both BMI and weight were negatively associated with percent density, however. Changes in BMI and weight may affect the non-dense breast tissue, rather than dense breast tissue where cancers arise.

[WG#381]


**Primary Question:**

**Summary of Findings:** The baseline total estrogen and its rate of change were not associated with an increased incidence. A low SHBG as well as a high total testosterone at entry appeared to increase the risk independent of their respective change over time. Both higher baseline values and greater rate of change in the relative androgen excess increased the incidence of developing the metabolic syndrome, independent of ethnicity.

**Primary Question:**

**Summary of Findings:** The ISQ’s high specificity suggests that a negative result with this instrument has a high probability of excluding those with insomnia. The high Positive Predictive Value indicates that the ISQ would have few false positives and useful in large observational studies in which the prevalence of insomnia is likely to be about 10%.


**Primary Question:**

**Summary of Findings:** Depressive symptoms were associated with a greater amount of aortic calcification for African-American, but not Caucasian women. Depressive symptoms were not associated with coronary calcification for either racial/ethnic group.


**Primary Question:**

**Summary of Findings:** Physically active women were less likely to experience pain and had higher levels of physical functioning over 3 years compared to less active women. This association was evident after taking into account menopausal status, sociodemographic factors, and medical conditions.


**Primary Question:**

**Summary of Findings:** Adenomyosis was found in about one-half of the SWAN women who had hysterectomies and for whom the study was able to obtain pathology reports. All the conditions examined, which are commonly reported as being related to adenomyosis (fibroids, endometriosis, abnormal bleeding and chronic pain), were equally common in women with and without adenomyosis. Adenomyosis is a common occurrence that does not cause symptoms in this population.

Primary Question:
Summary of Findings:  After simultaneous adjustment for multiple predictors in Cox Proportional Hazards analyses, baseline role functioning due to physical health (p<.0001, a lifetime history of an anxiety disorder (p=.03), and hot flashes (p=.02) and a very stressful life event (p=.05) prior to depression onset predicted a first episode of depression.

Primary Question:
Summary of Findings:  Happily married, Caucasian women had fewer sleep disturbances as compared to their unhappily married counterparts. This association was independent of other risk factors, suggesting that marital happiness is not merely a proxy for being a “happy” person. There was no association between marital happiness and sleep disturbance in African American, Hispanic, Chinese, or Japanese women.

Primary Question:
Summary of Findings:

Primary Question:
Summary of Findings:  Sleep characteristics differ by race. African American and Caucasian women who report that it is somewhat to very hard to pay for the very basics like food and housing have poorer sleep quality and a harder time falling and staying asleep at night, compared to women who report no difficulty paying for basics.

Primary Question:
Summary of Findings:  Both sensitivity and specificity of retrospective reporting for any vs. no vasomotor symptoms were high. Accuracy of retrospective reporting was highest among women with no symptomatic days or many symptomatic days in daily reporting, i.e., at the two extremes of symptom frequency.

507 Scuteri A, Vuga M, Najjar SS, Mehta V, Everson-Rose SA, Sutton-Tyrrell K, Matthews K, Lakatta EG. Education eclipses ethnicity in predicting the development of the metabolic syndrome in different ethnic groups in midlife: the Study of Women’s Health
Primary Question:
Summary of Findings: Approximately 10% of perimenopausal women developed the metabolic syndrome during the five year follow-up. SES, but not ethnicity, was an independent predictor of incident metabolic syndrome risk.


Primary Question:
Summary of Findings: The following menstrual and reproductive factors were found to be associated with greater or less mammographic density, a risk factor for breast cancer: older age at menarche (greater), history of premenstrual cravings and bloating (less), younger age at first full-term birth (less), being premenopausal (greater). However, the associations between mammographic density and the menstrual and reproductive factors listed above were not independent of other factors, such as body size, age, race/ethnicity, smoking, or the plasma sex hormone, sex hormone-binding globulin.


Primary Question:
Summary of Findings: There were competing CVD risk factor profiles when comparing premenopausal women and the same-aged women using HT. In the HT users, there were more favorable lipid profiles than the same aged premenopausal women but, concurrently, more negative oxidative/thrombotic/inflammatory profiles. These findings do not support assumptions that having only short-term time discontinuity before HT use is likely to replicate the environment in either premenopausal or immediately postmenopausal women.


Primary Question:
Summary of Findings: More rapid rate of follicle stimulating hormone (FSH) change was significantly associated with higher delta sleep percent, longer total sleep time (TST), but less favorable self-reported sleep quality from the Pittsburgh Sleep Quality Index (PSQI). Baseline estradiol (E2) was modestly and negatively associated with sleep quality. Women in the lowest total testosterone (T) quartile at baseline had more wake time after sleep onset (WASO) than women in the highest quartile. Lower E2/T ratio, an index reflecting the increasing androgenic environment with the menopause transition, was associated with less WASO. Therefore, more rapid rate of FSH change was associated with longer sleep duration but less favorable self-reported sleep quality. Women with higher T or who were moving
toward the completion of the transition process (as indexed by a lower E2/T) had less sleep discontinuity as characterized by WASO.  

[WG#397]

511 Thurston RC, Sutton-Tyrrell K, Everson-Rose SA, Hess R, Matthews KA. **Hot Flashes and Subclinical Cardiovascular Disease: Findings from the Study of Women’s Health Across the Nation Heart Study.** Circulation. 2008;118(12):1234-1240.  
**Primary Question:**  
**Summary of Findings:** Women with hot flashes were more likely to have evidence of subclinical disease (i.e., endothelial dysfunction, aortic calcification) than women without hot flashes.  

[WG#416]

**Primary Question:**  
**Summary of Findings:** Factors such as mood, symptom sensitivity, sleep problems, duration of vasomotor symptoms, age and race are associated with bother associated with vasomotor symptoms, above and beyond the frequency of vasomotor symptoms.  

[WG#399]

**Primary Question:**  
**Summary of Findings:** As testosterone increases over the menopausal transition, the prevalence of the metabolic syndrome increases, independently of age and other important covariates. This suggests that one pathway by which cardiovascular disease increases in women is via the menopause-related increasing androgenicity of the hormonal milieu.  

[WG#289]

**Primary Question:**  
**Summary of Findings:** Progression through the menopausal transition as indicated by 3 menopausal characteristics – symptoms, bleeding-defined stages, and endogenous hormone levels – is associated with self-reported sleep disturbances. Difficulty falling asleep and staying asleep increased through the menopausal transition, but early morning awakening decreased from late perimenopause to postmenopause. Women with more frequent VMS also were more likely to report each type of sleep difficulty. Women with decreasing E2 levels were more likely to report trouble falling and staying asleep, and those with increasing FSH levels were more likely to report trouble staying asleep. There were racial/ethnic differences in difficulties staying asleep and early morning awakening but no significant differences in falling asleep.  

[WG#138]

Primary Question:
Summary of Findings: Changes in timing of bleeding (interval and duration) are associated with anovulation. Changes in amount of bleeding (heavy bleeding or menorrhagia) are not associated with anovulation but are associated with fibroids and obesity. [WG#217A]


Primary Question:
Summary of Findings: C-reactive protein levels vary with ethnicity; the highest levels are found in African-American women, followed in order by Hispanic women, Caucasian, Chinese and Japanese women. Modifiable risk factors, particularly body mass index, account for much but not all of the differences in CRP levels between ethnic groups. [WG#274]


Primary Question:
Summary of Findings: The per cent of ovulatory cycles declined over a three year observation period (H1-H3). Luteal progesterone decreased over time in ovulatory cycles. Anovulatory cycles that did not end with a menstrual period appeared to be associated with progress through the menopausal transition. [WG#211]


Primary Question:
Summary of Findings: Poor HRQOL does not increase the likelihood of initiating HT, nor is HT use associated with subsequent improvements in HRQOL. The exception to this may be women who have high levels of menopausal symptoms. [WG#313]


Primary Question:
Summary of Findings: F2a-isoprostane concentrations were doubled in women who smoked compared to nonsmokers, indicating much more oxidative stress in women who smoked. With the exception of postmenopausal nonsmoking women, E2 was poorly
correlated with the F2a-isoprostanes, indicating that those with higher measured levels of estradiol were not necessarily likely to have less oxidative stress. Both 2-OHE1 and 16α-OHE1 were positively correlated with F2a-isoprostanes, with the exception of 2-OHE1 in postmenopausal smokers, suggesting that these estrogen metabolites behave more like markers of oxidative stress rather than antioxidants.


**Primary Question:**

**Summary of Findings:** Both menopause status and lower estrogen levels were associated with adverse alterations in the vascular system. These results may partially explain the increased risk of CVD with postmenopause.


**Primary Question:**

**Summary of Findings:** Increased abdominal adiposity is associated with a greater likelihood of reporting hot flashes among midlife women. Differences in reproductive hormones estradiol and follicular stimulating hormone did not account for the association between adiposity and hot flashes.


**Primary Question:**

**Summary of Findings:** Higher baseline intakes of dietary cholesterol and total and saturated fat, lower intake of fiber, along with higher BMI and lower levels of physical activity were consistently associated with greater functional limitations assessed 4 years later, even following adjustment for demographic variables and health conditions. These dietary associations were observed whether the data were expressed in relation to recommended intakes or in relation to nutrient intake quality with respect to total energy consumed. Greater subsequent functional limitations were also associated with lower baseline magnesium and lycopene intakes as well as fewer baseline fruit and vegetable servings.


**Primary Question:**

**Summary of Findings:** We found that breast density is associated with how physically active a woman is, but only for certain types of activities. If women have an active lifestyle...
(non-leisure activities) or are active in the household or in caregiving, their breast density may be lower. It appeared that women’s level of activity in their occupation or for recreation are not associated with breast density.

[WG#369]


Primary Question: Summary of Findings: Women with urinary incontinence in peri- and post-menopause are more likely to report improvement in their incontinence symptoms. Meanwhile, aging, increases in waist to hip ratio and weight cycling are associated with worsening incontinence symptoms.

[WG#248E]


Primary Question: Summary of Findings: A history of breastfeeding is associated with a lower prevalence of metabolic syndrome in midlife.

[WG#350]


Primary Question: Summary of Findings: There is little or no bone loss in the pre- and early perimenopause. Rates of both lumbar spine and total hip bone loss accelerate substantially in the late perimenopause and continue at a similar pace in the early postmenopausal years. Body weight is a major determinant of the rate of bone loss during the menopause transition, with women of lower body weight losing bone more rapidly. Observed ethnic differences in rates of menopausal bone loss are largely explained by differences in body weight.

[WG#174]


Primary Question: Summary of Findings: A skipped segment, a 10-segment running range >42 days and a segment of at least 60 days identify a similar moment in women’s reproductive lives, with the latter two identifying the exact same moment in two-thirds of women. All three markers occur in a greater proportion of women than the 90-day marker and are equally predictive of the FMP although they occur one to two years earlier. These findings support the STRAW recommendation that a shorter duration of amenorrhea be used as the bleeding criterion for
A standard deviation >6 or >8 days, persistent difference in consecutive cycles of >6 days, irregularity, and a cycle >45 days were evaluated. Most women experienced each of the changes in menstrual function described by the proposed bleeding markers of the early menopausal transition. Except for the persistent >6 day difference which occurs earlier, proposed markers of the early transition occur at a similar time in women’s reproductive life and at approximately the same age as the late menopausal transition in a large proportion of women. FSH levels were associated with occurrence of all the proposed markers. Selection of the optimal marker requires consensus regarding whether the biological concept of early transition is best described by ovarian activity consistent with earlier changes identified by the persistent >6 day difference or by that consistent with later menstrual changes.

[BG#345/346B]


Primary Question:
Summary of Findings: Women's cultural and personal characteristics influence the decision to use complementary and alternative medicine more than symptom experience or menopausal status.

[BG#262]


Primary Question:
Summary of Findings: Childhood abuse or neglect is associated with increased vasomotor symptom reporting during the menopausal transition. This relation was observed across multiple forms of abuse and neglect and in both African American and Caucasian women.

[BG#365]


Primary Question:
Summary of Findings: Higher total percentage of body fat is associated with a higher likelihood of reporting vasomotor symptoms among midlife women.

[BG#361]


Primary Question:
Summary of Findings: Vasomotor symptoms were less frequent in women with greater
ovarian function. Associations of other factors with vasomotor symptoms – smoking, physical activity, and possibly body mass index – varied by degree of ovarian function. [WG#210]

532 Tomey KM, Sowers MR, Li X, McConnell DS, Crawford S, Gold EB, Lasley B, Randolph JF, Jr. Dietary Fat Subgroups, Zinc, and Vegetable Components Are Related to Urine F2a-Isoprostane Concentration, a Measure of Oxidative Stress, in Midlife Women. Journal of Nutrition. 2007;137(11):2412-2419. Primary Question: Summary of Findings: There were consistent associations between higher trans fat intake and higher F2a-isoprostanes, and higher lutein and lower F2a-isoprostanes in smokers and non-smokers, cross-sectionally and across time. Among smokers and non-smokers, cross-sectional associations between F2a-isoprostanes and trans fatty acids were observed at the year 05 follow up visit, in analyses adjusted for recruitment site, age, race, body mass index (kg/m2), and physical activity. Regression models with adjustment showed that higher baseline intakes of trans fat and increased intake of trans fat from baseline to Y05 were significantly associated with higher levels of F2a-isoprostanes. In smokers and non-smokers, higher lutein intakes at year 05 were associated with lower F2a-isoprostanes at year 05. Higher baseline intakes of lutein from vegetables were significantly associated with lower levels of F2a-isoprostanes in both smokers and non-smokers. [WG#374]

533 Habel LA, Capra AM, Oestreicher N, Greendale GA, Cauley JA, Bromberger J, Crandall CJ, Gold EB, Modugno F, Salane M, Quesenberry C, Sternfeld B. Mammographic Density in a Multiethnic Cohort. Menopause. 2007;14(5):891-899. Primary Question: Summary of Findings: Mammographic density varied by race/ethnicity, but the pattern differed by method of classifying density. Density was not highest among those racial/ethnic groups with the highest breast cancer rates. Mammographic density was lower in more acculturated Asian women. [WG#300]

534 Crawford S. The roles of biologic and nonbiologic factors in cultural differences in vasomotor symptoms measured by surveys. Menopause. 2007;14(4):725-733. Primary Question: Summary of Findings: Cultural differences in VMS reporting on surveys reflect both differences in underlying biology or physiologic mechanisms, which are likely to affect VMS occurrence, and differences in non-biologic sociocultural factors likely to be related to VMS perception and/or reporting. [WG#391]

535 Avis NE, Colvin A. Disentangling cultural issues in quality of life data. Menopause. 2007;14(4):708-716. Primary Question: Summary of Findings: We found that controlling for covariates explained the majority of ethnic differences in HRQL. Degree of acculturation was related to several of the outcomes and may reflect cultural differences in the impact of physical and mental health on quality of life.

**Primary Question:**

**Summary of Findings:** In multivariate models, dietary factors were largely not associated with any of the symptom groupings. Caffeine intake was positively associated premenstrual anxiety and mood changes. Alcohol was negatively associated with premenstrual anxiety and mood changes and headaches. Active and passive smoke exposure were positively associated with a number of premenstrual symptoms. Number of comorbidities, depressive symptoms, symptom sensitivity, increased BMI and early perimenopause (compared to premenopause) were positively associated with a number of premenstrual symptoms, and reporting of symptoms varied by race/ethnicity.


**Primary Question:**

**Summary of Findings:** Extensions of the statistical work originally developed and published by Zhang, Lin, and Sowers allow the use of longitudinal and non-linear data (like that occurring in menstrual cycles) to be related to bone mineral density.


**Primary Question:**

**Summary of Findings:** Rates of regular binge eating, dissatisfaction with eating patterns, and marked fear of weight gain were 11%, 29.3%, and 9.2%, respectively. African Americans were likelier than were Whites to report fasting. In multivariable analyses, high BMI (or waist circumference), depressive symptoms, past depression, and history of childhood/adolescence abuse were significantly associated with the binge eating and preoccupation with body image and weight subscale scores (comprised of 7 to 16 items).


**Primary Question:**

**Summary of Findings:** The higher the mammographic breast density, the lower the bone mineral density. This observation was especially apparent in early perimenopausal women, and less obvious in premenopausal women.

Primary Question:
Summary of Findings:

[WG#405]


Primary Question:
Summary of Findings: Age, menstrual cycle interval, smoking behavior, and the hormones FSH and estradiol can all help a woman predict when her menstrual periods will cease at the time of the menopause transition.

[WG#260B]


Primary Question:
Summary of Findings: A woman’s age, and her estimate of more variability or lengthening of her menstrual cycles help to predict how much longer she will continue to get her period. Whether or not she smokes or is exposed to smoke, and hormone levels can make this prediction more precisely. Women who exercise may take longer to go through menopause than women who don’t. A woman’s ethnic group may also be a factor that can help her tell when her periods will end.

[WG#260]


Primary Question:
Summary of Findings: This empirical assessment supported the STRAW recommendations that a) >=60-days of amenorrhea be used to define the late menopausal transition and b) that early transition is consistent with a persistent 7 or more day difference in length of consecutive cycles. Serum FSH values >= 40 IU/L was an independent marker of the transition and when occurring together with a bleeding marker increased prediction of FMP.

[WG#345/346C]


Primary Question:
Summary of Findings: We identified multiple differences in hormone profiles associated with variation in cycle length. Very short and longer than typical cycles were characterized by increasingly chaotic variability. An estrone conjugate follicular/luteal phase asymmetry differed across body mass index categories.

[WG#234]

**Primary Question:**

**Summary of Findings:** Our findings suggest that there is no relation between cognitive test performance and menopause stage. Likewise no association was found between cognitive performance and FSH or estradiol levels.

[Searched Index #225]


**Primary Question:**

**Summary of Findings:**

[Searched Index #359]


**Primary Question:**

**Summary of Findings:** Women with higher levels of depression have higher levels of fibrinogen, a measure of blood coagulation, even after taking into account other health and lifestyle factors. Obesity is strongly related to markers of inflammation and hemostasis. In addition to obesity, markers of hemostasis are also elevated among late perimenopausal and postmenopausal women compared to premenopausal women.

[Searched Index #272]


**Primary Question:**

**Summary of Findings:** We found higher levels of religious involvement among Black and Hispanic women compared to White and Asian women. White and Japanese women reported similar levels of involvement for all measures of religion. Compared to the White women, the Chinese women reported similar levels of worship attendance and religious social support, but lower levels for the other 3 measures of religion. These racial/ethnic differences were not explained by differences in religious preference, acculturation or socio-demographic factors.

[Searched Index #61]

Bromberger JT, Matthews KA, Schott LL, Brockwell S, Avis NE, Kravitz HM, Everson-Rose SA, Gold EB, Sowers M, Randolph JF Jr. **Depressive symptoms during the menopause transition: The Study of Women’s Health Across the Nation (SWAN).** Journal of Affective
Primary Question:
Summary of Findings: Midlife women are more likely to experience high levels of depressive symptoms when peri- or postmenopausal or using hormone therapy than when premenopausal. Premenopausal women who have low depressive symptom levels at baseline (relative to women with high levels) are at a somewhat greater risk for higher symptoms during the peri- and post menopause. Menopausal status, as well as other health and lifestyle factors, influences depressive symptoms during the menopause transition.


Primary Question:
Summary of Findings: Over half of women used some type of CAM. Use of most types of CAM differed significantly by race/ethnicity, except use of ginkgo biloba, glucosamine and yoga. Use of most types of CAM did not differ significantly by menopausal status or vasomotor symptoms, except use of soy supplements which was significantly greater in late and surgically menopausal women who were not using hormones. Women reporting somatic symptoms were significantly more likely to use glucosamine. Women reporting psychological symptoms were significantly more likely to use ginkgo biloba and soy supplements. Number of comorbidities, moderate or high socioeconomic status, number of healthy behaviors, symptom sensitivity, age and dietary genistein intake were significantly positively associated with use of several types of CAM.


Primary Question:
Summary of Findings: First reported incontinence that develops in mid-life is mild, with a higher proportion of the urge type and different risk factors. African American and overweight women appear to be at the greatest risk of developing incontinence in mid-life.


Primary Question:
Summary of Findings: Midlife women with elevated levels of depressive symptoms displayed decreased mitogen-stimulated production of proinflammatory cytokines IL-6, IL-1β and TNF-α, reflecting diminished immune competence. Importantly, the relationship between depression and immune competence remained significant following control for such health-related variables as age, BMI, recent sleep disruption, physical activity level and psychotropic medication use.

**Primary Question:**

**Summary of Findings:** Of the 3215 SWAN women with complete information at baseline, 2466 (76.7%) received the same menopausal status classification at baseline and 749 (23.3%) received different classifications. While the two algorithms may classify a given woman differently on a given day, both approaches track progression through the transition over time. Choosing which to use should depend on the study population, including the proportion of women who are not cycling due to health reasons, and on the ability to obtain samples for hormone assays. Further work is needed to more precisely define optimal criteria for staging menopausal aging.


**Primary Question:**

**Summary of Findings:** Lower BMD was related to a higher degree of calcification in the aorta but not the coronary arteries.


**Primary Question:**

**Summary of Findings:** We found that hostility was positively related to extent of carotid artery intimal-medial thickening (IMT), a subclinical marker of heart disease risk. Women with high hostility scores had significantly greater IMT compared with women with low hostility scores, after taking into account the effects of age, race, study site, obesity, smoking and blood pressure. The level of risk associated with hostility was similar to the excess risk conferred by obesity, age and blood pressure, known risk factors for heart disease. Hostility was not related to presence of plaque in the carotid arteries.


**Primary Question:**

**Summary of Findings:** Direct measures of urinary hormones rather than menstrual cycle ovulatory characteristics were associated with lower levels of BMD.

**Primary Question:**

**Summary of Findings:** A skipped segment, a 10-segment running range >42 days and a segment of at least 60 days identify a similar moment in women’s reproductive lives, with the latter two identifying the exact same moment in two-thirds of women. All three markers occur in a greater proportion of women than the 90-day marker and are equally predictive of the FMP although they occur one to two years earlier. These findings support the STRAW recommendation that a shorter duration of amenorrhea be used as the bleeding criterion for the late transition.

[WG#345]

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**Primary Question:**

**Summary of Findings:** We identified two polymorphisms, one for the ERα and one for ERβ, whose association with circulating hormone E2 levels may have physiological meaning. In both instances, one genotype in each polymorphism was associated with lower levels of E2.

[WG#304]

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**Primary Question:**

**Summary of Findings:** Three aromatase gene SNPs were associated with variation in serum androgen concentrations, within and between racial groups. The CYP19 6306 AA genotype was associated with a significant difference in the T:E2 ratio, especially among African-American women. Japanese women with the CYP19 9292 AA genotype had lower E2 and T levels and higher SHBG when compared to Japanese women with CYP19 9292 AG or GG genotypes.

[WG#309]

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**Primary Question:**

**Summary of Findings:** The CYP1A1 rs2606345 polymorphism may play an important role in estrogen metabolism in pre- and peri-menopausal women. Japanese women with the CC genotype had lower E2 concentrations than Japanese women with the AC genotype, of this polymorphism, while Chinese women with the CC genotype had higher 2-OHE1 concentrations than Chinese women with the AC genotype. Further, African-American women with the CC genotype had higher 16α-OHE1 concentrations compared to those with other genotypes.

Primary Question:
Summary of Findings: Specific associations of BMD and ESR1 or ESR2 genotypes varied according to race group. The ESR2 rs1256030 or rs1256065 SNPs should have further evaluation with bone mineral density measures in Chinese and Caucasian populations.


Primary Question:
Summary of Findings: Prevalence of VMS reporting increased in all race groups from baseline to the 6th annual follow-up visit. After adjustment for covariates, several SNP’s encoding genes responsible for estrogen metabolism and estrogen receptors were associated with decreased odds of reporting VMS: including CYP1B1 rs1056836 GC genotype in African Americans, 17HSD rs615942 TG, rs592389 TG, and rs2830 AG genotypes in Caucasians, and the CYP1A1 rs2606345 AC genotype in Chinese women. Clarification of the mechanisms of the associations and confirmation in other populations is warranted.


Primary Question:
Summary of Findings: While associations were identified with the estrogen receptor alpha and beta SNP variants and lipids in premenopausal women, these associations were not consistently observed across the four contributing race groups. Nor were the associations consistently inclusive of both HDL-c and ApoA1. These genetic variants provide limited evidence of associations with lipids that may explain the cardioprotective effect of being a premenopausal woman.


Primary Question:
Summary of Findings: Allele frequencies differed significantly by race. There was substantial linkage disequilibrium among many of the SNPs and only a few SNPs showed significant Hardy-Weinberg disequilibrium within race. Finally, there are a number of haplotype patterns that vary according to race, including a ‘yin-yang’ pattern for 17HSD among Caucasian, Chinese, and Japanese women, but not among African-American women.

**Primary Question:**

**Summary of Findings:** There is evidence that two genotypes of the estrogen receptor alpha may have advanced more toward the menopause that women having other genotypes. This occurs following adjustment for chronological age, body size, and race. More rapid advancement was characterized in Daily Hormone Study enrollees using evidence of luteal activity, the menstrual cycle length, and deviations from expected hormone profiles.

[WG#305]


**Primary Question:**

**Summary of Findings:** Single nucleotide polymorphisms (SNPs) from 3 genes involved in the estrogen system were significantly associated with a high level of depressive symptoms in premenopausal and perimenopausal women: CYP1A1 in Caucasian and African-American women, CYP19A in Japanese women, and HSD17B1 in Chinese women. These genes may influence vulnerability to increased depressive symptoms. The specific relevant estrogen-related genetic polymorphism(s) varied by ethnicity.

[WG#308]


**Primary Question:**

**Summary of Findings:** There were strong associations with genes for sex hormone biosynthesis and action with insulin sensitivity, the metabolic syndrome, and diabetes. Significant associations of CYP 19 genotypes and insulin sensitivity were observed in African-American, Caucasian, and Japanese women, while selected ESR1 and ESR2 genotypes were associated with insulin sensitivity and metabolic syndrome only in Japanese and Chinese women. The strongest associations related 17HSD genotypes (and haplotypes) to diabetes in Caucasian women, with odds ratios ranging from 4.4 to 7.5 and confidence intervals that excluded the null value.

[WG#312]


**Primary Question:**

**Summary of Findings:** Allele frequencies and distances differed substantially in the 4 race-specific groups evaluated, leading to variable patterns of association with health-related measures. Several SNPs were associated with multiple outcomes, and some associations were much more prominent in specific races. Importantly, women in the Genetics Study were
typical of women in the community-based SWAN sample.  

569  
Kravitz HM, Meyer PM, Seeman TE, Greendale GA, Sowers MR.  
**Cognitive Functioning and Sex Steroid Hormone Gene Polymorphisms in Women at Midlife.**  

**Primary Question:**

**Summary of Findings:**  
Estrogen-related polymorphisms, particularly from ESR1, 17HSD, and CYP 19, were associated with differences in cognitive performance among four racial groups of mid-life women. Most of the significant findings involved either East Boston Memory Test (a test of episodic memory) or Digit Span Backward (test of working memory). Only one of the polymorphisms was associated with differences in cognitive performance on the Symbol Digit Modalities Test (a test of perceptual speed). We conclude that selected genes involved in estrogen synthesis and metabolism may be associated with performance on cognitive function tests that measure new learning in a multi-racial cohort of mid-life women.  

570  
**The Value of Follicle-Stimulating Hormone Concentration and Clinical Findings as Markers of the Late Menopausal Transition.**  

**Primary Question:**

**Summary of Findings:**  
FSH predicts the final menstrual period, but is not as good a predictor as menstrual bleeding patterns. Hot flashes are not predictive of the final menstrual period once we already have information on bleeding patterns and FSH.  

571  
Brown C, Matthews KA, Bromberger JT, Chang Y.  
**The Relationship between Perceived Unfair Treatment and Blood Pressure in a Racially/Ethnically Diverse Sample of Women.**  

**Primary Question:**

**Summary of Findings:**  
Our findings indicate that unfair treatment is common among midlife women and that it differs by race and ethnicity. Racial/ethnic differences in blood pressures were evident, however, these findings indicate that perceived unfair treatment was not a predictor of blood pressure.  

572  
**Longitudinal Analysis of the Association Between Vasomotor Symptoms and Race/Ethnicity Across the Menopausal Transition: Study of Women’s Health Across the Nation.**  

**Primary Question:**

**Summary of Findings:**  
Transition to late perimenopause was the strongest predictor of VMS (adjusted odds ratio [AOR]=6.64, 95% CI 4.80, 9.20). VMS reporting was highest in African Americans (AOR=1.63, 95% CI 1.21, 2.20). Age (AOR=1.17, 95% CI 1.13, 1.21), lower education (AOR=1.91, 95% CI 1.40, 2.61), increasing body mass index (AOR=1.03, 95% CI 1.01, 1.04) and smoking (AOR=1.63, 95% CI 1.25, 2.12), and anxiety (AOR=3.10,
95% CI 2.33, 4.12) were significantly independently related to VMS.

[HG#169]


**Primary Question:**

**Summary of Findings:** No associations between genistein intake and measures of cognitive performance were found in Japanese or Chinese participants. Our results did not support the hypothesis that genistein intake benefits cognitive performance.

[HG#205]


**Primary Question:**

**Summary of Findings:** Among 1490 perimenopausal women in the baseline sample, application of the recent ATP-III criteria show that 6.5% have LDL levels and risk profiles that would make them eligible for lifestyle modification and drug therapy. Hispanic, African American, and Caucasian women are more than three times more likely to be classified as requiring treatment than are Japanese and Chinese women. We also noted variability across sites within ethnic group, for the Caucasian and African American groups, which may reflect socioeconomic variability. Hypertension, current smoking and diabetes are the most common risk factors among these women. When perimenopausal women at baseline were classified according to JNC-VI criteria, overall, 10.3% were classified as hypertensive. The proportion hypertensive varied significantly by ethnic group, with 17% of African American, 16.5% of Hispanic, 7.5% of Caucasian, 6% of Chinese and 4% of Japanese women classified as hypertensive (p<0.001). As we found in the cholesterol analyses, there was also significant variation in the prevalence of hypertension across sites within ethnic group for the African Americans and Caucasians. Among women who reported current treatment for hypertension at baseline, (N=206), approximately a third (34.5%) had elevated blood pressure levels on treatment. The proportion of treated women with elevated blood pressure was highest among African Americans and Hispanics, and lowest among Caucasians and Japanese women. (p>.001)

[HG#96]


**Primary Question:**

**Summary of Findings:** Exposure to “everyday” discrimination over the course of five years was significantly associated with the presence of coronary artery calcification at year five in African-American women, even after taking into account the effects of age, education and standard cardiovascular risk factors. Exposure to recent discrimination (in the 12 months preceding the coronary artery calcification assessment) was only marginally associated with
the presence of coronary artery calcification. The association between chronic “everyday”
discrimination and coronary artery calcification appeared to be driven by exposure to
discrimination from multiple sources, rather than exposure to racial/ethnic discrimination
alone.

Selected Diet and Lifestyle Factors Are Associated with Estrogen Metabolites in a
Primary Question:
Summary of Findings: We found that 2- and 16α-hydroxyestrone concentrations were
higher in African American and Caucasian women compared to Chinese, Japanese, and
Hispanic women. Women in the highest weight quartile had lower 2-hydroxyestrone
concentrations compared to women in the lowest weight quartile. Women who smoked 20 or
more cigarette per day had higher 2-hydroxyestrone concentrations than non-smokers as well
as increased 16α-hydroxyestrone concentrations vs. smokers although there were clearly
greater differences in the 2-hydroxyestrone than 16α-hydroxyestrone concentrations. Wine
consumption was related to 2-hydroxyestrone concentrations while caffeine consumption was
associated with 16α-hydroxyestrone concentrations, adjusted for race/ethnicity, smoking, and
body size. We conclude that modifiable lifestyle and behavioral factors are independently
related to estrogen metabolites and may offer a strategy for modifying disease risk.
Additionally, individual metabolite levels were more informative and interpretable than their
ratio.

[Sowers M, Jannausch ML, Gross M, Karvenen-Gutierrez CA, Palmieri RM, Crutchfield M,
Richards-McCullough K. Performance-based Physical Functioning in African-American
and Caucasian Women at Midlife: Considering Body Composition, Quadriceps
Strength, and Knee Osteoarthritis. American Journal of Epidemiology. 2006;163(10):950-
958.
Primary Question:
Summary of Findings: The prevalence of x-ray-defined OAK was 20%, based on the
Kellgren-Lawrence criteria of 2 or greater. Women with x-ray defined OAK had slower
descent downstairs and less leg strength. Almost one-third of the population reported knee
joint pain and these women had slower speeds, longer ascent and descent times on stairs,
but no diminution in leg strength. Women with both OAK and self-reported knee joint pain
were most compromised having less leg strength, slower speeds, and greater likelihood of
hand rail use

[Dugan SA, Powell LH, Kravitz HM, Everson-Rose SA, Karavolos K, Luborsky J.
331
Primary Question:
Summary of Findings: One in six women at the third follow-up year of the SWAN report
daily aches and pain symptoms. One in seven women reports cutting down on the amount of
time she spends on work or other activities due to pain in the previous four weeks. After
adjusting for demographic, medical, and lifestyle factors and depression, early
perimenopausal women still reported significantly greater functional limitations from pain than premenopausal women.

[WG#233]


**Primary Question:**

**Summary of Findings:** Few risk factors differed between women who did and did not evidence of having an ovulatory cycle. Among women with evidence of an ovulatory cycle, lower hormone levels or longer cycle length with associated with a more atherogenic risk factor profile, which were reduced in number statistically after controlling for body mass index. Higher estrone levels during the follicular phase were associated with lower risk factor levels.

[WG#239]


**Primary Question:**

**Summary of Findings:** Over the 4-year observation period, there was a 5.6%, 3.9%, and 3.2% LS BMD loss, respectively, among pre- and early perimenopausal women who became postmenopausal (natural), postmenopausal (surgical) or late perimenopausal. This is the first study that has shown that baseline FSH concentration and 4-year FSH rise predicted 4-year spine and hip BMD loss. The manuscript identifies how much bone might be lost based on the level of FSH at the baseline and how much FSH changes over the 4-year period. The combination of baseline E2 and its 4-year change were not predictive of BMD loss. Further, neither testosterone, Free Androgen Index, nor dehydroepiandrosterone-sulfate concentrations were associated with BMD changes.

[WG#173]


**Primary Question:**

**Summary of Findings:** Vasomotor symptoms had higher prevalence among early perimenopausal women than premenopausal women and were even greater among late perimenopausal women. Other symptoms had higher prevalence among early perimenopausal women, but then leveled off. These findings suggest that vasomotor symptoms follow a different pattern than other symptoms.

[WG#298]


**Primary Question:**

**Summary of Findings:** Sleep was best at mid-cycle and worst at the extremes (ie, early
follicular and late luteal phases) in the menstrual cycles with increases in progesterone metabolite (Pdg) excretion compatible with ovulation. Pdg was the only one of the 4 hormones (FSH, LH, E1c, Pdg) we examined that was significantly related to trouble sleeping. Mood and vasomotor (hot flashes/flushes, night sweats) symptoms and use of pain medication also were associated with more trouble sleeping, and the fall and summer seasons (compared with winter season) were associated with less trouble sleeping. Increase in progesterone may have a negative effect on sleep quality in middle-aged women who have cycles with luteal activity.

[WG#221]


Primary Question:
Summary of Findings: We conclude that, when modeled together longitudinally, FSH, but not E2, T, DHEAS, FTI or FEI, is associated with both the prevalence and frequency of vasomotor symptoms in women at midlife.

[WG#229]


Primary Question:
Summary of Findings: Lower estradiol levels were associated with higher levels of PAI-1 and tPA-ag and higher FSH concentrations were associated with higher PAI-1 and Factor-VII levels. Menopause status classifications were not associated with significant differences in levels of hemostatic factors; however, hsCRP concentrations were approximately 25% higher and PAI-1 concentrations approximately 20% lower among women who initiated hormone therapy (HT) compared to non-users. Endogenous estrogens may reduce CVD risk by modulating fibrinolytic factors, a response which could be consistent with an increased clearance of fibrinolytic factors. Notably, circulating endogenous estradiol and exogenous HT use were not related to the hemostatic factors in the same manner. Thus, conclusions derived from studies of exogenous hormones and CVD risk may not parallel or explain the effect of endogenous hormones or perimenopausal hormone changes on CVD risk.

[WG#213A]


Primary Question:
Summary of Findings: Higher androgen levels were associated with less favorable levels of PAI-1, t(PA), and hsC-RP, three factors associated with greater CHD risk. Lower levels of SHBG, which impacts the amount of free testosterone androgen in the bloodstream, was associated with significantly less favorable levels of these fibrolytic and inflammatory factors.

**Primary Question:**

**Summary of Findings:** Compared with Caucasian women, African-American and Hispanic women have significantly higher prevalence of hypertension independent of other factors, whereas Chinese and Japanese women have a similar prevalence. Treatment rates vary considerably across ethnicities. In addition, we demonstrate the important joint effect of BMI and waist-hip ratio on hypertension status.


**Primary Question:**

**Summary of Findings:** Women have a positive sense of well-being at midlife. Dispositional optimism was the only significant correlate of women’s self-reported sense of identity and security at midlife. African American and Caucasian women shared many similar perceptions; African American women reported a greater sense of security and identity at midlife. Further, African American women with high stress and greater financial need had higher identity and security, while the opposite was true of Caucasian women.


**Primary Question:**

**Summary of Findings:** Sex hormone binding globulin (SHBG), and to a lesser extent, circulating androgens, were most strongly related to the presence of the metabolic syndrome. Relationships between adrenal androgens and physical functioning and self reported health were strongest. Sexual interest was related to both circulating testosterone and SHBG.


**Primary Question:**

**Summary of Findings:** We have found that women who report not speaking English well or at all are less likely to receive breast and cervical cancer screening than women who speak English and that these differences are not explained by sociodemographic factors and contact with health care.

**Primary Question:**

**Summary of Findings:** A higher level of physical activity, particularly vigorous physical activity, is associated with a lower percentage of body fat and a smaller waist circumference. Late peri- and post-menopause is associated with lower levels of lean muscle mass. [WG#268]

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**Primary Question:**

**Summary of Findings:** African Americans had an 86% higher rate of elective hysterectomy, and Asian Americans had an 84% lower rate, than Caucasians. These differences were not accounted for by socioeconomic status, fibroids, obesity, or the availability of medical insurance. It is unknown whether ethnic differences represent informed choices or disparity in appropriate care. [WG#26]

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**Primary Question:**

**Summary of Findings:** We found that women who had a history of recurrent major depression were 4 times more likely to have high calcium levels of the coronaries, and 3 times more likely to show high calcium levels in the aorta. These risks were present even when we took into account the woman’s age, body size, blood pressure, race and whether she smoked. Our results suggest the need for identifying and treating women with major depression in an effort to prevent progression of atherosclerosis and subsequent heart disease. [WG#207]

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**Primary Question:**

**Summary of Findings:** African American and Hispanic women have the highest levels of risk factors whereas Japanese and Chinese women have the lowest. However, statistical controls for socioeconomic status, obesity, cigarette smoking, cardiovascular health history, and age substantially attenuated the magnitude of the ethnic differences, suggesting that these factors play a role in understanding why ethnic groups differ in risk factors. [WG#95]

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Primary Question:
Summary of Findings: Past depression significantly predicted mood symptoms, body pain, poor role functioning as a result of physical health, and poor social functioning. For somatic symptoms there was a marginally significant effect of past depression (p=.06), specifically for recurrent depression. Compared to no past depression the odds ratios of recurrent depression were higher for somatic symptoms, body pain, poor role functioning as a result of physical health, and poor social functioning. The effect of subsyndromal and single episode depression varied depending on the health outcome.

[Sow#144]

595


Primary Question:
Summary of Findings: A substantial number of mid-aged women (about 1 in 10) had lean mass loss, in spite of an average increase in weight and this loss of lean mass was strongly related to leg strength and less strongly related to gait speed. Additionally, the associations of lean and fat mass with measures of physical function were important after adjusting for age.

[Sow#231]

596


Primary Question:
Summary of Findings: Women with the highest solvent exposure were more than twice as likely to report forgetfulness as working women with no exposure. Women with low solvent exposure reported the best general health of all groups of women.

[Sow#91A]

597


Primary Question:
Summary of Findings: Hormone factors related to androgens are strongly related to cardiovascular risk factors in SWAN women. Thus, increases in androgens rather than decreases in estrogens may drive the change in risk of heart disease after menopause.

[Sow#243A]

598


Primary Question:
Summary of Findings: We observed significant racial differences in the effects of socioeconomic status (measured by education) on weight for middle-aged women. At baseline, African-American women at all levels of education were equally heavy, while
Caucasian women were thinner with each incremental increase in educational attainment. Over time, women of both races and all educational levels gained equally (about 1.3 pounds each year). Consequently, the absolute level differences observed at baseline persisted over time.

-primary-link-


Primary Question: Summary of Findings: Rather than replacing conventional health services, women who use CAM also use more conventional health care. Additionally, women with more consistent CAM use also had increasing conventional health care contacts throughout a 2 year period.

-primary-link-


Primary Question: Summary of Findings: Analysis of the patterns of hormones in early perimenopausal women who did not ovulate indicate that the brain is less sensitive to estrogen with reproductive aging.

-primary-link-


Primary Question: Summary of Findings: Women with a lifetime history of recurrent MDD reported less sexual arousal, less physical pleasure and less emotional satisfaction within their partnered sexual relationships. Although the depression history groups did not differ in reports of sexual desire or frequency of partnered sexual behaviors, women with a lifetime history of MDD reported a higher frequency of masturbation as compared with never-depressed women. Reports of decreased physical pleasure with partnered sex and increased frequency of masturbation remained significant after controlling for current depressive symptoms, study site, marital status, psychotropic medication use, and lifetime history of anxiety or substance abuse/dependence disorders.

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Primary Question: Summary of Findings: Compared to Caucasian women, African-American women with a symptom score of 16 or higher on our measure of depression showed elevated risk of developing diabetes over 3 years of follow-up that could not be explained by known diabetes risk factors. Depressed African-Americans similarly showed significant increases in insulin
resistance over time, compared to non-depressed women. Depression was not related to changes in insulin resistance among the other racial groups.

603


Primary Question:
Summary of Findings: Weight and waist circumference increased on average, but was not related to change in menopausal status. Women who increased participation in sports/exercise and daily routine activity had less of an increase in weight and waist, while those who decreased their activity level had the greatest gains.

604


Primary Question:
Summary of Findings: Progression through the menopause was significantly related to decreases in pinch and grip strength in African American women only, after controlling for age, HRT use, smoking, marital status, income, education, obesity and physical activity. Age and HRT use were not associated with declines in arm strength. The most important predictor of loss of arm strength was physical inactivity.

605


Primary Question:
Summary of Findings: Unadjusted analyses showed that rates of depression (Center for Epidemiological Studies depression scale (CES-D) score greater than or equal to 16) varied significantly by ethnicity. They were highest among African American and Hispanic and lowest among Japanese and Chinese women. Separate analyses showed that adjustments for social economic status and demographic factors in one, and health factors in another, attenuated the effects of ethnicity. The final model showed that health, physical activity, stress, and social support were each significantly associated with depression.

606


Primary Question:
Summary of Findings: Depressed women had high levels of all four coagulation factors, ps < .05. After controlling for smoking, ethnicity, prevalent cardiovascular disease, and the use of medications (including psychotropics), depressed women still had elevated levels of
fibrinogen (mean ± SD, 304.1 ± 72.2 mg/dl vs. 290.6 ± 66.8 mg/dl, p= 0.0001) and Factor VIIc (125.2 ± 53.1 ng/dl vs. 118.8 ± 35.5 ng/dl p= 0.001) levels.

WG#180


**Primary Question:**

**Summary of Findings:** High Depressive symptom burden was independent predictor of lower odds of cancer screening in women. Depression may be a modifiable factor in improving rates of cancer screening in women.

WG#203


**Primary Question:**

**Summary of Findings:** Significantly more African American and Hispanic women and significantly less Chinese and Japanese women reported vasomotor symptoms. Increased reporting of vasomotor symptoms was also significantly independently associated with passive smoke exposure and increased dietary cholesterol, as well as a history of premenstrual symptoms or gynecologic surgery.

WG#104

609 Avis NE, Assmann SF, Kravitz HM, Ganz PA, Ory M. **Quality of life in diverse groups of midlife women: Assessing the influence of menopause, health status and psychosocial and demographic factors.** *Quality of Life Research.* 2004;13(5):933-946.

**Primary Question:**

**Summary of Findings:** Early perimenopausal women reported lower global QOL, compared with premenopausal women in unadjusted analysis, but menopausal status had little effect on QOL when analyses adjusted for other variables. Being married and having low levels of perceived stress were consistently related to global QOL across all ethnic groups. Other variables related to global QOL among some ethnic groups were education, difficulty paying for basics, self-assess health, physical activity, attitudes towards aging, and social support.

WG#14


**Primary Question:**

**Summary of Findings:** Older age, larger body size, and Hispanic ethnic background were all associated with a greater likelihood of having an anovulatory cycle in women in the early stages of the menopause transition. Cigarette smoking, although known to affect the age at
menopause, was not associated with major menstrual cycle alterations in this sample. [WG#128A]


Primary Question:
Summary of Findings: SWAN is the first multi-ethnic longitudinal study of the menopause transition ever performed in the United States. Current models are challenging some prevailing notions about the menopause transition—that obesity protects against vasomotor symptoms, that DHEAS decreases inexorably in everyone over time, and that decreasing ovarian reserve is associated with a progressive decline in estrogen. Further elucidation of the process of menopause will allow for a distinction between ‘early’, ‘late’, ‘fast’ and ‘slow’ transitions, an improved prediction of the timing of the final menses, and an ability to forecast symptomatology and encourage preventive measures or appropriate interventions. [WG#238]


Primary Question:
Summary of Findings: Serum E2 concentrations decreased significantly with age, with a steeper decline at higher ages. FSH concentrations increased significantly with age, with a steeper increase at higher ages. Similar patterns in the decline of E2 and the increase in FSH with age were found across ethnic groups, but the levels of these hormones differed by race/ethnicity. These ethnic differences in E2 and FSH were independent of menopausal status. The effect of BMI on serum E2 and FSH levels varied by menopausal status. [WG#181]


Primary Question:
Summary of Findings: Including an open-ended question (“Any other foods?”) contributes trivially to estimates or ranking. Asking ethnic foods of Caucasian respondents contributes trivially. [WG#135]


Primary Question:
Summary of Findings: Chinese Americans, Japanese Americans and African Americans are less insulin sensitive than non-Hispanic white women. The non-Mexican American Latino women have a similar level of insulin sensitivity as non-Hispanic white women. Chinese American and Japanese American women do not have the compensatory increase in beta cell function seen in African American women. Beta cell function in non-Mexican American
Women is similar to that of non-Hispanic white women.

[WG#157A]


Primary Question:
Summary of Findings: In unadjusted analyses, perimenopausal women were more likely to have impaired functioning on all 5 domains. However, in analyses adjusting for other variables, menopausal status was no longer significantly related to impaired functioning. Ethnicity was also related to impaired functioning on all 5 domains in unadjusted analyses and remained significant in adjusted analyses for all domains but role-physical. In general, health and psychosocial factors for most related to all 5 health-related quality of life domains.

[WG#105]


Primary Question:
Summary of Findings: We showed that SHBG (which influences the amount of available testosterone and estradiol as well as have an independent hormone-like action) was associated with both hemostatic factors and insulin, and significantly modified the association of the hemostatic factors with insulin resistance. Women with the greatest insulin resistance had the lowest SHBG concentrations and highest homeostatic marker levels, even after adjusting for covariates.

[WG#99]


Primary Question:
Summary of Findings: There was a slight increase over time in cognitive functioning as measured in terms of working memory and perceptual speed. It was not significantly associated with menopausal status or progression through the menopausal transition.

[WG#171]


Primary Question:
Summary of Findings: Insulin resistance was not significantly related to Lp(a) after controlling for ethnicity. Among healthy women, the direct effect of insulin resistance on Lp(a) was small compared with the indirect effects through body weight and ethnicity. Unlike race/ethnicity and body weight, estrogen, androgens and insulin resistance accounted for very little variation in Lp(a) concentrations.

Primary Question:

Summary of Findings: Rates of frequent mood symptoms were higher among early perimenopausal (14.9%-18.4%) than among premenopausal (8%-12%) women. Early perimenopausal women had higher odds of irritability, nervousness, and frequent mood changes, but not feeling blue. The effect of being early perimenopausal on overall dysphoric mood was greatest among women with less than a high school/GED education and with no “possible PMS” in the previous year.


Primary Question:

Summary of Findings: Overall, 79% of the sample had engaged in sex with a partner in the last 6 months, and 33% considered sex to be quite or extremely important in their life. For those who engaged in sexual activity, a high level of emotional and physical satisfaction was reported. Perimenopause status was associated only with higher frequencies of masturbation and pain during intercourse. Early perimenopause had little effect on frequency of sexual practices or function, but ethnic variation remained in most measures even after adjusting for socioeconomic factors.


Primary Question:

Summary of Findings: No difference in HAL between Japanese-American, Japanese women resident in the US, and Caucasian-American SWAN participants were observed at the UCLA site.


Primary Question:

Summary of Findings: African Americans reported greater stress and had higher carotid intima-media thickness (IMT) compared to Caucasians. Among African Americans only, greater accumulated stress and unfair treatment was associated with higher IMT.


**Primary Question:**

**Summary of Findings:** Serum estradiol and sex hormone-binding globulin levels were lower in Japanese and Chinese women than in Caucasians, African-Americans, or Hispanics. Serum testosterone levels were lower in Hispanics than in women belonging to the other 4 ethnic groups. Serum DHEAS (dehydroepiandrosterone sulfate) levels were higher in Chinese, Japanese and Caucasian women than in African-American or Hispanic women. Serum DHEAS levels were negatively correlated with age but not menopausal status. There were no ethnic differences in serum follicle-stimulating hormone levels, but it was highly correlated with menopausal status. All hormone concentrations were significantly correlated with body composition.

[WG#126]


**Primary Question:**

**Summary of Findings:** In women aged 42-52, the prevalence of TSH levels outside the normal range was 9.6%. Thyroid status was associated with bleeding length and self-reported fearfulness, but not with other menopausal symptoms or reproductive hormone concentrations, including Follicle Stimulating Hormone (FSH). There was a marked ethnic difference in TSH levels for which currently there is no explanation.

[WG#148]


**Primary Question:**

**Summary of Findings:** Higher leisure and home physical activity were independently associated with higher bone mineral density in each ethnic group. To our knowledge, this is the first demonstration of an association between home activity and BMD. It highlights the need to use physical activity scales that measure this important component of women’s activity.

[WG#121]


**Primary Question:**

**Summary of Findings:** Adaptations of widely used algorithms for assessing menstrual cyclicity in midreproductive aged women were adapted to the SWAN Daily Hormone Study cohort. Robust algorithms were derived that agreed closely with subjectively rated cycles by trained observers. Inter and intra-rater agreement was also assessed. We conclude that simple methods for determining luteal function and the day of luteal transition can be applied to the study of cycles in perimenopausal women.

**Primary Question:**

**Summary of Findings:** In these pre- and early perimenopausal women, higher FSH concentrations, but not other serum reproductive hormone concentrations such as estradiol, are positively associated with greater bone turnover even prior to the last menstrual period.

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**Primary Question:**

**Summary of Findings:** After controlling for biological and behavioral risk factors for carotid atherosclerosis, lifetime history of recurrent major depression more than doubled the risk of plaque relative to no history of major depression. Depressive symptoms or a lifetime history of a single major depressive episode afforded no increase risk for plaque. Neither depressive symptoms nor major depression were associated with intima media thickness (IMT).

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**Primary Question:**

**Summary of Findings:** BMD was lower in perimenopausal women than pre-menopausal women. Women with higher Follicle Stimulating Hormone (FSH) concentrations had lower BMD. Serum FSH concentrations, but not serum estradiol, testosterone, or Sex Hormone Binding Globulin (SHBG), were significantly associated with BMD in a multi-ethnic population of women. This supports the hypothesis that alterations in hormone environment are associated with BMD differences before the final menstrual period.

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**Primary Question:**

**Summary of Findings:** The stage of the menopausal transition is significantly associated with self-reported difficulty sleeping, apart from the effects of other factors. However, other factors may play an important role in contributing to the difficulty sleeping that middle-aged women going through the menopausal transition may experience and should be further investigated. Older age per se was not significantly associated with difficulty sleeping.

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Luborsky JL, Meyer P, Sowers MF, Gold EB, Santoro N. *Premature menopause in a multi-

Primary Question:
Summary of Findings: POF was reported by 1.1% of all women and varied by ethnicity. Health factors associated with POF also vary by ethnicity. This is the first paper to examine POF in multiple ethnic groups under a single study design.


Primary Question:
Summary of Findings: Twenty-five percent of midlife women experienced UI at moderate to severe levels, i.e., at least enough leakage to warrant a change of undergarments several days per week. Significant predictors of severity included Body Mass Index (BMI), perimenopausal status, diabetes mellitus, and current smoking, but not age or ethnicity.


Primary Question:
Summary of Findings: A score of 1 is part of the advancement to emergent OAK and suggests the following criteria to characterize individuals who are at an intervenable stage on the pathway toward OAKnee: age ≥40, BMI ≥30, and K-L score of ≥1. From the perspective of both the individual and the examiner, these assessment characteristics are as reliable as the assessment of pain in the knee joint.


Primary Question:
Summary of Findings: Almost half of the women in SWAN used some kind of CAM at baseline, including herbs (18%), nutritional remedies (32%), psychological methods (20%), physical methods (20%) and folk medicine (6%). Women who reported psychological symptoms or used complementary and alternative medicines at baseline were mostly likely to be using CAM at the first year follow-up.


Primary Question:
Summary of Findings: Terminal digit for year at hysterectomy was more evenly distributed across all 10 digits than was terminal digit for year at natural menopause. The latter, however, was similar to a reference distribution based on prevalence data, suggesting that self-report is accurate. Results did not differ by ethnicity.

Primary Question: Summary of Findings: Many differences in macro-and micronutrient intakes in the 5 SWAN ethnic groups were observed, which may contribute to differences in a number of outcomes of interest, such as bone mineral density, menopausal symptoms, and cardiovascular risk factor profile.


Primary Question: Summary of Findings: An ultra sensitive, semi-automated estradiol-17beta immunoassay was developed on the Bayer Diagnostics, Automated Chemiluminescent System (ACS-180) with analytical sensitivity (~1.0 pg/mL) that is adequate to quantify estradiol reproducibly in the sera of men, post-menopausal women, and children. The availability of this method has greatly facilitated the rapid analysis of large numbers of samples with good precision, low labor and reagent costs per result, and rapid turnaround times.


Primary Question: Summary of Findings: Higher C-RP concentrations were associated with both prevalent and incident OAK, and were predictive after adjusting for obesity. C-RP, as a measure of an acute phase response and moderate inflammation, may permit earlier or more definitive detection of OAK or act as a predictor prior to its presentation on x-ray.


Primary Question: Summary of Findings: There is no uniform predictable decline in circulating dehydroepiandrosterone (DHEAS) in women undergoing the menopause transition. Circulating DHEAS concentrations transiently increase in some individuals, and this transient increase is linked to the later stages of the menopause transition. Changes and variability of DHEAS in the later menopause transition differed among the different ethnic groups. The linkage of ovarian function to adrenal function underscores the importance of characterizing ovarian status when studying women, and highlights the need for further mechanistic elucidation of the pathways responsible for transient adrenal androgen activation.

Primary Question:
Summary of Findings: The traditional view is only true when bone density is considered without adjustment for ethnic variation in factors that have major effects of bone density, particularly body weight. When bone density is adjusted for these factors, it remains highest in African-American women and is lowest in Caucasians. Depending on the skeletal site, adjusted bone density in Asian women is either similar to that of African-Americans or intermediate between African-Americans and Caucasians. These data help explain some of the well-known ethnic variations in fracture rates that heretofore have seemed paradoxical.


Primary Question:
Summary of Findings: Serum osteocalcin levels are highest in Caucasian women, next highest in African-American women, and lowest in Asian women. Urinary N-telopeptide levels are higher in Caucasian and African women than in Asian women. Interestingly, however, the pattern of ethnic variation in bone turnover is quite different from the pattern of ethnic variation in BMD, suggesting that factors other than the current state of bone turnover, such as differences in bone accretion, are responsible for ethnic variation in BMD.


Primary Question:
Summary of Findings: In focus groups, consisting of European-American English speaking, Japanese-American Japanese speaking, and Japanese-American English speaking pre-, peri- and postmenopausal women, the constructions of menopause varied by ethnicity, language, and current menopausal status. This highlights the need to have culturally-appropriate research designs in order to address relevant questions that women may have.


Primary Question:
Summary of Findings: Latinas emphasize three themes: 1) The primacy of health and the importance of harmony and balance; 2) El cambio de vida – something you have to go
through; and 3) This time is for me: reorientation and restructuring. This life phase was marked by rediscovery and redefinition as opposed to being defined by physical symptoms. [WG#50]

Primary Question:
Summary of Findings: Caucasian women were primarily concerned about menopause as it altered physical appearance to be less congruent with the societal ideal of youth. In comparison, African-American women viewed menopause as a normal, even welcome part of life. A language of emancipation and awareness of gender-bias were prominent in the women’s stories regardless of menopausal status or race. [WG#55/56/60]

Primary Question:
Summary of Findings: Soy isoflavone intake was associated with higher bone mineral density (BMD) in women of Japanese, but not Chinese, ethnicity in SWAN. (Intakes were too low in African American and Caucasian women to permit analysis of relation to BMD). These results open exciting avenues for additional study to confirm the apparent differences between Japanese and Chinese women's response to isoflavones and to explore possible mechanisms of this ethnic interaction. [WG#114/123]

Primary Question:
Summary of Findings: Intrinsic health variables (including diabetes, heart condition, arthritis, osteoporosis, surgical menopause) and extrinsic variables (including body size, unemployment, difficulty paying for basics, high stress) were associated with functional physical limitations. [WG#70]

Primary Question:
Summary of Findings: Even at the relatively early ages of 40-55 years, approx. 20% of women self-reported limitation in physical functioning. Surgical menopause, post-menopause and the use of hormones were more frequently observed among women with "some" and "substantial" physical limitation, even after adjusting for economic status, age, body mass index, and race/ethnicity. [WG#3/4]

**Primary Question:**

**Summary of Findings:** Rates of psychological distress (feeling tense, depressed, and irritable in the previous 2 weeks) were highest in early perimenopause and lower in premenopause and postmenopause. In comparison with premenopausal women, early perimenopausal women were at a greater risk of distress, even after adjustment for vasomotor and sleep symptoms, suggesting that the difference in negative mood/distress is independent of vasomotor symptoms and sleep difficulties. In adjusted analyses, odds of distress were significantly higher for whites than for the other racial/ethnic groups.

[WG#17]

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**Primary Question:**

**Summary of Findings:** African-American women (but not European-Americans) who report experiencing subtle forms of mistreatment due to their race show an elevated diastolic blood pressure during a laboratory task that bears similarities to an encounter with racial prejudice. This is not seen for a non-similar task. These findings suggest that racial discrimination is a chronic stressor that might impact negatively on African-American’s cardiovascular health.

[WG#116]

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**Primary Question:**

**Summary of Findings:** Joint pain in African-American women was more likely to be associated with radiographic OAK when compared with Caucasian women. This suggests differences in these two groups in both how pain is experienced in the OAK process and in the prevalence of non-OAK related pain in knee joints.

[WG#155]

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**Primary Question:**

**Summary of Findings:** Self-reported weight adjusted for height was similar in women reported a natural menopause and in premenopausal women. However, women who had a hysterectomy were heavier and women who used hormone replacement therapy were lighter. The effects of menopause and hormone use were small relative to those of physical activity and ethnicity.

[WG#34]

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Avis NE, Crawford SL. **SWAN: What It Is and What We Hope to Learn.** _Menopause_

Primary Question:
Summary of Findings: Some of the key findings reported from the cross-sectional data that will be mentioned include prevalence of symptoms, factors related to age of menopause, and attitudes towards menopause.

[WG#161]

Primary Question:
Summary of Findings: Japanese women had significantly later and Hispanic women an earlier menopause. Current smokers had a significantly earlier menopause than former or never smokers, by about 1-2 years. Women who had never given birth, never used oral contraceptives, were less educated, or with a history of heart disease had significantly earlier menopause.

[WG#6/13]

Primary Question:
Summary of Findings: Perimenopausal women, hormone users, and women who had surgical menopause reported significantly more vasomotor symptoms but not more psychosomatic symptoms. Caucasian women reported significantly more psychosomatic symptoms than other ethnic groups. African-American women reported significantly more vasomotor symptoms. The pattern of symptom reporting argues against a universal menopausal syndrome consisting of a variety of vasomotor and psychological symptoms.

[WG#15/16]

Primary Question:
Summary of Findings: A cross-calibration study was used to develop an accurate method to measure hip axis length (HAL) using the Hologic 4500A fan-beam densitometer.

[WG#84]

Primary Question:
Summary of Findings: Self-reported rating of physical activity level relative to other women of respondent’s age does not capture the expected race/ethnic group differences in activity level, but within each race/ethnic group, physical activity is associated similarly with factors such as education and body mass index. This suggests that this global question is not appropriate for race/ethnic comparisons but is useful for ranking individual women by activity level within their race/ethnic group.
Relation of Demographic and Lifestyle Factors to Symptoms in a Multi-Racial/Ethnic 

Primary Question:
Summary of Findings: The most important factor affecting reporting of hot flashes and 
night sweats was menopausal status. Women who were in the early stages of menopause or 
had finished menopause were 2 to 4 times as likely to report these symptoms as women 
whose periods were still regular. In addition, these symptoms were reported more frequently 
by African American and Hispanic women than Caucasian women; and Japanese and 
Chinese women reported fewer symptoms than Caucasian women. Also, women who were 
less educated, smoked, or reported less physical activity than other women their age, 
reported significantly more symptoms than women who were more educated, non-smokers or 
who reported more physical activity.

Pope SK, Sowers M. Functional Status and Hearing Impairments in Women at Midlife. 
Journals of Gerontology Series B--Psychological Sciences & Social Sciences. 

Primary Question:
Summary of Findings: Hearing loss measurable by an audiometer is often not perceived 
by the participant. Self-reported hearing impairment appears to be associated with lower 
physical and mental functioning. Identification of self-reported hearing loss at mid-life or 
earlier may facilitate prevention of further hearing loss.

Conceptualizing menopause and midlife: Chinese American and Chinese women in the 

Primary Question:
Summary of Findings: Most women who had gone through menopause regarded it as 
natural, even a new beginning. But many who had not gone through it had concerns for its 
effect on them physically, emotionally, and socially.

Sowers M, Lachance L, Hochberg M, Jamadar D. Radiographically defined osteoarthritis 
of the hand and knee in young and middle-aged African American and Caucasian 

Primary Question:
Summary of Findings: By age 40, radiographically defined osteoarthritis emerges in both 
the hands and knees in both black and white women. Prevalence of knee OA was higher in 
black females (23.1%) compared with white females (8.5%), and although prevalence of hand 
OA was more comparable between black (25.5%) and white females (19.2%), the joint sites 
affected differed. The major risk factors reported in studies of older populations are present in 
this younger population where OA is newly emerging.

**Primary Question:**
**Summary of Findings:** Income and the subjective stress of lower SES were significantly related to sleep, after controlling for age, race, menstrual status and education. Lower income and moderate to severe difficulty making ends meet were significantly associated with poorer subjective sleep quality. In a separate set of analyses, difficulty in making ends meet was shown to fully mediate the relationship between income and subjective sleep quality. [WG#87]


**Primary Question:**
**Summary of Findings:** African-American women had the most positive attitudes toward menopause, and Chinese-American and Japanese-American women had the least positive attitudes. Ethnic groups within the US vary slightly, but reliably, in their attitudes toward menopause and aging. Menopausal status was not a consistent predictor of attitude across ethnic groups. [WG#20/29/39]

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**MS E-PUB AHEAD OF PRINT**

**IN PRESS & PROVISIONALLY ACCEPTED MANUSCRIPTS**

Dugan SA, Crawford SL, Wente K, Waetjen EL, Karvonen-Gutierrez C, Harlow SD *The Association of Urinary Incontinence and Disability Among a Diverse Sample of Mid-life SWAN Women* Menopause

**Primary Question:** Does the relationship over 2 years between Urinary Incontinence (UI) and Disability, differ by UI type?
Does the relationship over 2 years vary by UI frequency?
Does the relationship over 2 years vary by UI amount?

**Summary of Findings:** Urinary incontinence has strong association with multiple areas of disability after two years. It is important to address UI earlier in symptom onset. Screening for mixed UI (both Stress and Urge) and UI that occurs more frequently and in larger amounts more specifically may yield better information regarding an individual’s future disability risk. [WG#975]

**Primary Question:** Do obesity and metabolic syndrome have unique effects on cardiovascular risk?

**Summary of Findings:** There are a significant proportion of metabolically healthy obese individuals within SWAN. The findings from this study suggest that there is only a minimal impact of obesity on carotid artery thickness over the effect of metabolic syndrome alone. [WG#1034]


**Primary Question:**
1) Are LDL subclasses change over the menopause transition independent of aging?
2) Are LDL subclasses during midlife associated with the presence of coronary artery calcification and carotid intima-media thickness?
3) Will these associations vary by the timing of these measures as related to the final menstrual period (FMP)?

**Summary of Findings:** Women experience significant atherosclerotic increases in LDL subclasses that increases their risk of having greater cIMT levels and higher CAC prevalence. The reported associations were more profound during perimenopause stage. [WG#1081]


**Primary Question:** What is the distribution of vaginal microbiota (classified by community state types-CSTs) in a diverse cohort of postmenopausal women? What are the relationships among genitourinary syndrome of menopause symptoms (vaginal dryness, vulvovaginal irritation, sexual pain, dysuria, urinary urgency), CSTs, estrogen, and vaginal atrophy biomarkers (vaginal maturation index and vaginal pH)?

**Summary of Findings:** While close relationships exist among estrogen, the structure of the vaginal microbiota, vaginal atrophy biomarkers (vaginal maturation index and vaginal pH), sexual pain was the only genitourinary syndrome of menopause symptom associated with the structure of vaginal microbiota and vaginal atrophy biomarkers. [WG#977MS1]


**Primary Question:** Our goal was to develop a complex Bayesian joint model for baseline prevalence and longitudinal incidence of MetS components and to use this model to ascertain what factors are associated with prevalence of particular MetS components at
baseline, and their incidence, if possible considering the complexity of the problem.  
(2) Since we were able to accomplish (1), our next goal was to ascertain the effect of 
race/ethnicity on development of MetS modified by menopausal status.  
(3) We also assessed the effect of particular MetS configurations at baseline on the 
predictive probabilities of particular MetS constellations using a Markov chain approach.  

**Summary of Findings:** Having central adiposity at baseline, alone or in combination with 
another MetS component, is the major factor that increases predictive probability of 
subsequent development of MetS. The predictive probability of development of MetS varies 
by race/ethnicity and is somewhat modified by menopausal transition stage. Later 
menopause is protective of developing component MetS.  

[WG#1083]

Metabolic Syndrome and Carotid Remodeling in Non-diabetic Middle-aged Women: The 
Study of Women’s Health Across the Nation  
**Primary Question:**  
**Summary of Findings:** The presence of MetS is associated with maladaptive remodeling of 
the common carotid artery in non-diabetic middle-aged women independent of select 
inflammatory, metabolic, and hemodynamic risk factors. Different patterns of remodeling 
were observed by race/ethnicity, and how these patterns of remodeling could potentially be 
related to the variation in risk of stroke warrant further examination  

[WG#703]

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**BOOK CHAPTERS**

1 Karlamangla AS, Shieh A, Greendale GA. *Hormones and Bone Loss Across the 
Menopause Transition* Vitamins and Hormones 2021;115:401-417. doi: 
**Primary Question:**  
**Summary of Findings:**  

[WG#1041MS]

2 Avis NE, Crawford S. *Menopause: Recent Research Findings.* The Baby Boomers Grow 
Up: Contemporary Perspectives on Midlife (SK Whitbourne, SL Willis) Mahwah, NJ 2006:75- 
109 (Chapter 4).  
**Primary Question:**  
**Summary of Findings:**  

[WG#254]

3 Sowers MF. *Studying the Complexity of the Menopause Transition from an 
**Primary Question:**
Summary of Findings: The stages of the menopausal transition can be defined based on menstrual bleeding, symptoms, hormone concentrations or health status. Integral to the menopause transition itself include duration of the transition and age at menopause as well as a marker of the intensity of the experience, observed as symptoms, shifts in hormone concentrations and ovarian function. The SWAN study provides prospective data of the menopausal transition stages using a multi-ethnic population.


Primary Question: Summary of Findings: This manuscript documents the study design and study implementation of the SWAN cross-sectional study that ultimately characterized more than 16,000 women at seven sites. The manuscript also documents the study populations, design, and implementation for the cohort study that includes more than 3300 women.

Presented Abstract with Journal Citation


   Primary Question: Summary of Findings:
   [WG#1023C]

2. Barnes M, Dugan S, Fitchett G, Janssen I, Kravitz H. Does Religion and Spirituality Buffer the Harmful Association Between Discrimination and Stress Among Midlife Women: the Study of Women's Health Across the Nation (SWAN)

   Primary Question: Summary of Findings: Background
   Across various racial and ethnic groups, midlife women have been subjects of discrimination as a result of their gender, race/ethnicity, appearance and other factors. Furthermore, discrimination has been associated with stress, and stress has been associated with adverse health behaviors, health outcomes and poor quality of life. Additionally, religion and spirituality have been shown to have positive effects on physical and mental health.

   Methods
   The study used participants from the longitudinal cohort Study of Women Across the Nation (SWAN) using data from the baseline year and follow-up years one through four which span from 1996 to 2002. The initial data set consisted of 2,655 participants who had data in response to perceived stress questions in follow-up year 4. The deletion of participants
missing data for the exposure, or outcome, or potential effect modifier created a data set of 1,686 participants. A restricted analysis of African-American women who selected race or ethnicity as a reason for their perceived discrimination consisted of 171 participants.

The exposure of discrimination used the Everyday Discrimination Scale (EDS), the outcome of perceived stress used the Perceived Stress Scale (PSS), and the potential effect modifier of spiritual and religious coping used the Daily Spiritual Experience Scale (DSES). Covariates included age, race, marital status, financial strain; meaning how hard it is to pay for basics, their study site, and menopause status. The statistical methods for both the full and restricted data sets included univariate analysis, correlation analysis of the exposure, outcome, and potential effect modifier, and four multiple linear regression models.

Results
Among the entire study sample, the mean age, perceived stress score, discrimination score, and spiritual and religious coping score were 49.9 years, 7.86, 1.69, and 34.17 respectively. 65.2% stated religion was very important to them and 70% said they get a great deal of strength and comfort from their faith. Among the restricted analysis study sample, the mean age, perceived stress score, discrimination score, and spiritual/religious coping score were 50 years, 8.19, 2.25, and 37.68 respectively. 81.9% said religion was very important to them and 87.7% said they get a great deal of source and strength and comfort from their faith.

For the entire study sample, the correlation between perceived stress and every day discrimination r=0.19, and spiritual/religious coping r= -0.18 were statistically significant at P <.0001. For the restricted study sample, the correlation between perceived stress and every day discrimination r=0.28 (P <0.001), and spiritual/religious coping r= -0.27 (P <0.001) were statistically significant. In the regression model adjusted for covariates, discrimination had a positive association with perceived stress in both the full 1.84 (95% CI: 0.66,3.29; P <0.001) and the restricted samples 1.98 (95% CI: 0.66, 3.29; P 0.004). In this model, the main effect of spiritual and religious coping had a statistically significant inverse association with perceived stress in both the full -0.06 (95% CI: -0.08, -0.05; P <.0001) and restricted samples -0.08 (95% CI: -0.15, -0.03; P 0.005). There was no significant association between the interaction of discrimination and religious/spiritual coping and perceived stress in either the full or restricted sample.

Conclusions
There is a positive association between discrimination and stress among midlife women. It appears there is a stronger correlation between perceived stress and spiritual/religious coping and discrimination in the African American women, restricted, sample as compared to the entire sample. Spiritual/religious coping has an independent and inverse association/relationship with stress, however, it did not modify the effect of the association between discrimination and stress for the sample as a whole or for African American women in the restricted sample.

[WG#900A]  

Stewart A, Brooks MM, Barinas-Mitchell E, El Khoudary S, Matthews KA, Jackson L, Magnani J. Social role stress, reward and the American Heart Association Life’s Simple 7 in midlife women: The Study of Women’s Health Across the Nation Abstract MP56: Social Role Stress, Reward and the American Heart Association Life’s Simple 7 in Midl Primary Question: Summary of Findings: Title: Social role stress, reward and the American Heart Association
Life's Simple 7 in midlife women: The Study of Women’s Health Across the Nation

Background: American women can occupy multiple social roles, such as employee, caregiver, mother, and spouse during midlife. These roles can be both stressful and rewarding, which may influence adherence to heart-healthy behaviors and risk factors. The aim of this study was to test the association of social role stress and reward with achievement of the American Heart Association Life’s Simple 7 risk factors in a cohort of midlife women in the United States.

Methods: The Study of Women’s Health Across the Nation (SWAN) is a longitudinal cohort study initiated in 1996-1997 of women aged 42-52 who were premenopausal. At the fifth annual follow-up visit women first were asked if they occupied four social roles (employee, caregiver, spouse, mother), and then were asked to rate how stressful and how rewarding each occupied role was, using five point scales. Average role-related stress and reward were calculated for each woman (range 1-5). Ideal cardiovascular risk factors were assessed at the same follow-up visit using anthropometric measurement (body mass index, blood pressure), blood draw (glucose, cholesterol), and validated questionnaires (physical activity, diet, and smoking). Multivariate linear regression was used for cross-sectional analyses of the number of ideal factors, using average role stress and reward as exposures. Adjusted logistic regression models were used to estimate odds of achieving the ideal level of each individual risk factor. Models were adjusted for age, race, site, education, and menopause status.

Results: At the fifth SWAN follow-up visit, 1,777 women had data on all seven risk factors, and reported occupying at least one social role. The mean (standard deviation) of the number of ideal risk factors was 3.2 (1.3). Only 5% of the sample had five or more ideal factors. Women who reported greater role-related stress achieved fewer ideal factors, and a higher reward score was related to more ideal factors. A one unit higher role stress score was associated with 18% lower odds of having a healthy diet, and 18% reduced odds of having a BMI under 30. Women with a one unit higher role reward score had 56% greater odds of ideal physical activity, and 34% greater odds of being a non-smoker. Higher job stress was associated with 13% reduced odds of having a healthy blood pressure. There was no evidence of an interaction between stress and reward. Adjusting for depression and social support attenuated, but did not eliminate the significant relationships between role stress and reward and cardiovascular risk.

Conclusion: Midlife women experience stress from multiple social roles while simultaneously deriving reward from these roles, which may be beneficial for their cardiovascular disease risk factors. Understanding the influence and determinants of role stress and reward may be important when designing interventions to improve diet, physical activity, and smoking behaviors in midlife women.

Authors: Emma Barinas-Mitchell, PhD; Karen Matthews, PhD; Samar El-Khoudary, MPH, PhD; Lisa Jackson, MD, MPH; Jared Magnani, MD, MSc

[WG#850E]
5  Gold EB. **Vasomotor and Other Symptoms of the Menopause Transition: Prevalence and Risk Factors, Including Racial/Ethnic Differences** North American Menopause Society (NAMS) NAMS, 10/06/2016, Orlando, FL
Primary Question:
Summary of Findings:
[WG#842A]

6  Finkelstein JS, Darakananda K, Yu E, Lin D, Bouxsein M, Putman M **Differences in trabecular microstructure between African American and Caucasian Women** ASBMR ASBMR, 9/19/2016; Atlanta, GA
Primary Question:
Summary of Findings:
[WG#601E]

7  Barinas-Mitchell EJ, Broadwin R, Brooks MM, Duan C, Matthews KA., Talbott E **Exposure to PM2.5 and Ozone and Progression of Subclinical Atherosclerosis among Women Transitioning through Menopause** International Society for Environmental Epidemiology International Society for Environmental Epidemiology, 09/02/2016, Rome, Italy
Primary Question:
Summary of Findings:
[WG#819A]

8  Duan C, Broadwin R, Talbott E, Brooks M, Matthews K , Barinas-Mitchell E. **Exposure to PM2.5 and Ozone and Progression of Subclinical Atherosclerosis among Women Transitioning through Menopause: Study of Women's Health Across the Nation (SWAN)** International Society for Environmental Epidemiology International Society for Environmental Epidemiology, Sept 1-4, 2016, Rome, Italy
Primary Question:
Summary of Findings:
[WG#819D]

9  Casement M, Hall M, Bromberger J, Harlow S, Kline C, Kravitz H, He F, Matthews KA, Zheng H(. **Variability in Sleep Duration Mediates the Relationship Between Chronic Stress and Symptoms of Depression and Anxiety in Midlife Women: The SWAN Sleep Study**
Primary Question:
Summary of Findings:
[WG#769C]

10 Lee JS, Gold EB, Johnson WO, Wong J. **Synergy between Circulating Androgens and Estradiol in Relation to the Risk of Uterine Fibroids: Study of Women's Health Across the Nation (SWAN)**
Primary Question:
Summary of Findings:
[WG#782A]
Snoring prevalence in women increases in midlife and may increase the risk of adverse health outcomes, including cardiometabolic diseases. However, most studies examining snoring-related risks rely exclusively on self-reported measures. No published study has examined associations among objectively-assessed snoring and cardiometabolic morbidity. This study evaluated whether objective snoring was associated with increased risk of the metabolic syndrome and its components in a community sample of midlife women.

Snoring was measured overnight by microphone in 248 participants in the SWAN Sleep Study (age=50.9±2.2 years, 45% African American). Snoring index (SI) was calculated as the ratio of objectively-scored snoring epochs (≥2 snores per 20-sec. sleep epoch) to sleep epochs. Metabolic syndrome criteria included hypertension (SBP≥130, DBP≥85, anti-hypertensive medication), fasting glucose ≥100 mg/dL, waist circumference ≥88 cm, triglyceridemia ≥150 mg/dL, and HDL <50 mg/dL. The metabolic syndrome was determined as meeting criteria for ≥3 components. Odds ratios for metabolic syndrome and components were calculated using logistic regression models and adjusted for apnea-hypopnea index, age, race, depression, sleep duration, menopausal status, alcohol use, exercise, and smoking. Snoring was significantly associated with increased ORs for the metabolic syndrome in fully adjusted models (OR= 6.7, 95% CI=1.4-31.2). Snoring was not associated with increased risk for hypertension or HDL. Moderate snoring was associated with elevated glucose (OR=3.8, 95% CI=1.1-14.0). Snoring was associated with waist circumference (SI: OR=65.8, 95% CI=6.5-671.5) and elevated triglycerides (SI: OR=6.1, 95% CI=1.2-31.9). All effects persisted after adjusting for sleep apnea. Sensitivity analyses revealed that associations between objective snoring and the metabolic syndrome were found only in obese participants. Objectively assessed snoring is associated with increased cross-sectional risk of metabolic syndrome and adiposity-related components. These associations are present in obese midlife women and may be mediated by adiposity. However, the direction of associations remains unclear; prospective analyses are needed to determine whether objective snoring frequency confers risk for incident metabolic syndrome above and beyond the effect of obesity.

The Study of Women's Health Across the Nation (SWAN) has grant support from the National Institutes of Health (NIH), DHHS, through the National Institute on Aging (NIA), the National...
Institute of Nursing Research (NINR) and the NIH Office of Research on Women’s Health (ORWH) (Grants U01NR004061; U01AG012505, U01AG012535, U01AG012531, U01AG012539, U01AG012546, U01AG012553, U01AG012554, U01AG012495). The content of this abstract is solely the responsibility of the authors and does not necessarily represent the official views of the NIA, NINR, ORWH or the NIH.

Burns J, Bruehl S, Appelhans B, Dugan S, Janssen I, Kravitz H, Matthews KA, Quartana PJ. Chronic Pain and Increases in SBP over 10 Years in Midlife Women: Tests of Direct and Mediated Relationships in SWAN

Primary Question: Chronic pain has detrimental effects on health and quality of life beyond the influence of pain itself. Results suggest that chronic pain from musculoskeletal or other nonmalignant conditions is related to elevated SBP, but reported findings are exclusively cross-sectional. It is also not clear whether links between chronic pain and SBP are due to unique aspects of chronic pain or are mediated by other behavioral, psychological and metabolic factors, such as depressive symptoms, physical activity, and obesity. Using longitudinal data from the Study of Women’s Health Across the Nation (SWAN) (N = 1931 women), we examined with multiple regressions whether Bodily Pain scores from the SF-36 averaged over the baseline (Year 0) and first 2 SWAN annual assessments predicted increases in SBP from Year 2 to Year 12, and whether this association was mediated by depressive symptoms, physical activity and BMI at Year 6. Controlling for Study Site, Race/Ethnicity, menopausal status, education and Year 2 SBP, Bodily Pain was related significantly to Year 12 SBP (beta = .10; p<.001). Tests of mediation indicated that physical activity and BMI at Year 6 partially mediated this association (Sobel test z’s > 2.87; p’s <.002), whereas depressive symptoms did not. Also, the direct links between Bodily Pain and Year 12 SBP were also significant (sr’s > .08; p’s<.002). Thus, high bodily pain averaged over 3 years at the start of SWAN assessments was related to greater increases in SBP over a subsequent 10-year period. Mediation analyses suggest that part of this relationship was conveyed by low physical activity and high BMI assessed at Year 6, but that chronic bodily pain may still exert unique and direct effects on increases in SBP. These longitudinal data suggest a potential causal link, and suggest that chronic pain may have a meaningful impact on public health beyond disability and suffering. To the extent that chronic pain contributes to increases in SBP, a known CVD risk factor, and is often unremitting, chronic pain may emerge as a new treatment target for reducing cardiovascular morbidity and mortality.

Reeves K, Hart V, Avis N, Crawford S, Gold EB, Habel L. Menopausal vasomotor symptoms and mammographic density in the Study of Women’s Health Across the Nation

Primary Question: Background: Declines in endogenous estrogen during menopause have been linked to the onset of menopausal vasomotor symptoms (VMS) and to reduced breast cancer risk. Percent mammographic density (PMD) is viewed as a marker for breast cancer susceptibility. Establishing a relationship between VMS and PMD may improve understanding of breast cancer etiology and justify future investigations of VMS and breast cancer risk.
Methods: We investigated this association in the Study of Women’s Health Across the Nation (SWAN) Mammographic Density Substudy (N=833). Women were pre- or perimenopausal at enrollment and followed through menopause. VMS were assessed at annual SWAN visits. PMD was ascertained from routine screening mammograms. A linear mixed effects model was used to evaluate the longitudinal association between VMS and PMD.

Results: Women contributed a total of 4,748 mammograms (2-10 per woman) over a median 5.4 years of follow-up. We observed no overall association between VMS and PMD. When stratified by menopausal status, VMS was associated with lower PMD among perimenopausal women (β = -1.29%, 95%CI -2.58, -0.001) and those with unknown menopausal status due to hormone use during the study period (β = -3.62%, 95%CI -7.17, -0.07). VMS was not associated with absolute dense area in any analyses. Among women who transitioned to postmenopausal, VMS was not associated with change in PMD across the menopausal transition.

Conclusion: Although our findings do not suggest a strong association between VMS and PMD, we observed a significant effect among perimenopausal women and those using hormones during menopause. Further prospective studies are needed to establish a relationship between VMS and breast cancer risk, and to ascertain the extent to which this relationship may be mediated by PMD.

[VG#615C]

14 Reeves K, Avis N, Hart V, Crawford S, Gold EB. Vasomotor symptoms and breast cancer risk in the Study of Women’s Health Across the Nation

Primary Question:

Summary of Findings: Vasomotor symptoms and breast cancer risk in the Study of Women’s Health Across the Nation

Katherine Reeves, Vicki Hart, Nancy Avis, Ellen Gold, Sybil Crawford

Two previous retrospective studies reported a significantly decreased breast cancer risk among women who experienced menopausal vasomotor symptoms (VMS). It is possible that VMS are a marker of declining sex hormone levels during menopause. Elevated sex hormone levels have been associated with increased breast cancer risk, suggesting that VMS may be indicative of lower susceptibility to breast cancer. We evaluated this relationship in the prospective Study of Women’s Health Across the Nation (SWAN), which includes annual data on VMS and endogenous hormone levels for 3,098 women who were pre- or early perimenopausal at enrollment. We evaluated the effect of VMS on breast cancer risk using discrete survival analysis. Over an average 11.4 years of follow-up, 129 breast cancer cases were self-reported and approximately 50% of participants reported some VMS. Women reporting VMS at any current or previous visit had a reduced risk of breast cancer compared to those never experiencing VMS (OR 0.63, 95% CI 0.39, 1.02). Results were strengthened in the subgroup of women who fully transitioned to postmenopausal during follow-up (N=80 cases, OR 0.45, 95% CI 0.26, 0.77). Associations were unchanged upon adjustment for endogenous hormone levels. VMS appear to be a marker of reduced breast cancer risk. Future research is needed to fully understand this relationship, which does not appear to be mediated by endogenous hormone levels.

[VG#615B]
12-year changes in body mass index and sexual functioning in midlife women

Primary Question:

Summary of Findings: Associations between 12-year changes in body mass index and sexual functioning in midlife women

[WG#727A]

Lee JS, Gold EB, Johnson WO, Ward E. Mapping the Metabolic Syndrome Components during the Menopausal Transition: A Multi-Ethnic Study

Primary Question:

Summary of Findings: Mapping the Metabolic Syndrome Components during the Menopausal Transition: A Multi-Ethnic Study

Jennifer S. Lee, MD, PhD1; Elizabeth Ward2, MA; Wesley Johnson, PhD2; Ellen Gold, PhD3

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The constellations of components of the Metabolic Syndrome (MetS) that occur during midlife in a woman offer a composite of her cardiovascular (CV) condition and risk of CV disease. We hypothesized that the constellations of MetS components, in women who develop MetS during the menopausal transition (MT), depend on race/ethnicity, behavioral factors, and MT stage. The Study of Women Across the Nation (SWAN) followed pre-/early peri-menopausal women as they underwent the MT. MetS diagnosis meant having at least 3 of 5 components: triglyceride >150mg/dL (hTG), HDL-cholesterol < 50mg/dL (lHDL-C), fasting glucose >=100mg/dL (hGluc), waist circumference > 88cm (80cm for Asians) (Obese), and blood pressure >130/85mmHg (HTN). We included 2,367 women, who did not have MetS at baseline. In women who developed MetS (median followup = 7 years), frequencies of all observed MetS component constellations by race/ethnicity (Caucasian, African American, Hispanic, Japanese, Chinese) and MT stage (pre-, early peri-, late peri-, post-menopause, hormone therapy) were assessed at MetS diagnosis. Discrete time Cox regression models identified factors associated with risk of developing the most frequent constellations of MetS components. Models included age, study site, alcohol use, MT stage, race/ethnicity, physical activity (PA), current smoker, and fiber intake. Of the 159 women who developed MetS in the MT, 7.5% had no MetS components at baseline; the most frequent components were obesity (47%) and lHDL-C (45%). The most frequent constellations at MetS diagnosis were: Obese/hTG/lHDL-C (23% of those who developed MetS); Obese/HTN/lHDL-C (21%); Obese/HTN/hTG (14.7%); and Obese/HTN/hGluc (14.7%). In multivariable models, greater PA conferred a 20% lower risk for the two most frequent MetS constellations (HR 0.79, 95% CI 0.6-0.99 and HR 0.77, 95% CI 0.6-0.97, respectively). Current smokers had a greater risk (HR 2.64, 1.11-6.29) of having Obese/hTG/lHDL-C than non-smokers. African Americans had a lower risk (HR 0.05, 0.01-0.37) of having Obese/hTG/lHDL-C than Caucasians. Conclusion: In women who develop MetS during the MT, their specific constellations of MetS components were associated with race/ethnicity and behaviorally modifiable factors.

[WG#752B]
El Khoudary SR, Shields K, Budoff M, Barinas-Mitchell EJ, Janssen I, Everson-Rose SA, Matthews KA. Heart Fat Depots, but not Peri-aortic Fat Depot are Significantly Associated with Presence and Severity of Coronary Calcification in Women at Midlife: The Study of Women’s Health Across the Nation (SWAN) Ectopic Cardiovascular Fat Ancillary Study

Primary Question: The importance of vitamin D for bone health as well as its potential role in nonskeletal health has garnered much recent attention. Population-based studies investigating temporal trends in 25-hydroxyvitamin D (25OHD) have reported conflicting results. Our goal was thus to investigate changes in mean 25OHD levels over time and predictors of these changes in the Study of Women’s Health Across the Nation (SWAN), a multi-center, racially and ethnically diverse cohort of women. 1582 women had 25OHD measured in 1998-2000 (at age 48±3 years) and again in 2009-2011 (at age 60±3 years). 25OHD was measured by liquid chromatography-tandem mass spectrometry in a single batch. Over this interval, the mean 25OHD level increased by 6.5 ng/mL (95% CI 5.9 to 7.0), from 21.5±9.8 to 28.0±11.5 ng/mL (p<0.001 after adjustment for age, BMI, menopausal status, study site, and season of blood draw). As expected, baseline mean 25OHD levels
varied by race/ethnicity (14.0 ng/mL (African-American), 25.4 ng/mL (Caucasian), 19.8 ng/mL (Chinese), 18.3 ng/mL (Hispanic), and 24.0 ng/mL (Japanese) (p<0.001)). However, the magnitude of increase was similar among groups, ranging from 5.3 ng/mL (Caucasian) to 8.7 ng/mL (Chinese) (Figure 1). The observed increases in 25OHD did not vary by socioeconomic status (SES), education level, or acculturation. At the 2009-2011 visit, 49% of subjects reported taking a multivitamin or vitamin D supplement; the adjusted increase in 25OHD was higher among supplement users (10.1 ng/mL vs. 3.2 ng/mL, p<0.001). Using the Institute of Medicine definition of vitamin D deficiency as 25OHD < 20 ng/mL, the proportion of deficient women decreased from 43% to 24% (p<0.001) over the interval. Among those who reported using supplements at the 2009-2011 visit, the proportion deficient decreased from 35% to 6% (p<0.001) while the proportion decreased from 51% to 39% among non-users (p<0.001). Rates of 25OHD < 20 ng/mL were significantly lower among supplement users of all racial/ethnic groups (p<0.001 for all comparisons at the 2009-2011 visit) (Figure 2). In summary, we observed an increase in average 25OHD levels as well as a decrease in the proportion of subjects with vitamin D deficiency in this observational cohort over an approximately 11 year interval. Subjects of all races/ethnicities as well as of differing SES, level of education, and degree of acculturation had similar changes. Use of vitamin supplements was a major determinant of changes in 25OHD levels.

Yu E, Putman M, Bouxsein. Defects in cortical microarchitecture among postmenopausal African-American women with DM2

Primary Question:

Summary of Findings: Purpose: Fracture risk is increased in patients with type 2 diabetes mellitus (DM2) despite normal bone mineral density (BMD). In populations comprised predominantly of Caucasians, cortical porosity is higher in diabetics than in non-diabetics. Although DM2 is more common in African-Americans than in Caucasians, it is not known whether African-American women with DM2 also have cortical bone deficits. Methods: We measured BMD at the spine, hip, and total body by DXA, and volumetric bone density and microarchitecture at the distal radius and tibia by HR-pQCT in 22 type 2 diabetic and 78 non-diabetic postmenopausal African-American women participating in the Study of Women Across the Nation (SWAN). Microfinite element analysis was performed to estimate bone strength. We measured fasting glucose and insulin and calculated HOMA-IR.

Results: There were no significant differences in age (60 ± 3 yr vs. 59 ± 3 yr, p=NS) or weight (87 ± 20 kg vs. 84 ± 19 kg, p=NS) between the diabetic and non-diabetic groups. DXA BMD was similar in the diabetics and non-diabetics at all bone sites. At the radius, cortical porosity and cortical pore volume were greater (P<0.04 for both) and cortical BMD and tissue mineral density were lower (p<0.05 for both) in diabetics than in non-diabetics (Table). There were no differences in radius total BMD or trabecular BMD between groups. Measures of cortical bone strength were significantly lower in the diabetic women though overall failure load was similar (Table). There were no significant associations between cortical parameters and either the duration of DM2 or with HOMA-IR. In the full cohort, fasting glucose levels were associated with worse cortical porosity (r=0.25, p=0.02) and lower cortical BMD (r=-0.35, p<0.01). In particular, cortical porosity and cortical pore volume were higher among those who had fasting glucose >100 mg/dL (p<0.05 for both). There were no differences in tibial bone density or microarchitecture between diabetic and non-diabetic women. These findings remained similar after adjustment for use of diabetes or osteoporosis medications.

Conclusions: DM2 and higher fasting glucose are associated with unfavorable changes in cortical bone at the non-weight-bearing radius in postmenopausal African-American women.
These structural deficits may contribute to the increased fracture risk among women with DM2. Further our results suggest that hyperglycemia may be involved in mechanisms of skeletal fragility associated with DM2.

Primary Question:
Summary of Findings: Circulating 25(OH)D has been linked to fracture risk but to our knowledge, there is no information on whether 25(OH)D predicts fracture over the menopausal transition or whether 25(OH)D is associated with changes in BMD over the menopausal transition. We studied 1620 women enrolled in the bone cohort of the Study of Women’s Health across the Nation (SWAN). Women attended up to 11 clinic visits for an average follow-up of 9.5 years. 25(OH)D was measured at the 02 clinic visit, 2 years after enrolling in SWAN. At this time, 1207 (74.5%), were pre or early perimenopausal; 116(7.2%) late perimenopausal, 77(4.8%) postmenopausal based on bleeding patterns. Menopausal status or had hysterectomy was unknown for 220 (13%). The mean 25(OH)D (ng/ml) was 21.6 but differed markedly by race/ethnicity; White, 25.2; Black, 14.1; Chinese, 20.1 and Japanese, 23.5, p<0.000) 703 (43%) had a value < 20ng/ml. The mean age of the women at time of 25(OH)D measure was 48.5 ± 2.7, with no difference by race/ethnicity. Body mass index (BMI) (kg/m2) was greatest in Black women, 31.8; lower in White women, 28.2 and lowest in Japanese, 23.5 and Chinese, 23.2 women. Incident non-traumatic fractures that occurred after visit 02 were ascertained at each annual visit initially by self-report and later, confirmed by radiographic report. A total of 88 women experienced an incident non-traumatic fracture. Cox proportional hazard models were used to calculate the hazard ratio (HR) (95% confidence interval (CI)). Each 10 ng/ml increase in 25(OH)D was associated with a 25% lower fracture risk, even after adjusting for BMI, BMD and other important confounding variables, Table. Women with 25(OH)D >20 ng/ml had a 42% lower risk of fracture. Exclusion of women who were already postmenopausal at visit 02 had no effect. Longitudinal analyses of BMD across the menopausal transition were confined to the subset of 791 women for whom a final menstrual period (FMP) could be determined. The mean 25(OH)D level in this subgroup (21.2 ng/ml) was similar to the total population. We compared rates of spine and hip BMD changes in women from -5 to -1 yr before the FMP, 1 year before to 2 years after FMP and 2 to 5 years after FMP. We found no association between (25(OH)D and transmenopausal bone loss. We conclude that women with higher 25(OH)D levels at midlife have a lower risk of subsequent fractures. Vitamin D supplementation may be warranted in women with 25(OH)D <20 ng/ml.

Primary Question:
Summary of Findings: Background: Several studies have reported associations between
long-term air pollution exposures and cardiovascular mortality. However, the biological mechanisms connecting them remain uncertain.

Objectives: Examine effects of fine particles (PM2.5) and ozone on serum markers of cardiovascular disease (CVD) risk in a cohort of midlife women.

Methods: We obtained information from women enrolled at six sites in the multi-ethnic, longitudinal Study of Women's Health Across the Nation, including repeated measurements of high-sensitivity C-reactive protein (hs-CRP), fibrinogen, tissue-type plasminogen activator antigen (tPA-ag), plasminogen activator inhibitor Type 1 (PAI-1), and Factor VIIc. We obtained residence-proximate PM2.5 and ozone monitoring data for a maximum five annual visits, calculating prior year, six-month, one-month, and one-day exposures and their relations to serum markers using longitudinal mixed models.

Results: For the 2,086 women studied, after adjusting for age, race/ethnicity, site, body mass index, smoking and recent alcohol use, PM2.5 exposures were significantly associated with blood marker levels, especially year-prior exposures for hs-CRP (20.88% increase per 10 µg/m3 PM2.5, 95% CI: 6.59, 37.10), tPA-ag (8.61%, 95% CI: 1.82, 15.86), and PAI-1 (34.64%, 95% CI: 18.70, 52.72). Findings did not change significantly after further adjustment for health and lifestyle characteristics. Significant associations with ozone were observed less but also present.

Conclusions: Our findings suggest that prior year exposures to PM2.5 and ozone adversely affect inflammatory and hemostatic pathways for cardiovascular outcomes in midlife women.

Acknowledgements:
The Study of Women's Health Across the Nation (SWAN) has grant support from the National Institutes of Health (NIH), DHHS, through the National Institute on Aging (NIA), the National Institute of Nursing Research (NINR) and the NIH Office of Research on Women's Health (ORWH) (Grants U01NR004061; U01AG012505, U01AG012535, U01AG012531, U01AG012539, U01AG012546, U01AG012553, U01AG012554, U01AG012495). The content of this abstract is solely the responsibility of the authors and does not necessarily represent the official views of the NIA, NINR, ORWH or the NIH.


Primary Question:
Summary of Findings: Subclinical atherosclerosis indices, such as carotid artery intima-media thickness (IMT) and plaque, have been linked to future CHD, MI and stroke events, are more prevalent in postmenopausal women and vary by race/ethnicity. In most studies, African-American women have greater IMT (especially in the common carotid artery; CCA) and larger carotid arterial adventitial diameter (AD; a measure of vascular adaption). These differences may reflect the higher levels of CVD risk factors in African-Americans. However,
population-based studies have reported lower carotid plaque and coronary calcification in African-American women compared to Caucasian women. Less is known about late midlife women of other racial/ethnic groups including Hispanic and Chinese women. We hypothesized that, in late midlife women, there are racial/ethnic differences in subclinical atherosclerosis and in the associations between these measures and CVD risk factors.

Methods: Participants (n=1406; 85% postmenopausal; mean±SD age 60±3 years) from the Study of Women's Health Across the Nation, who were free of CVD and had CCA-IMT, AD or presence of carotid plaque assessed at the 12th annual visit, were included in these analyses. Multivariable regression models were run to determine the relationship between race/ethnicity and CCA-IMT, AD (linear) and plaque (logistic) adjusted for CVD risk factors (Table 1). Results: Compared to Caucasian women, CCA-IMT was greater in African-American, AD greater in African-American and Chinese women and plaque prevalence was lower in African-American and Hispanic women independent of CVD risk factors. Independent correlates of CCA-IMT were age and SBP for all groups and BMI and glucose in Caucasian and Chinese women only. Independent correlates of AD were SBP, BMI and height in Caucasian, African-American and Chinese women, insulin and antihypertensive medications in African-American and glucose in Caucasian women. Smoking and lower education were independently associated with plaque in African-American women (age, smoking and glucose in Caucasian women).

Conclusions: In this cross-sectional study of late midlife women, the extent of subclinical atherosclerosis and associations with CVD risk factors vary by race/ethnicity, indicating that vascular adaptation to CVD risk factors may differ across racial/ethnic groups.

Table 1: Markers of subclinical atherosclerosis by race/ethnicity in late mid-life women

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>N (%)</th>
<th>CCA-IMT (mm)</th>
<th>AD (mm)</th>
<th>Plaque, N(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caucasian</td>
<td>712 (50.6%)</td>
<td>0.78±0.11</td>
<td>7.09±0.63</td>
<td>327 (45.9%)</td>
</tr>
<tr>
<td>African-American</td>
<td>417 (29.7%)</td>
<td>0.83±0.12*</td>
<td>7.35±0.72**</td>
<td>155 (37.2%)*</td>
</tr>
<tr>
<td>Chinese</td>
<td>189 (13.4%)</td>
<td>0.76±0.11</td>
<td>7.21±0.59*</td>
<td>92 (48.7%)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>88 (6.3%)</td>
<td>0.80±0.11</td>
<td>7.04±0.63</td>
<td>24 (27.3%)*</td>
</tr>
<tr>
<td>Total</td>
<td>1406</td>
<td>0.79 ±0.12</td>
<td>7.18 ±0.66</td>
<td>598 (42.5%)</td>
</tr>
</tbody>
</table>

*p<0.001, **p<0.05 compared to Caucasian women adjusting for age, site, SBP, BMI, height (for AD model only), current smoking, HDL-C, triglyceride levels, glucose, insulin, antihypertensive and lipid lowering medications, menopausal status and education.

[WG#694A]

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Primary Question: Study Objectives: Mexican immigrants to the US report longer sleep duration and fewer sleep complaints than their US-born counterparts, but the reasons underlying this “healthy immigrant effect” remain uncertain. To investigate whether this effect extends to other immigrant groups, we examined whether prevalences of self-reported sleep complaints are lower among Hispanic, Chinese, and Japanese immigrant women compared to their US-born ethnic counterparts. We also examined whether (1) sociodemographic and psychosocial characteristics and (2) language acculturation accounted for these differences. Design: Cross-sectional observational study. Setting: Multi-site study in Oakland, Los Angeles, and Newark.
Participants: Hispanic (n=197), Chinese (n=230), and Japanese (n=275) women (mean age=46) participating in the Study of Women’s Health Across the Nation (SWAN), 414 of whom are first-generation immigrants.

Interventions: None

Measurements and Results: Questionnaires were used to assess sleep complaints, race/ethnicity, immigrant status, language acculturation (use of English language), and sociodemographic and psychosocial variables. Approximately one quarter of first-generation immigrant women reported any sleep complaint compared to 37% of those who were US-born. Multivariable adjusted logistic regression analyses showed that first-generation immigrants had lower odds of reporting any sleep complaints (OR = 0.45, p<.001), compared to US-born women of the same race/ethnic group. Women without full language acculturation had lower odds of reporting sleep disturbances; adjustment for language acculturation statistically mediated 51.5% (95% CI 34.4-98.2) of the association between immigrant status and sleep complaints.

Conclusion: Hispanic, Chinese, and Japanese immigrants were less likely to report sleep complaints than their US-born ethnic counterparts; a finding largely explained by level of acculturation.

[WG#529A]

24 Thurston R, Mackey R, Matthews KA. **Childhood and adulthood socioeconomic status in relation to adult subclinical cardiovascular disease in The Study of Women’s Health Across the Nation**

**Primary Question:**

**Summary of Findings:** Background: The relation between low adult socioeconomic status (SES) and cardiovascular disease (CVD) is well-known. However, life-course perspectives underscore the importance of childhood SES to the development of CVD disparities. The relative contributions of childhood and adult SES to CVD are not understood. Examining these relations using subclinical CVD indices capturing early disease development is useful to avoiding SES biases in event presentation and detection. The study aim was to examine the relative relations of childhood and adult SES to carotid intima media thickness ((IMT), an index of atherosclerosis) and brachial artery flow mediated dilation ((FMD), an estimate of endothelial dysfunction).

Methods: Aims were tested among Pittsburgh participants of the Study of Women’s Health Across the Nation (SWAN), a prospective study of midlife women (N=245, 30% AFRICAN AMERICAN, 70% CAUCASIAN). Relations between childhood SES (maternal and paternal education, home ownership, family being on public assistance) and adult SES (education, income, difficulty paying for basics) in relation to each subclinical CVD index were examined in linear regression models with one adult and one childhood SES measure (covariates: age, race, BMI, SBP, smoking, and for FMD, baseline lumen diameter).

Results: For IMT, lower childhood SES (maternal education: <= vs. >high school: b(SE)=.03(.01),p=0.04; being on public assistance: b(SE):.03(.02),p=.04), but not adult SES, was related to higher IMT. For FMD, adult SES (current education < vs. >= college: b(SE)=-.17(.07), p=.01), but not childhood SES, was related to poorer FMD. An interaction between race and current financial strain (p<.05) indicated that difficulty paying for basics was associated with somewhat poorer FMD among AFRICAN AMERICANS (b(SE)=.23(.12),p=.06) but not CAUCASIANS (b(SE)=-.04(.09),p=.63) There were no interactions between childhood and adult SES.
Conclusions: Low childhood SES may be most important to processes that develop over a lifetime (e.g., atherosclerosis). Conversely, low adult SES may be most relevant to dynamic processes (e.g., acute endothelial dysfunction). These results point to the specificity of the timing of adverse exposures in relation to the timing of differing CVD processes.

SWAN has grant support from the NIH, DHHS, through the NIA, the NINR, the NHLBI, and the NIH ORWH (Grants NR004061; AG012505, AG012535, AG012531, AG012539, AG012546, AG012553, AG012554, AG012495, HL065591). The content of this abstract is solely the responsibility of the authors and does not necessarily represent the official views of the NIA, NINR, ORWH, NHLBI, or the NIH.


Primary Question:

Summary of Findings: Title: IMPACT OF SMOKING ON THE AGE AT NATURAL MENOPAUSE IN BRCA1/2 MUTATION CARRIERS IN NORTHERN CALIFORNIA

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Objective: Timing of fertility preservation and risk-reducing salpingo-oophorectomy is of great concern for BRCA1 and BRCA2 mutation(BRCA1/2) carriers. Our preliminary analyses suggested BRCA1/2 carriers may have an earlier age at natural menopause, consistent with findings from a recent study relating BRCA1 to occult primary ovarian insufficiency. The aim of this study was to examine the association of BRCA1/2 and age at natural menopause, and possible effect modification of smoking,a possible exogenous modifiable risk factor.

Design: Retrospective study with historical control

Materials and Methods: 166 Caucasian BRCA1/2 carriers in Northern California with natural menopause or still menstruating were identified within UCSF Cancer Risk Program registry and compared to 765 Caucasian women in Northern California included in the Study of Women's Health Across the Nation (SWAN) cohort. We compared median age at natural menopause and any effect modification of smoking,using the Kaplan-Meier approach for unadjusted analyses and Cox proportional hazards regression analyses to adjust for confounding factors.

Results: The median age at natural menopause in BRCA1/2 carriers was statistically significantly earlier than normal population (48 vs 53years,log-rank p-value<0.0001). The
unadjusted hazard ratio of natural menopause was 3.94 (95% confidence interval 2.34, 6.65), 4.05 (2.30, 7.12) after adjusting for smoking and oral contraception pills. For BRCA1/2 carriers who were current heavy smokers (≥20 cigarettes/day), the median age at natural menopause was 45.5, significantly earlier than never or past smokers or current light smokers (<10, 10-19 cigarettes/day) (log-rank p-value=0.0021).

Conclusions: BRCA1/2 is associated with significantly earlier age at natural menopause, and heavy smoking poses additional risk for even earlier menopause. As the relationship between menopause and end of natural fertility is considered fixed, this finding of earlier menopause and the impact of smoking is important for counseling BRCA1/2 carriers and is suggestive of the underlying mechanism.

Support: NIH/DHHS grant AG012554 [WG#612A]


Primary Question: Summary of Findings:

Women gain visceral fat during pregnancy. Whether post-partum behaviors, such as lactation, modify women’s subsequent body composition is unknown.

Purpose
To examine the extent to which lactation was associated with visceral adiposity in a sample of US women.

Methods
Cross-sectional analysis of 351 women aged 45-58, who were free of clinical cardiovascular disease and had not used oral contraceptives or hormone replacement therapy in the three months prior to enrollment in the Study of Women’s Health Across the Nation-Heart Study (2001-2003). History of lactation was self-reported. Computed tomography was used to precisely measure abdominal adiposity.

Results
On average, women were 51 years old and 19 years had passed since their last birth. Among premenopausal/early peri-menopausal mothers, those who did not breastfeed had 28% greater visceral adiposity (95%CI:11-49, p=0.001), 20% greater visceral to total abdominal fat ratio (95%CI:2-40, p=0.03), 4.7% greater waist-hip ratio (95%CI:1.9-7.4, p<0.001), and 6.49cm greater waist circumference (95% CI:3.71-9.26, p<0.001) than mothers who consistently breastfed in models adjusting for study site, age, parity, years since last birth, socioeconomic, lifestyle, and family history variables, early adult BMI and current BMI. In comparison to women who were nulliparous, mothers who consistently breastfed had no more visceral fat. In contrast, premenopausal/early peri-menopausal mothers who had not breastfed had significantly greater visceral adiposity (42%(95%CI:17-70), p<0.001), ratio of visceral to total abdominal adiposity (32%(95%CI:10-60), p=0.004), waist circumference (6.15cm(95%CI:2.75-9.56), p<0.001), and waist-hip ratio (3.7%(95%CI:0.69-6.8), p=0.02) than nulliparous women. No significant relationships were observed among late peri-menopausal/postmenopausal women.
Conclusions
Mothers who did not consistently breastfeed were significantly more likely to retain metabolically-active visceral fat than mothers who consistently breastfed. These results provide a potential physiologic basis for prior findings that women who do not breastfeed their children are at increased risk for diabetes, the metabolic syndrome, and cardiovascular disease.


Primary Question:

Summary of Findings: Depressive symptoms are associated with adiponectin levels in middle-aged women.

Susan A. Everson-Rose, PhD; Cari Jo Clark, ScD; Qi Wang, MS; Hongfei Guo, PhD; Peter Mancuso, PhD; Jared Goldberg, BS; Howard Kravitz, DO; Joyce T. Bromberger, PhD; MaryFran Sowers, PhD.

Depressive symptoms are associated with obesity, diabetes, and cardiovascular diseases (CVD). Mechanisms underlying these associations are not fully understood, but evidence suggests inflammatory processes may be particularly important. Adipocytokines play a critical role in obesity and obesity-related disorders, including type 2 diabetes, insulin resistance, dyslipidemia, hypertension, and coronary artery disease. Adiponectin is the most abundant anti-inflammatory adipocytokine secreted by fat cells. Very few studies have investigated whether depression is related to adiponectin, though this is a biologically plausible pathway linking depression to obesity and CVD risk. This study examined the association between depressive symptoms, assessed by the 20-item Center for Epidemiologic Studies Depression scale (CES-D), and circulating levels of adiponectin in a cohort of 581 women (38.7% black; 61.3% white; mean (SD) age = 45.6 (2.5) years). Participants were from the Study of Women’s Health Across the Nation. Adiponectin was measured from stored serum specimens and assayed in duplicate using a commercially available enzyme linked immunosorbent assay. The mean (SD) adiponectin value was 9.90 (4.92) ìg/mL [range, 1.7 to 30.0; median, 8.92 ìg/mL]. Values were log-transformed for analyses due to skewness of the distribution. An adjusted linear regression model showed that compared to women with few depressive symptoms, those with elevated depressive symptoms (CES-D >16) had 9.6% lower median adiponectin levels (95% CI, 1.4 to 17.0%), controlling for age, race, sex hormone binding globulin, smoking, alcohol consumption, diet and physical activity. This association was somewhat reduced with further adjustment for body mass index [estimate for CES-D > 16 = -0.082; SE = .043; p=0.057]. This study provides unique epidemiologic evidence of an association between depressive symptoms and circulating adiponectin levels in healthy, middle-aged women. Findings suggest that the pathway between depression and obesity, CVD and related disorders may include critical obesity-related inflammatory markers. [Supported by NIH/DHHS grants HL091290, AG012505, AG012546, MH59770, AG17719.]

**Primary Question:**

**Summary of Findings:** Background: Obese (BMI ≥30 kg/m²) individuals without cardiometabolic abnormalities have no apparent increased risk of CVD in comparison to non-obese individuals. Why the “benign” obese remain free of CVD risk factors and CVD events remains unclear. We hypothesized that diet patterns that were higher in antioxidants, fiber, fruits and vegetables, and lower in saturated and trans fats would be associated with greater odds of benign obesity.

Methods: Cross-sectional analyses of obese (BMI ≥30 kg/m²) black and white SWAN women, aged 42-52, who were categorized as “at-risk” or “benign” based on the presence (at-risk) or absence (benign) of any of the following at baseline: 1) blood pressure ≥130/85 mmHg or antihypertensive medications; 2) HDL<50 mg/dL; 3) triglycerides ≥150 mg/dL; 4) glucose ≥100 mg/dL or antidiabetes medications; and 5.) C-reactive protein >5.6 mg/dL (top quartile). Usual dietary intake over the previous year was assessed with the Block food frequency questionnaire.

Results: Of the 2,242 women with complete risk factor data, 39% (n=884) were obese with 9% (n=80) of obese having the benign phenotype. Benign obese women were more likely to be white and had a lower mean BMI (34.0 vs. 36.0 and 38.1 kg/m², respectively) and waist circumferences (95.7 vs. 101.1 and 108.4 cm, respectively) compared to those obese women with 1-2 or ≥3 risk factors. Energy intake did not differ significantly between the three groups (1680 vs. 1821 and 1855 kcal/day, respectively), nor did energy-adjusted daily intake of saturated (11.9 vs. 12.5 and 12.4 g/1,000 kcal, respectively) or trans fats (3.1 vs. 3.5 and 3.5 g/1,000 kcal, respectively). Benign obese women had significantly higher energy-adjusted daily intakes of vitamin B6 (0.83 vs. 0.77 and 0.73 mg/1,000 kcal, respectively) vitamin E (5.0 vs. 4.5 and 4.5 mg /ATE/1,000 kcal, respectively), dietary fiber (6.5 vs. 5.8 and 5.7 g/1,000 kcal, respectively) and vegetables (1.5 vs.1.2 and 1.3 servings/d, respectively) with significantly less meat servings (1.6 vs.1.9 and 1.7 servings/d, respectively). After adjustment for important covariates including BMI, each standard deviation higher energy-adjusted daily intake of Vitamin E, Vitamin B6, and fiber was associated with 42% (OR 1.42; 95% CI 1.15-1.75), 27% (1.27; 1.01-1.61), and 28% (1.28; 1.01-1.61) greater odds of having the benign phenotype, respectively. Higher energy-adjusted intake of omega-3 fatty acids was associated with benign obesity (OR1.27; 95% CI 1.01-1.61). Additionally, higher intakes of vitamin B1, folate and iron were significantly associated with benign obesity in blacks but not whites.

Conclusions: Among obese women at mid-life, higher intake of vitamin B6, vitamin E, and fiber may contribute to normal CVD risk factor levels despite adiposity. These data highlight the potential contribution of diet patterns independent of energy intake or body weight.

[Tomey K, Sowers M, Brines S, Schlemmer E. **Neighborhood poverty and physical functioning-related variables in mid-life rural and urban women living in the Midwestern United States.** Health Over the Life Course Conference in London, Ontario.]

**Primary Question:**

**Summary of Findings:** No free-standing abstract will be published for this conference, just
the manuscript (see accompanying concept proposal). I will be giving an oral presentation based on the contents of the manuscript.

[WG#506A]


**Primary Question:**

**Summary of Findings:** Background: There is almost no longitudinal information about measured cognitive performance during menopause transition [MT].

Methods: We studied 2362 participants from the Study of Women’s Health Across the Nation for four years. Major exposures were time spent in MT stages, hormone use prior to the final menstrual period (FMP) and postmenopausal current hormone use. Outcomes were longitudinal performance in three domains: processing speed (Symbol Digit Modalities Test [SDMT]), verbal memory (East Boston Memory Test [EBMT]) and working memory (Digit Span Backward [DSB]).

Results: Premenopausal, early perimenopausal and postmenopausal women scored higher with repeated SDMT administration (p < 0.0008), but scores of late perimenopausal women did not improve over time (p=0.2). EBMT delayed recall scores climbed during pre- and postmenopause (p<0.01), but did not increase during early or late perimenopause (p >0.14). Initial SDMT, EBMT-immediate and EBMT-delayed tests were 4-6% higher among prior hormone users (p< 0.001). On the SDMT and EBMT, compared to the premenopausal referent, postmenopausal current hormone users demonstrated poorer cognitive performance ( p < 0.05) but performance of postmenopausal non-hormone users was indistinguishable from that of premenopausal women.

Conclusions: Consistent with transitioning women’s perceived memory difficulties, perimenopause was associated with a decrement in cognitive performance, characterized by women not being able to learn as well as they had during premenopause. Improvement rebounded to premenopausal levels in postmenopause, suggesting that MT-related cognitive difficulties may be time-limited. Hormone initiation prior to the FMP had a beneficial effect whereas initiation after the FMP had a detrimental effect on cognitive performance.


**ACKNOWLEDGMENTS**

The Study of Women’s Health Across the Nation (SWAN) has grant support from the National Institutes of Health (NIH), DHHS, through the National Institute on Aging (NIA), the National Institute of Nursing Research (NINR) and the NIH Office of Research on Women’s Health (ORWH) (Grants NR004061; AG012505, AG012535, AG012531, AG012539, AG012546, AG012553, AG012554, AG012495). The content of this abstract is solely the responsibility of the authors and does not necessarily represent the official views of the NIA, NINR, ORWH or the NIH.

[WG#376B]

**Primary Question:**

**Summary of Findings:** Use of selective serotonin reuptake inhibitors is associated with lower bone mineral density in middle-aged women


Recent work has suggested a possible detrimental effect of selective serotonin receptor inhibitors (SSRIs) on bone mineral density (BMD), although most work has been limited by a focus on the elderly. To test the hypothesis that middle-aged women who use SSRIs have lower BMD, we assessed current use of SSRIs using an interviewer-administered questionnaire and measured lumbar spine and hip BMD in a cohort of 1755 women (mean age 50.0 yrs) attending the 5th exam of the Study of Women's Health Across the Nation (SWAN), a prospective cohort study of women in mid-life. We verified medication use from medication containers and classified type of medication from product brand or generic names obtained from containers using a computerized medication dictionary. We categorized women according to their reported SSRI use as users (use at least twice a week in the last month) vs. non-users. Individual drug use within the user category included fluoxetine, paroxetine, sertraline, fluvoxamine, and citalopram. Users of other classes of antidepressants at the visit were excluded. Depressive symptoms were measured using the CES-D. Mean BMD at the lumbar spine, hip, and femoral neck were calculated by category of SSRI use. All results were adjusted for the following characteristics measured at the visit: age, site, ethnicity, BMI, menopausal stage, and CES-D score.

<table>
<thead>
<tr>
<th>BMD site</th>
<th>Non-user (n=1628)</th>
<th>SSRI user (n=127)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumbar spine</td>
<td>1.059 (1.052, 1.065)</td>
<td>1.034 (1.011, 1.058)</td>
<td>0.04</td>
</tr>
<tr>
<td>Total hip</td>
<td>0.951 (0.946, 0.956)</td>
<td>0.931 (0.912, 0.951)</td>
<td>0.05</td>
</tr>
<tr>
<td>Femoral neck</td>
<td>0.828 (0.823, 0.833)</td>
<td>0.805 (0.786, 0.824)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Use of SSRIs in this cohort is associated with lower BMD at the lumbar spine and hip, after controlling for several potentially confounding factors. Prospective analyses of rate of change in BMD in SSRI users vs. non-users are necessary to confirm these findings.


**Primary Question:**

**Summary of Findings:** SWAN (the Study of Women’s Health Across the Nation) has previously reported a rise in circulating DHEAS during the late menopausal transition. We now expand that original study to include ten consecutive annual measurements on 2886 women from five ethnic groups who were 42-52 years of age on entry into the study. Women with a hysterectomy and/or bilateral oophorectomy and observations concurrent with hormone use were excluded and data were adjusted for ethnicity, clinical site, smoking (including passive smoke exposure), weight, and height. Cross-sectional analysis of covariance of circulating dehydroepiandrosterone sulfate (DHEAS) in premenopausal women at baseline
indicates a uniform decline in circulating DHEAS with increasing age. In contradistinction, longitudinal linear mixed modeling including observations from premenopause through late postmenopause (more than 24 months past the final menses, FMP) identified a significant late-transition rise in DHEAS when women were analyzed by ovarian status. An average increase in mean circulating DHEAS was observed between early perimenopause and late perimenopause (3.95%, p=0.003) when the entire cohort was analyzed. Levels tended to plateau between late perimenopause and early postmenopause (within 24 months LMP) (p>0.05) but then declined significantly (p=0.03) between early and late postmenopause (p=0.03). Levels were similar between early perimenopause and late postmenopause indicating the observed rise in DHEAS was transient and related to changes in ovarian function. Of 1423 women with at least one observation during the late transition or early postmenopause, 1202 (84.5%) had an estimated within-woman increase in DHEAS during the menopausal transition. The proportion of women exhibiting a rise and the trajectory of circulating DHEAS rise was similar for all five ethnic groups. Women who exhibited a detectable rise in DHEAS were more likely to be early perimenopausal at baseline with higher mean baseline DHEAS. Women with no detectable rise in DHEAS did not differ significantly from those with a DHEAS rise with respect to age, smoking, BMI, circulating estradiol or circulating testosterone. Baseline SHBG was lower in women with a detectable rise in DHEAS, but not statistically significantly so (p=0.06). Our findings of a late menopause transition-associated rise in DHEAS in most women underscore the importance of longitudinal observational data, as cross-sectional studies have led to a widely held assumption that DHEAS declines inexorably in adulthood. Elucidation of how this contribution to the sex steroid milieu affects the health of middle-aged women is warranted.


Primary Question: A common hypothesis about how religion/spirituality affects health is by improving host resistance to the negative effects of stress. Daily spiritual experiences have been thought to play a key role in this process. Having a valid and reliable measure of daily spiritual experiences is a prerequisite for testing this hypothesis. We employed the Rasch model to examine the psychometric properties of the Daily Spiritual Experiences Scale (DSES). The Rasch model estimates the probability of item endorsement based on person ability and item difficulty. Data were taken from 420 white and African-American midlife women participants in the Chicago site of SWAN. We found the DSES had reasonably good person and item reliability, but there were problems with the response scale, with multidimensionality, item misfit, and assessment of the continuum of the construct. Developing additional items that measure a continuum of daily spiritual experiences will improve the scale.

SWAN has grant support from the National Institutes of Health, DHHS, through the National Institute on Aging, the National Institute of Nursing Research and the NIH Office of Research on Women's Health (Grants NR004061; AG012505, AG012535, AG012531, AG012539, AG012546, AG012553, AG012554, AG012495). This research was also supported by AG020145 (G Fitchett).
Primary Question:

Summary of Findings: Extensive scientific evidence exists supporting the numerous health benefits of regular physical activity (Physical Activity Guidelines Advisory Committee). These benefits include reduced risks of premature mortality, coronary heart disease, hypertension, diabetes, obesity, osteoporosis, and colon and breast cancer, and improved mental health and overall quality of life. In addition, evidence suggests that age-related declines in physiological capacity (e.g. aerobic capacity, muscular strength) are attenuated by physical activity. However, whether or not physical activity modifies the adverse effects of the menopausal transition on outcomes, such as onset of vasomotor symptoms, increases in central adiposity, and increased risk of depression, is not well established.

SWAN, a multi-site, multi-ethnic, observational study of the natural history of the menopause, offers a unique opportunity to examine the relation of physical activity to a number of different outcomes relevant to women as they transition from pre- to post-menopause. The primary focus of this presentation will be on a comparison of active women with inactive women with regard to changes in weight and waist circumference over time, with time defined as years from the final menstrual period (FMP). Physical activity will be examined both as an effect modifier of the impact of time from the final menstrual period (FMP) on body size as well as a confounder of that relation. The differences between active and inactive women in terms of other outcomes, such as vasomotor symptoms and depression, will also be discussed.

Primary Question:

Summary of Findings: Other SWAN investigators have previously demonstrated a significant relationship between depression and visceral fat accumulation in women transitioning through menopause, and it is commonly believed that this relationship is mediated by cortisol. It is also commonly accepted that hypercortisolism is associated with depression, however, the literature examining the relationship between depression and cortisol demonstrates considerable inconsistency in results. The characterization of HPA axis dysfunction is complicated and likely affected by a multitude of variables, including age, sex, race, severity of psychological insult, and technique of cortisol sampling and evaluation, any of which could influence this relationship.

Method/Proposed Methods:
We first reviewed the literature on the relationship between cortisol and depression and observed considerable inconsistency in results. There are many possible reasons for the inconsistency in the literature linking cortisol to depression, and the analyses that are planned or underway include looking at the following relationships/variables:
• The relationship may not be linear such that depressed people demonstrate both hypo- and hypercortisolemic patterns.
• The association between depression and cortisol may exist only among the more severely depressed people.
• The techniques of cortisol assessment in the literature include salivary, urinary, and plasma sampling in the morning, evening, and throughout the day and this variability may influence results; we therefore will examine our salivary samples as individual time points as well as the diurnal slope.
• Finally, extraneous factors such as physical activity, smoking, age, income, education, caffeine, recent food intake, race, menopausal status, hormone replacement therapy, BMI, and alcohol affect cortisol levels and failure to account for these variables could affect the association.

Discussion/Significance:
We aim to study the relationship between depression and salivary cortisol assessments in midlife women. This is a significant undertaking for several reasons. First, this study has the potential to clarify the physiologic mechanisms relating psychological functioning to cortisol response. This study is of clinical importance since perimenopausal women, particularly those in the late stage of the menopausal transition, are vulnerable to depressed mood. With the loss of protective sex hormones during this time period, depressed mood may have particularly adverse physiological effects. The delineation of an at-risk hypercortisolemic depressive subtype would be valuable clinically in helping target those at particular risk for somatic effects of depressive illness. Our findings may help guide future efforts to assess cortisol in large-scale epidemiologic cohorts, as this cohort is larger and more representative of a natural environment than many previous studies examining effects of mood on cortisol.


Primary Question:
Summary of Findings: The opposing carcinogenic and antiestrogenic properties of tobacco smoke may explain the inconsistent associations between smoking and breast cancer. Mammographic density, a strong risk factor for breast cancer, appears to be lower among current smokers, compared to never smokers. However, few studies have evaluated whether active smoking influences mammographic density after controlling for secondhand smoke (SHS) exposure. We used multivariable linear regression to assess the association between active smoking and SHS exposure, and mammographic density among 799 pre- and early perimenopausal women in the Study of Women’s Health Across the Nation (SWAN). SHS exposure was defined as at least one hour of exposure in the past seven days at home, work, or other setting. Smoking status was defined as follows: (1) never smokers with and (2) without SHS; (3) former smokers with and (4) without SHS; and (5) current smokers. We observed a trend of lower mean percent density (dense tissue area/breast area) across increasing levels of smoke exposure, from 48.1% among never smokers without SHS to 38.4% among current smokers (p<0.001). Smoking status remained inversely associated with percent density after adjusting for age, race/ethnicity, study site, body mass index, and parity (beta= -6.49, SE=2.3, p=0.01 for current smoking versus never smoking without SHS). SHS exposure was not associated with percent density among never or former smokers. Among ever active smokers, statistically significant inverse associations were observed for starting to smoke before age 18 (beta= -5.3, SE=2.4, p=0.03) and smoking 20 or more
cigarettes per day (beta= -8.17, SE=3.0, p=0.02). The inverse association with smoking status and percent density was confined to parous women, or those who had at least one full-term birth (beta= -7.84, SE=2.5, p<0.01 for current smoking versus never smoking without SHS). Our data support an antiestrogenic hypothesis for the relation between smoking and breast cancer in parous women. Supported by NIH/DHHS grants NR004061, AG012554, AG012539, AG012546, and NCI grant R01CA89552.

Matthews K, Bromberger J. Childhood Abuse and Neglect are Associated with Body Fat Distribution in Adulthood. American Psychosomatic Society. 03/2009, Chicago, IL.

Primary Question:
Summary of Findings: Childhood abuse and neglect are traumatic early-life stressors that may be risk factors for central adiposity. Our objective was to examine the association between childhood abuse/neglect and body fat distribution in a sample of 311 women (106 Black, 205 White) from the Pittsburgh site of the Study of Women’s Health Across the Nation (SWAN). SWAN included a baseline measurement of women in midlife (mean age=45.7) and 8 follow-up visits during which waist circumference (WC) and body mass index (BMI) were measured. The Childhood Trauma Questionnaire, given at visit 8, retrospectively assessed 5 domains of abuse and neglect in childhood and adolescence: emotional, physical, and sexual abuse; emotional and physical neglect. ANCOVAs were used to determine whether a history of any abuse/neglect, or each type of abuse or neglect, was associated with WC, controlling for age. Results showed that women with a history of any abuse/neglect had significantly higher WC at visit 8 than women with no abuse history (M=90.8, SE=1.2; M=96.1, SE=1.5; F(1, 308)=7.7, p=.01). Of the specific types of abuse, only physical abuse was significantly related to WC at visit 8 (M=91.7, SE=1.0; M=97.9, SE=2.3; F(1,308)=6.2, p=.01). A history of any abuse/neglect, or specific types of abuse or neglect, were not associated with increased WC from baseline to visit 8 (ps>.05) in the full sample. However, among women with a BMI<30, a history of any abuse/neglect, emotional abuse, physical abuse, sexual abuse, or physical neglect predicted increased WC over time. For all analyses, adjustment for BMI reduced the relationship between abuse and WC to non-significant because of a high correlation between WC and BMI (r=.91, p<.001). Additional mediation analyses showed that Trait Anger scores mediated some relationships between abuse/neglect and WC. This study suggests that traumatic early-life stressors are associated with adulthood body fat distribution, especially among normal-weight and overweight women. Supported by NIH/DHHS AG012546 and MHO59689. The content of this abstract is solely the responsibility of the authors and does not necessarily represent the official views of the NIA, NIMH, or the NIH.

Venkitachalam L, Wildman RW, Mackey RH, Edmundowicz D, Johnston J, Sutton-Tyrrell K. Segment-specific Variation in the relationship between Ovarian Aging and Aortic Diameter In The Study Of Women's Health Across The Nation (SWAN) Heart Study. Conference on Cardiovascular Disease Epidemiology and Prevention, Palm Harbor, FL, March 12-14, 2009

Primary Question:
Summary of Findings: Acknowledgment: Dr. Venkitachalam was supported by the American Heart Association Predoctoral fellowship (award number: 0615369U) from the Pennsylvania-Delaware affiliate. The Study of Women’s Health Across the Nation (SWAN) has grant support from the National Institutes of Health, DHHS, through the National Institute
Background: Ovarian aging is known to influence cardiovascular risk in women. The specific impact on arterial structure, however, remains unknown. We hypothesized that indicators of ovarian aging (menopausal status and sex hormones) will exhibit segment-specific relationship with aortic diameter in 345 Caucasian and 199 African-American women (mean age: 50 years), enrolled in the Pittsburgh and Chicago sites of SWAN, an ongoing longitudinal study of the menopausal transition. Methods: Aortic diameter was recorded at five segments - aortic root (AR), ascending (AA), descending (DA), thoracic (TA) and abdominal aorta (AbA) - using a novel, reliable electron beam tomography protocol. Sex hormones evaluated include estradiol, testosterone, and androgen excess (free androgen index/log estrogen). Results: In the overall cohort, 42% of women were in late peri or post menopause and possessed larger aortic diameters compared to those in pre/early peri menopause. Age and weight adjusted models showed interaction of menopausal status with arterial segment (Figure). A 10-unit increase in estrogen levels was associated with smaller diameters in all segments (parameter estimates in millimeters: AR: -0.01, AA: -0.003, DA: -0.02, TA: -0.02, AbA: -0.004). Increase in androgen excess on the other hand was associated with larger descending and thoracic aortic diameters (P interaction with segment: 0.02). Conclusion: These novel findings reflect the complex, segment-specific impact of ovarian aging on central vasculature. Further research is needed to evaluate this interaction as a potential mechanism for accelerated atherosclerosis observed with menopausal transition.


Primary Question: MEASURING SLEEP: HOW DO DIARIES AND WRIST ACTIGRAPHY COMPARE WITH POLYSOMNOGRAPHY?

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Sleep plays a critical role in health and functioning. Polysomnography (PSG), which involves recording multiple physiologic signals during sleep, is often considered to be the gold standard method for assessing sleep. Limitations to its use include access to expertise and equipment, cost and participant burden. It is, thus, important to understand how alternative methods for quantifying sleep compare to PSG. We used within-person multivariate repeated
linear models to compare important indices of sleep measured by PSG to measures derived from self-report daily diaries and wrist actigraphy, which estimates sleep and wakefulness based on motor activity. Participants were 302 mid-life women enrolled in the multi-site Study of Women across the Nation Sleep Study. All data, including PSG, were collected in participants' homes over 3 consecutive nights. Sleep outcomes were sleep duration (minutes), sleep latency (minutes to sleep onset), minutes of wakefulness after sleep onset (WASO) and sleep efficiency (time spent asleep/time spent in bed x 100). The latter 3 variables were log transformed prior to analyses. Model covariates were race, hot flashes/night sweats, body mass index (BMI), symptoms of depression and use of medications that affect sleep. Significant differences were observed between PSG and diary-assessed measures of sleep duration (Beta = 12.62, p<.01), latency (Beta = -0.38 p<.001), WASO (Beta = -3.17, p<.001) and efficiency (Beta = 0.79, p<.001). In contrast, the only actigraphy-assessed measures shown to differ significantly from PSG were sleep latency (Beta = -1.07, p<.001) and WASO (Beta = -0.63, p<.001). Compared to PSG values, diary reports underestimated the amount of time spent awake at night by over 25 minutes and overestimated sleep efficiency by approximately 7% in reference group participants (white, no hot flashes/night sweats). Actigraphy-based estimates of sleep duration and efficiency, each of which has been widely-linked to health and functioning, did not differ significantly from PSG. Supported by NIH/DHHS AG012505, AG012546, AG012554, NR04061, AG019360, AG019361, AG019362, AG019363.

[WG#420A]

40 Matthews K. **Midlife Aging: Lessons from Study of Women's Health across the Nation.** American Psychosomatic Association 2009 Scientific Session. March 5-7 Chicago ILL.

Primary Question:

Summary of Findings:  No abstract - Invited presentation

[WG#486A]


Primary Question:

Summary of Findings:  No abstract - Invited presentation

[WG#486A]


Primary Question:

Summary of Findings:  Title: Longitudinal Influence of Anthropometry on Mammographic Breast Density

Authors: Katherine W. Reeves, MPH,1 Roslyn A. Stone, PhD,2 Francesmary Modugno, PhD, MPH,1 Roberta B. Ness, MD, MPH,1 Victor G. Vogel, MD, MHS,3 Joel L. Weissfeld, MD, MPH,1,4 Laurel Habel, PhD,5 Barbara Sternfeld, PhD,5 Jane A. Cauley, DrPH, MPH1

1Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, Pennsylvania
Objectives/Research Questions: In cross-sectional studies BMI is negatively associated with percent breast density, a strong risk factor for breast cancer. We sought to evaluate longitudinal associations between changes in BMI and mammographic breast density.

Methods: We studied a prospective cohort of 834 women enrolled in an ancillary study to the Study of Women’s Health Across the Nation (SWAN). Height and weight were measured at annual clinic visits. Routine screening mammograms were collected and read for breast density using manual planimetry. Longitudinal associations between changes in BMI and changes in dense breast area and percent density were evaluated with random effects regression models.

Results: Mean follow-up was 4.8 years (SD 1.8), and the mean number of observations per participant was 5.6 (range 1-8). Mean annual weight change was +0.22 kg/year. In fully adjusted models, changes in BMI and weight were not associated with changes in dense breast area ($\beta$=-0.0105, $p$=0.34 and $\beta$=-0.0055, $p$=0.20, respectively), but were strongly negatively associated with changes in percent density ($\beta$=-1.18, $p$<0.001 and $\beta$=-0.44, $p$<0.001, respectively).

Conclusions: This study demonstrates that longitudinal changes in BMI and weight are not associated with the dense area, yet are negatively associated with percent density. Effects of changes in anthropometry on percent breast density may reflect effects on non-dense tissue, rather than on the dense tissue where cancers arise.

Implications for Public Health: These results improve our understanding of how increased BMI acts to promote breast cancer, and may lead to opportunities for disease prevention and early detection in the future.

[WG#381C]

Santoro N. Differences in menopause symptoms across different ethnic groups. NAMS Annual Meeting, 09/24/08-09/27/08 Orlando FLA.

Primary Question:
Summary of Findings: The menopausal experience is known to differ across cultures worldwide. These differences can be attributed to the overall context in which menopause occurs. It is less clear whether women of different ethnic backgrounds who exist under a similar [apos]dominant[apos] culture experience menopause differently. Data emerging from SWAN, the Study of Women[apos]s Health Across the Nation, suggest that some of the differences in menopause experience are associated with culture and others are explained by lifestyle or behavioral characteristics associated with that culture within the dominant ethnic group. For example, the increase in self reported hot flashes among African-American women is largely explained by increased adiposity in this group of women. On the other hand, there are in stances in which interaction with the dominant culture may exert deleterious effects on the menopause experience, an issue that seems to be the case for Hispanic women. While acculturation appears to be beneficial for many ethnic groups because it increases access to
health care resources and improves educational attainment, Hispanic women in SWAN and in other studies appear to derive little benefit from acculturation and sometimes even demonstrable adversity. The effects of acculturation may be related to country of origin among Hispanic women. Puerto Rican women appear to have increased vulnerability to adverse effects of acculturation. They also appear to experience more menopausal symptoms such as vaginal dryness, worse sleep and increased depressive symptoms, when compared to other Hispanic subgroups in SWAN. In contrast to the negative effects of acculturation seen in some Hispanic populations, acculturation among Japanese women in SWAN is associated with low overall levels of most menopausal symptoms. A similar reduction in symptoms is seen in Chinese women compared to Caucasians, African-Americans and Hispanics in SWAN. The extent to which contact with the dominant culture, a consequence of acculturation, increases exposure to experiences of discrimination and mistreatment needs to be taken into account when evaluating symptom data on immigrant ethnic groups. A model is proposed to address these complex issues. (supported by AG12535).


Primary Question:
Summary of Findings: Hopelessness, depression and carotid atherosclerosis in women at mid-life: The Study of Women's Health Across the Nation (SWAN) Heart Study

Mary Whipple, Susan Everson-Rose, Department of Medicine, University of Minnesota, Minneapolis, MN, Tené Lewis, Epidemiology & Public Health, Yale School of Medicine, New Haven, CT, Lynda Powell, Preventive Medicine, Rush Medical Center, Chicago, IL, Karen Matthews, Kim Sutton-Tyrrell, Epidemiology, University of Pittsburgh, Pittsburgh, PA

Background
Depression and hopelessness are associated with increased cardiovascular disease (CVD) and mortality risk, and several studies have suggested that the effects of hopelessness may be stronger than the effects of depression. Few studies have compared the effects of these two constructs early in the atherogenic process, especially in women and minorities.

Research Design and Methods
We examined the association between self-reported depressive symptoms and hopelessness and carotid artery intimal-medial thickening (IMT) in 576 white and African American women (mean (SD) age, 50.3 (2.8) years) from two of the 7 sites of the Study of Women’s Health Across the Nation (SWAN), a prospective study of the menopausal transition, who participated in an ancillary study of subclinical CVD (SWAN Heart Study). The 20-item Center for Epidemiologic Studies Depression Scale (CES-D) and 2-item Kuopio Ischemic Heart Disease Study Hopelessness Scale were used to measure depressive symptoms and feelings of hopelessness, respectively. Non-invasive B-mode ultrasonography was used to assess mean and maximal IMT of the left and right carotid arteries.

Results
Means (SD) were 0.67 (0.10) mm for average IMT and 0.87 (0.13) for maximum IMT. In models adjusted for age, race, site, body mass index (BMI), resting systolic blood pressure
(SBP), and smoking status, CES-D score was weakly related to mean IMT (P=.062) whereas each 1-point higher CES-D score related to a significant 0.001-mm greater level of maximum IMT (P=.039). Each 1-point higher hopelessness score predicted a significant 0.001-mm greater level of mean IMT (P=.011) and a 0.008-mm greater level of maximum IMT (P=.022). With hopelessness and CES-D score modeled simultaneously, the effect of hopelessness remained significant for both mean IMT (P=.021) and maximum IMT (P=.041), whereas CES-D score was no longer significant (P>0.10). Age, race, site, BMI, and SBP were significant covariates in the model whereas smoking was nonsignificant.

Conclusions
Hopelessness and depression are associated with greater IMT in women at mid-life, independent of age, race, BMI, SBP, and smoking status, but our results indicate hopelessness likely is more atherogenic than depression. Additional research is needed to understand mechanisms that may mediate the effect of hopelessness on subclinical atherosclerosis.

Acknowledgments: Supported by NIA (U01 AG012505, U01 AG012546), NHLBI (R01 HL065581, R01 HL065591), the NIH Office of Research on Women’s Health and the Program for Health Disparities Research at the University of Minnesota Medical School.


Primary Question:
Summary of Findings: Objective. Recent studies show that women with greater body weight and fat have increased risk of menopausal hot flashes. These findings challenge traditional thinking that body fat is associated with fewer hot flashes due to estrone production in adipose tissue, instead supporting thermoregulatory models emphasizing insulating properties of fat. However, because studies have been cross-sectional, the directionality or causal nature of these relations is uncertain. The present study’s aim was to examine whether gains in body fat were associated with increased reporting of hot flashes over time.

Design. 1801 Study of Women’s Health Across the Nation participants ages 42-52 years at entry, who had their uterus and ≥1 ovary at annual visits 6-9, and underwent bioelectrical impedance analysis comprised the study sample. At visits 6-9 they answered questions about hot flashes, provided a blood sample for measurement of hormone concentrations, and had bioelectrical impedance measured for body fat. Associations between change in percent body fat and hot flashes (any/none) were examined in repeated measures logistic regression models (generalized estimating equations). Visits with reported hormone therapy use were excluded.

Results. Gains in percentage of body fat were associated with significantly increased odds of hot flash reporting (per each additional % body fat gain: OR=1.04, 95%CI 1.01-1.08, p=0.01), controlling for age, site, race, menopausal status, education, parity, smoking, and anxious symptoms, current % body fat, and hot flashes at the previous visit. Associations persisted when additionally controlled for estradiol, the free estradiol index, or follicular stimulating hormone concentrations.
Conclusions. Gains in body fat were associated with increased odds of reporting of hot flashes over time. Gains in body fat, which commonly occur during the menopausal transition, may contribute to the onset and persistence of hot flashes over time.

SWAN has grant support from the NIH, DHHS, through NIA, NINR and the NIH ORWH (NR004061, AG012505, AG012535, AG012531, AG012539, AG012546, AG012553, AG012554, AG012495) [WG#444A]


Primary Question:

Summary of Findings: Vascular health and its interaction with cardiovascular (CV) risk factors have been extensively studied but with emphasis on arterial function. Methods: We examined the association of central artery structure with CV risk factors in a bi-racial cohort of 544 women (mean age: 50 years, 37% African-Americans, mean BMI of 29 kg/sq.m) from the Pittsburgh and Chicago sites of SWAN, an ongoing multi-ethnic, multi-site longitudinal study of the menopausal transition. Aortic diameter was measured at five segments – aortic root (AR), ascending (AA), descending (DA), thoracic (TA) and abdominal aorta (AbA) – using previously recorded electron beam tomography scans. Parameter estimates were obtained using regression analysis that accounted for within-person correlation. Results: African-american women possessed larger diameters in every segment, albeit with varying significance, compared to their Caucasian counterparts (age, weight, site and education-adjusted estimates (SE) - AR: 0.18 (0.34), AA: 0.46 (0.32), DA: 0.81 (0.19), TA: 0.54 (0.18), AbA: 0.01 (0.20)). Significant interaction with arterial segment was also seen with the following risk factors: systolic (SBP) and diastolic blood pressures, glucose, insulin, visceral adipose tissue, lipoprotein A1 and Factor VII (Table). Exploratory stratified analysis by race revealed differences in segment-specific correlates of aortic diameter that needs to be further understood. Conclusion: Cardiovascular risk factors exhibit segment-specific association with central artery (aorta) diameter. The effect of related treatment strategies on central vasculature, therefore, needs to be further examined.

Table: Segment-specific associations of race and cardiovascular risk factors with aortic diameter.


Primary Question:

Summary of Findings: PURPOSE:
To determine whether self-reported physical activity at baseline is associated with physical functioning and musculoskeletal pain over three subsequent years in a multi-ethnic population of community-dwelling middle aged women after considering sociodemographics, menstrual
status, smoking, depression score, body size and chronic medical conditions.

METHODS:
Design: Longitudinal study.
Participants: Participants were over 2,200 women from the Study of Women’s Health Across the Nation (SWAN).
Measurements: Baseline physical activity level (including active living and sports indices) was the independent variable. The SF-36 Role-Physical Index and the SF-36 Bodily Pain Index were the dependent variables measured from FU 01 to 03.
Data Analysis:
Our main approach to analysis was logistic regression for the binary outcomes of the SF-36 Role-Physical (modeled as the probability of a woman having High Role-Physical) and Bodily Pain (modeled as the probability of a woman having Low Bodily Pain) for each of the 3 follow-up years. The main predictor, baseline physical activity, was a continuous variable consisting of the sum of the sports/exercise and active living domains. Due to the longitudinal nature of the outcomes (each woman could provide up to 3 responses) we used general estimating equations (GEE).
Separate analyses were conducted for each outcome. Three models were fitted using time dependent outcomes and covariates except site, ethnicity and education which were time independent variables measured at baseline only. In model 1, we adjusted for site and age. In model 2, we added ethnicity, education, and self-reported menopausal status. In model 3, we added BMI, CESD, smoking status and chronic health conditions.

RESULTS:
Baseline physical activity was significantly correlated with High Physical-Function (OR=1.07; 95% confidence interval (CI)=1.02-1.28) and Low Bodily Pain (OR=1.10; CI=1.04-1.17) at follow-up years 01 to 03 independent of age, race, menopausal status, educational level, BMI, CESD, smoking or chronic medical conditions.

Conclusions: This study demonstrates a statistically significant association between baseline physical activity and self-reported pain and physical function over the next three years regardless of menopausal status, sociodemographics, and medical conditions. Motivating women to increase their physical activity during their middle years can positively modify age-related decline in function and increase in pain.

Acknowledgments: Funded by the NIA (U01 AG012505, U01 AG012546) and NHLBI (R01 HL065581, R01 HL065591) and the NIH Office of Research on Women’s Health.


Primary Question:
Summary of Findings: Depressive symptoms and intra-abdominal fat in Caucasian and African-American women at mid-life

Susan A. Everson-Rose, Kelly Karavolos, Tené T. Lewis, Deidre E. Wesley, Lynda H. Powell, Preventive Medicine, Rush University Medical Center, Chicago, IL

Depression has been associated with excess risk of cardiovascular disease (CVD) in women and men, but the mechanisms underlying this association are not fully understood. One
potential pathway is via central adiposity. Visceral or intra-abdominal fat (IAF) is more metabolically active and confers greater cardiovascular risk than subcutaneous fat. Several studies have documented an association between depression and central adiposity but few have examined abdominal fat distribution in relation to depressive symptoms. We investigated the association between depressive symptoms, assessed by the Center for Epidemiological Studies Depression Scale (CES-D), and IAF and subcutaneous fat, assessed by CT, in a sample of 316 middle-aged women (66.8% Caucasian, 33.2% African-American; mean age=50.4 years) participating in the Chicago site of the Study of Women's Health Across the Nation (SWAN). After adjusting for age, race, menopausal status, and total fat mass (assessed by DEXA), each 1-point higher score on the CES-D was associated with 0.76 cm³ greater IAF (p<0.018). With CES-D scores dichotomized we found that depressed women (CES-D score=16 or greater) had 18.4% greater IAF than non-depressed women (CES-D<16) (p=0.02). Further adjustment for smoking, parity, physical inactivity and education did not alter the findings. Associations did not vary by race or menopausal status. Depressive symptoms were unrelated to subcutaneous fat (p=0.55). Findings support the hypothesis that depressive symptoms are associated with visceral fat, and not with subcutaneous fat, in women at mid-life. Greater deposition of intra-abdominal fat may be one pathway by which depression contributes to increased risk for cardiovascular disease.

Acknowledgments: SWAN is supported by NIH through NIA, NINR, and the Office of Research on Women's Health (Grants NR004061, AG012505, AG012535, AG012531, AG012539, AG012546, AG012553, AG012554, AG012495). This ancillary study also is supported by HL/AG67128.

[WG#339A]


Primary Question:

Summary of Findings: The Associations Among Depression History, Life Stress, and Coronary Artery Calcification in Midlife Women.
Joyce T. Bromberger, PhD, Karen A Matthews, PhD

We evaluated the association between life stress and coronary artery calcification (CAC) and whether life stress mediates the previously reported association between recurrent major depression (RMD) and CAC. 210 women, aged 47-57, from the Pittsburgh site of the Study of Women's Health Across the Nation (SWAN) participated in a study of electron beam tomography (EBT) measures of CAC. Women reported no history of heart disease, diabetes, and were not taking hormones. They reported on demographic, psychosocial, and biological factors and participated in the Structured Clinical Interview for the Diagnosis of DSM-IV Axis I Disorders (SCID) at baseline and annually. History of depression was dichotomized as RMD vs no history or single depression episode. CAC score was dichotomized as <10 or > 10. Stress was measured as a stressful life event in the last year or a stressful ongoing problem for more than one year. To determine the effect of each stressor on the association between depression and CAC, each was added to separate multiple logistic regression analyses. 99 women reported a stressful life event and 38 reported a stressful ongoing problem. Both types of stress were associated with CAC > 10, p=.04 for a life event and p=.0003 for an ongoing problem and RMD (p=.004; p=.0003, respectively). In the analysis without stress, compared to women without RMD, those with RMD had a 2.71 odds of having CAC > 10. In the analysis
with a stressful life event, the latter was not significant, but RMD remained significantly associated with CAC > 10 (odds ratio (OR)=2.57; 95%CI=.99, 6.69, p=.05). The inclusion of a stressful ongoing problem reduced the OR for RMD to nonsignificance, p = .13, whereas the ongoing problem was marginally significant (OR=2.55; 95%CI=.89, 7.30, p=.08). These results indicate that stressful ongoing problems are associated with elevated CAC and attenuate the association between RMD and CAC. Chronic problems may be one pathway connecting depression history with CAC.


**Primary Question:**

**Summary of Findings:**

**Background.** Intra-abdominal fat (IAF) increases from pre- to post-menopause independently of age, but the reasons for this increase are unclear. This cross-sectional study examined correlates of several reproductive hormones and intra-abdominal fat (IAF) in Caucasian and African American women at various stages of the menopausal transition in the Diabetes Risk Study, an ancillary study of the Study of Women’s Health Across the Nation (SWAN).

**Methods.** From the 410 women in the total cohort, 151 AA and 194 CAU participants were selected if they: (1) were either pre, peri- or post-menopausal, (2) never took hormone therapy, (3) did not undergo a hysterectomy or double oophorectomy. IAF was measured with a CT scan, and total body fat was measured with a DEXA scan. Reproductive hormones (testosterone, estradiol, and SHBG) were measured from a blood draw at day 2-5 of the menstrual cycle.

**Results.** Women of both ethnicities were comparable in age (mean±SD=50.5±3.8yr), SHBG (55.0±31.4nM), free testosterone (3.81±3.38ng/dL/nM) and the ratio of log(free testosterone) and log(free estradiol) (0.32±0.27). Compared with Caucasian women, African American women had larger total fat mass (46.2±7.8 vs 41.2±8.7%, p<.0001). IAF was lower in AA than in CAU women (84.1±48.2 vs. 102.0 ±42.2kg, p=0.0005) after adjusting for age and percent total fat mass. IAF increased from pre- to post-menopause (p=0.022), but no ethnic differences were found between the trends. After adjusting for age and percent total fat mass, IAF was correlated with SHBG (r=-0.290, p<0.0001), with free testosterone (r=0.285, p<0.0001), and with the ratio of free testosterone to free estradiol (r=0.303, p<0.0001). These associations were similar after adjusting for education, alcohol consumption, smoking, physical activity, number of pregnancies, and depression. They did not differ in AA and CAU women.

**Conclusions.** The increasing androgenicity of the hormonal milieu in women at various stages of the menopausal transition is related to increases in IAF. If validated in longitudinal analyses, this suggests that testosterone is a risk factor for an important component of the metabolic syndrome in women.


**Primary Question:**

**Summary of Findings:**

**Background.** The balance of androgens relative to estrogen may be
a novel, menopause-related risk factor for sub-clinical cardiovascular disease. However, there are several ways to calculate this balance. The purpose of this paper is to provide validation for one or more of these measures of androgen/estrogen balance by comparing their patterns across the peri-menopause with patterns of cardiovascular risk factors over the same time period.

Methods. This was a longitudinal 6-year study of 779 participants in the Study of Women’s Health Across the Nation (SWAN), an investigation of the natural history of the menopause transition. Participants were selected from the 3302 women in the total cohort if they: (1) reached menopause and (2) never took hormone therapy. Annual measures of reproductive hormones (testosterone, estradiol and SHBG) and CV risk factors (elevated blood pressure, metabolic syndrome, and BMI) were graphed over a ten year period centered at the final menstrual period (FMP), each woman contributing up to 6 of data in different parts of the ten year time frame. Three measures of androgen excess were investigated: T/E2, FTI/E2, and FTI/FEI where FTI, the free testosterone index, is testosterone adjusted for SHBG and FEI, the free estrogen index, is estradiol adjusted for SHBG. Associations were examined visually from the graphs and statistically using generalized estimation equations to account for within-woman correlation of repeated assessments.

Results. Of the 3 calculations of androgen excess, FTI/E2 showed the clearest link to menopausal status, with a flat line in the pre- and early peri-menopause and an increase in the late peri-menopause and post-menopause. The other two calculations showed more curvature. The likelihood of higher than normal BP (SBP>120mmHg or DBP>80mmHg) increased significantly with FTI/E2 (p=0.0230), as did the likelihood of having metabolic syndrome (p=0.0007), or being overweight (p=0.0047). Associations were similar for the FTI/FEI models. The weakest associations were observed using measures of androgen excess without adjustment for SHBG.

Conclusions. This criterion validity study suggested that a link between androgen excess and cardiovascular risk is strongest when androgen excess is measured as FTI/E2. Further exploration of this link is needed.

[KG#289A]


Primary Question:

Summary of Findings: Background: The observed association between metabolic syndrome (MS) and coronary artery calcification (CAC) may be mediated through abnormalities that accompany core criteria including a prothrombotic state, proinflammatory state, and insulin resistance. The relative association of each of these factors with CAC was evaluated in a study of 559 perimenopausal women (mean age 50 years, 37% African-American).

Methods: We assessed CAC by electron beam computed tomography. MS core criteria included waist circumference, high density lipoprotein cholesterol, triglyceride, high blood pressure, and fasting glucose and the MS was defined by the presence of 3 of 5 of these core criteria. We measured the following additional markers: prothrombotic (tissue plasminogen activator[tPA], plasminogen activator inhibitor-1[PAI-1], factor VII[FVII]); proinflammatory (C-reactive protein[CRP], fibrinogen); and insulin resistance (homeostasis model assessment
Non-MS covariates included age, smoking, physical activity, education, race, and alcohol use. We used multivariable-adjusted logistic regression models to test the associations between MS components and CAC (presence or absence).

Results: CAC was present in 48% of the women. MS was present in 21% of women. MS was associated (logistic regression odds ratio (OR) and 95% confidence interval) with CAC (OR, 6.2 [3.4, 11.2]) after adjusting for non-MS risk factors. In a multivariable model incorporating MS, non-MS risk factors, prothrombotic markers, proinflammatory markers, and insulin resistance, the following were significantly related to CAC: MS (OR, 3.3 [1.6, 7.0]), alcohol use (OR, 0.57 [0.35, 0.93]), tPA (OR, 1.11 [1.02, 1.20]), FVII (OR, 1.01 [1.001, 1.016]), and CRP (OR, 1.12 [1.04, 1.21]).

Conclusions: In our cross-sectional study of middle-aged women, prothrombotic and proinflammatory markers were associated with CAC above and beyond the clinical definition of MS. These results are consistent with the hypothesis that distinct pathways related to the MS each contribute to the development of CAC.

Primary Question:
Summary of Findings:
Background: Metabolic syndrome (MS) core criteria and accompanying prothrombotic, proinflammatory, and insulin resistance components may each relate to the development of aortic calcification (AC). Data regarding the relations between MS components and AC are limited, particularly in middle-aged women.

Methods: We examined the cross-sectional relations of MS components with AC in a study of 557 middle-aged peri-menopausal women (mean age 50 years, 37% African-American). We assessed AC by electron beam computed tomography. MS was defined by presence of 3 of 5 core criteria including waist circumference, high density lipoprotein, triglyceride, high blood pressure, and fasting glucose. We measured the following additional markers: prothrombotic (tissue plasminogen activator, plasminogen activator inhibitor-1, factor VII); proinflammatory (C-reactive protein, fibrinogen); and insulin resistance (homeostasis model assessment index [HOMA]). Non-MS covariates included age, smoking, low density lipoprotein cholesterol (LDL-C), physical activity, education, race, and alcohol use. We used multivariable-adjusted logistic regression models to test the associations between MS components and AC (above or below median Agatston score =13).

Results: MS was present in 21% of women. MS was associated (logistic regression odds ratio (OR) and 95% confidence interval) with AC (OR, 7.2 [3.8, 13.8]) after adjusting for non-MS risk factors. Plasma fibrinogen was associated with AC (OR, 1.01 [1.002, 1.012]) after adjusting for MS and non-MS risk factors. HOMA was associated with AC (OR, 1.28 [1.01, 1.48]) after controlling for MS and non-MS risk factors. In a multivariable model incorporating MS, non-MS risk factors, prothrombotic markers, proinflammatory markers, and insulin resistance, the following were significantly related to AC: MS (OR, 4.6 [2.1, 10.3]), smoking (OR, 2.4 [1.2, 5.0]), LDL-C (OR, 1.01 [1.002, 1.018]), fibrinogen (OR, 1.01 [1.002, 1.012]), and HOMA (OR, 1.3 [1.06, 1.54]).

Conclusions: In our biracial sample of middle-aged women, clinically-defined MS, inflammation, and insulin resistance were each independently related to AC.

**Primary Question:**

**Summary of Findings:** Abstract: Hostility has been associated with increased risk of cardiovascular (CV) and all-cause mortality and incident coronary heart disease. Emerging evidence suggests hostility also may be related to subclinical CV disease. The majority of studies have been limited to Caucasian men; thus, less is known about the impact of hostility on CV risk or subclinical disease in women or minority populations. This study examined the association between low, moderate and high scores on a 13-item measure of cynical hostility and carotid atherosclerosis, assessed by B-mode ultrasonography, in a middle-aged sample of Caucasian and African-American women (N=553) from the Chicago and Pittsburgh sites of the Study of Women’s Health Across the Nation (SWAN). SWAN is an ongoing, multi-ethnic, multi-site, longitudinal study of the impact of the menopausal transition on CV risk and other health outcomes. With adjustment for age, study site, race, and education, high hostile women had higher levels of overall intimal-medial thickening (IMT) and maximal IMT compared to low hostile women (overall IMT means=0.693 and 0.671 mm, respectively, p=0.044; maximal IMT means=0.902 and 0.863 mm, respectively, p=0.014). Moderately hostile women did not differ from low hostile women. Further adjustment for body mass index and standard CV risk factors, as indexed by the Framingham Risk score, did little to diminish the observed associations. African-American women had significantly higher hostility scores and greater IMT than Caucasians but no race by hostility interactions were noted. Findings indicate that high levels of cynical hostility are related to greater subclinical atherosclerosis in women at mid-life.

Acknowledgments: Funded by the NIA (U01 AG012505, U01 AG012546) and NHLBI (R01 HL065581, R01 HL065591) and the NIH Office of Research on Women’s Health.


**Primary Question:**

**Summary of Findings:** Findings from animal models suggest that various forms of “stress” may be associated with the accumulation of adipose tissue over time; however few studies have prospectively examined these effects in humans. We examined the longitudinal association between negative life events assessed at baseline and weight gain over 4 years in a middle-aged sample of 2,017 African-American and Caucasian women from 4 sites of the Study of Women’s Health Across the Nation (SWAN). At baseline, negative life events were highest in African-American women (p<.0001), women with “some college” education (p=.008), and women who were obese (p=.002). Baseline weight was higher in women who were African-American (p<.0001) or reported their highest level of education as a HS degree or less (p<.0001). Negative life events were significantly associated with baseline weight (b=.34, p=.03) and increased weight gain over follow-up (b=.05, p=.003) after adjusting for age, education, parity, menopausal status, and chronic health conditions. Further
adjustments for behavioral risk factors (smoking, physical activity, total caloric intake, and percent fat intake), did not alter these associations. Although there were significant demographic differences in the occurrence of negative life events, the effects of life events on weight and weight gain did not differ by race, education, or baseline BMI category. Findings suggest that negative life events may be an important contributor to weight gain in middle-aged women, independent of their effects on behavioral risk factors such as smoking, diet and exercise. Reducing the emotional impact of life events and improving coping techniques may prevent the weight gain associated with mid-life aging.

Acknowledgements: SWAN is funded by the National Institutes on Aging and Nursing Research (U01 AG012495, U01 AG012505, U01 AG012531, U01 AG012546, U01 AG012553, U01 NR04061) and the NIH Office of Research on Women’s Health.


Primary Question:

Summary of Findings: There is substantial evidence for a role of depression in the pathogenesis of CHD and Type 2 diabetes, but little is known about potential pathways. Although central adiposity has been identified as a possible link between depression and disease, only one study has examined its relationship with depressive illness. Our objective was to examine the association between lifetime history of depression and central adiposity over time in a sample of middle-aged women. Participants consisted of 270 women (31% Black) from the Pittsburgh cohort of The Study of Women’s Health Across the Nation, a study of the menopausal transition. General linear modeling repeated measures ANOVAs, controlling for age and education, were used to evaluate the association between lifetime history of depression, measured at baseline by the SCID, and central adiposity measured by waist circumference (WC) across baseline and five annual visits. Results showed significant main effects of race F (1, 264) = 23.47, p < .001 and depression F (1, 264) = 9.37, p < .01 on WC across time, and a significant WC by race interaction F (1, 263) = 11.64, p < .01. Analyses stratified by race showed an effect of depression history in Blacks only F (1, 80) = 14.39, p < .001. Similarly, analyses of WC across follow-up visits only, controlling for baseline WC, showed a main effect of depression, F (1, 263) = 5.75, p < .05 and a trend for an effect in Blacks but not Whites. Results were independent of baseline BMI. Analyses also showed an association between depression history and BMI across time, but it was not independent of baseline WC. This study is the first to demonstrate that a lifetime history of depressive illness is associated with elevated central adiposity across time in middle-aged Black women. Black women may be vulnerable to the physiological sequelae of depression over time.

SWAN was funded by NIH NIA, NIMH, and NINR.

Primary Question:  
Summary of Findings:  
[WG#182A]


Primary Question:  
Summary of Findings:  
[WG#130A]


Primary Question:  
Summary of Findings:  
[WG#130B]


Primary Question:  
Summary of Findings:  
[WG#101A]


Primary Question:  
Summary of Findings:  
[WG#89]


Primary Question:  
Summary of Findings:  
[WG#85]


Primary Question:  
Summary of Findings:  
[WG#100]

Primary Question:
Summary of Findings:
[WG#68]


Primary Question:
Summary of Findings:
[WG#71]


Primary Question:
Summary of Findings:
[WG#94]


Primary Question:
Summary of Findings:
[WG#75C]


Primary Question:
Summary of Findings:
[WG#75B]


Primary Question:
Summary of Findings:
[WG#75A]


Primary Question:
Summary of Findings:

[WG#75E]


Primary Question:

Summary of Findings:

[WG#75]


Primary Question:

Summary of Findings:

[WG#75D]


Primary Question:

Summary of Findings:

[WG#93]


Primary Question:

Summary of Findings:

[WG#30B]


Primary Question:

Summary of Findings:

[WG#77B]


Primary Question:

Summary of Findings:

[WG#77A]

Primary Question:
Summary of Findings:

[WG#77D]


Primary Question:
Summary of Findings:
[WG#77C]


Primary Question:
Summary of Findings:
[WG#45]


Primary Question:
Summary of Findings:
[WG#23]


Primary Question:
Summary of Findings:
[WG#41]


Primary Question:
Summary of Findings:
[WG#38]


Primary Question:
Summary of Findings:
[WG#43]

84 Bradsher J for the SWAN Research Group. *Overview of the Study of Women's Health Across the Nation for the SWAN Research Group.* American Public Health Association


89  Janssen I, Derby CA, Dugan S, Kravitz H, Powell LH. IMPACT OF CARDIOVASCULAR HEALTH ON COGNITIVE AGING IN MIDLIFE: IS THERE A DIFFERENCE BY RACE? THE STUDY OF WOMEN'S HEALTH ACROSS THE NATION (SWAN)

90  Powell, LH, Dugan, SA, Derby, CA, Kravitz, HM, Janssen I. Does the impact of cardiovascular health on cognitive aging in midlife differ by race? The Study of
Women's Health Across the Nation (SWAN)

Primary Question:
Summary of Findings:

[WG#1123B]

PAPER PROPOSAL (PUBLIC USE DATA ONLY)

1

Leis AM, Jackson EA, Barlinas-Mitchell E, El Khoudary SR, Karvonen-Gutierrez CA

Carotid Intima Media Thickness and Comorbid Cardiometabolic Dysfunction in Women: The SWAN Study
Menopause

Primary Question: Do obesity and metabolic syndrome have unique effects on cardiovascular risk?

Summary of Findings: There are a significant proportion of metabolically healthy obese individuals within SWAN. The findings from this study suggest that there is only a minimal impact of obesity on carotid artery thickness over the effect of metabolic syndrome alone.

[WG#1034]

2


Low-density lipoprotein subclasses over the menopause transition and risk of coronary calcification and carotid atherosclerosis: The SWAN Heart & HDL Ancillary studies
Menopause

Primary Question: 1) Are LDL subclasses change over the menopause transition independent of aging?
2) Are LDL subclasses during midlife associated with the presence of coronary artery calcification and carotid intima-media thickness?
3) Will these associations vary by the timing of these measures as related to the final menstrual period (FMP)?

Summary of Findings: Women experience significant atherosclerotic increases in LDL subclasses that increases their risk of having greater cIMT levels and higher CAC prevalence. The reported associations were more profound during perimenopause stage.

[WG#1081]

3

Schiff MD, Mair CF, Barinas-Mitchell E, Brooks MM, Mendez DD, Naimi AI, Reeves A, Hederson M, Janssen I, Fabio A

Longitudinal Profiles of Neighborhood Socioeconomic Vulnerability Influence Blood Pressure Changes Across the Female Midlife Period

Primary Question: Does longitudinal exposure to neighborhood socioeconomic vulnerability throughout midlife impact blood pressure levels and their annual progression over time?

Summary of Findings: We used data from the Study of Women’s Health Across the Nation to characterize longitudinal patterns of neighborhood socioeconomic vulnerability and sociodemographic change over time, and to determine their influence on blood pressure levels and their annual progression among women across ten-year follow-up. We identified four unique profiles of neighborhood socioeconomic vulnerability, and found that women living in socioeconomically vulnerable neighborhoods throughout midlife – characterized by lower
SES, greater vacant housing, higher population density, and more non-Hispanic Black and Hispanic residents – had significantly higher SBP levels at study start, and experienced the fastest rate of annual SBP growth (at 0.93 mmHg/year) across ten-year follow-up. In our racially, ethnically, and geographically-diverse cohort of 2,738 women transitioning through menopause, neighborhood socioeconomic vulnerability was significantly associated with accelerated increases in systolic blood pressure throughout midlife. [WG#1023]


Primary Question: Do women with lower physical function during pre- or perimenopause have higher risk for a cardiovascular event compared to women with better physical function?

Summary of Findings: Women with lower physical function during pre- or perimenopause have higher risk of a cardiovascular event as they age. This association appears to be due to higher cardiovascular risk factors among women with lower physical function. [WG#1019]


Primary Question: Are sleep timing and regularity of sleep timing associated with psychological health?

Summary of Findings: Unhealthy sleep timing was associated with depressive symptoms. Irregular sleep was associated with depressive symptoms, anxiety symptoms, and worse psychological well-being. [WG#1063]


Primary Question: Are cardio-metabolic and inflammatory variables at baseline predictive
of neuropathy in SWAN women at visit 15?

**Summary of Findings:** We found that baseline metabolic syndrome is a significant predictor of neuropathy even after control for obesity and diabetes. Longitudinal CRP was also strongly predictive even after control for all three metabolic conditions, and mediated the relationship between both obesity and metabolic syndrome with peripheral neuropathy [WG#1055]


**Primary Question:** Are exposures to phthalates associated with hormones including estradiol, testosterone, FSH, SHBG, and AMH, and timing of natural menopause in midlife women?

**Summary of Findings:** We found that phthalates may affect circulating levels of testosterone in midlife women, especially in postmenopausal women, supporting antiandrogenic properties of phthalates.

[WG#878MS2]


**Primary Question:** The current study investigated whether pre-pandemic histories of childhood abuse or intimate partner violence (reported roughly 4-12 years prior to the COVID-19 pandemic) were prospectively related to elevated depression, anxiety, interpersonal conflict, and sleep problems during the pandemic among older women.

**Summary of Findings:**

[WG#1035]


**Primary Question:** We explored trajectories of palpitations over time, their risk factors, and their associations with subclinical cardiovascular disease.
Summary of Findings: We identified three distinct trajectories of palpitations: high probability of palpitations in the peri- to early postmenopause diminishing in the late postmenopause (15.9% of women), moderate probability of palpitations in the peri- to early postmenopause diminishing in the late postmenopause (34.3%), and sustained low probability of palpitations (49.8%). The high probability group had more financial strain, and a more adverse reproductive and health-related profile at baseline. Palpitations trajectories were not related to atherosclerosis or arterial stiffness.


Primary Question: Air pollution has been suggested to be associated with obesity; however, epidemiologic evidence is limited and has largely focused on body mass index (BMI). We examined longitudinal associations of air pollution exposure, including fine particulate matters (PM2.5), nitrogen dioxide (NO2), and ozone (O3) with weight, BMI, waist circumference, fat mass, lean mass, and proportion fat mass in midlife women.

Summary of Findings: In this prospective cohort study of 1,654 midlife women representing diverse racial/ethnic groups, exposure to air pollution was associated with adverse changes in body composition measures. In particular, PM2.5 and NO2 were positively associated with fat mass and proportion fat mass, and inversely associated with lean mass. In addition, O3 was positively associated with proportion fat mass and inversely associated with lean mass. Associations of PM2.5 and NO2 with body size and composition were modified by physical activity; associations were attenuated among participants with higher physical activity levels.


Primary Question: Is employment status a risk factor for poor physical function in midlife women?

Summary of Findings: Women with lower levels of employment from mid-life to older adulthood were more likely to experience severe impairment in physical function. These associations are not driven by adiposity, physical activity, or health-related variables.


Primary Question: Is menopause status a risk factor for lipoprotein subfractions and subclinical vascular health in middle aged women?

**Primary Question:**
Is there clear relationship between specific group of lipoproteins and subclinical atherosclerosis among perimenopausal women, after taking remaining lipoproteins into consideration? Does this relationship change by women’s menopausal status?

**Summary of Findings:** Carotid intimal medial thickening is positively associated with a cluster of small IDL particles in midlife women, and with a cluster of small and medium LDL particles after menopause.


**Primary Question:** Per- and polyfluoroalkyl substances (PFAS) can trigger a combination of pathophysiological responses that may lead to hypertension. However, human evidence to support this hypothesis is scant. We examined the association between PFAS and risks of developing hypertension.

**Summary of Findings:** We found that women with higher serum concentrations of perfluorooctane sulfonate (PFOS), perfluorooctanoate (PFOA), and 2-(N-ethyl-perfluorooctane sulfonamido) acetate (EtFOSAA) had a higher risk of developing hypertension. No significant associations were observed for perfluorononanoate (PFNA) and perfluorohexane sulfonate (PFHxS).


**Primary Question:** Changes in heart rate and breathing during physical activity can influence perceptions of exertion. This study compared estimates of physical activity with and without adjustments for perceived exertion.

**Summary of Findings:** Approximately three-fourths of participants reported any planned exercise activities or sports during the previous year. The most common planned exercise activity for all participants was walking and the most common perceived exertion level was a “moderate” increase in heart rate and breathing during physical activity. For most women, adjusting for perceived exertion did not substantially change estimates of physical activity.

**Primary Question:**

**Summary of Findings:**


**Primary Question:** Are higher volumes of abdominal visceral and cardiovascular (epicardial, paracardial and perivascular aortic) adipose tissue depots at midlife associated with a worse high-density lipoprotein (HDL) metric profile [lower HDL cholesterol efflux capacity (HDL-CEC), lower concentrations of HDL phospholipids (HDL-PL) and large HDL particles (HDL-P), smaller overall HDL size, and increases in levels of HDL triglycerides (HDL-Tg) and small HDL-P]?

Does insulin resistance mediate the observed associations between different adipose tissue depots and HDL metrics?

**Summary of Findings:** After adjusting for potential confounders, higher abdominal visceral adipose tissue volume was associated with lower concentrations of HDL-PL contents, HDL-cholesterol (HDL-C) and large HDL-P subclasses, and smaller overall HDL size. Higher paracardial fat (PAT) volume was associated with lower concentrations of HDL-C and large HDL-P, and smaller overall HDL size. Higher epicardial fat (EAT) volume was associated with more small HDL-P concentrations. Higher perivascular aortic adipose tissue (PVAT) was associated with lower HDL-CEC.

Insulin resistance (IR) partially mediated the associations between adipose tissue depots and HDL metrics as following:

IR mediated the associations between HDL-CEC, HDL-C, large HDL-P, and HDL size. IR also mediated the associations between PAT and HDL-C, large HDL-P and HDL size, and the associations between PVAT and HDL-CEC.

Napoleone JM, Boudreau RM, Lange-Maia BS, El Khoudary SR, Ylitalo KR, Kriska AM,
Primary Question: Do patterns of metabolic syndrome during midlife impact physical performance in early old age?

Summary of Findings: SWAN women with ≥3 metabolic syndrome (MetS; high-MetS) components compared to those with no MetS components had higher body mass index, pain, financial strain, and lower physical activity and self-reported health at visit 15 (p<0.0001). Compared to Caucasian women, African American and Hispanic women were more likely to be in the high-MetS group and had worse physical functioning along with Chinese women (SPPB, chair stand, stair climb, and gait speed but Hispanic women did not have worse gait speed). After adjustments, high-MetS compared to no MetS demonstrated significantly worse 40-ft walk (β: -0.08; 95% CI: -0.13, -0.03), 4-m gait speed (β: -0.09; 95% CI: -0.15, -0.02), SPPB (β: -0.79; 95% CI: -1.15, -0.44), and chair stands (β:0.69; 95% CI: 0.09, 1.28), though worse stair climb was not significant after adjustments. Excluding women with previous moderate or severe perceived physical function limitations did not change final models.

Primary Question: How do SWAN findings help us understanding racial/ethnic health disparities in women's midlife health?

Summary of Findings: This SWAN story documents the presence, magnitude, and longitudinal patterns of racial disparities in selected areas of women's midlife health (menopause symptoms, sleep, mental health, health-related quality of life, cardio-metabolic health, and physical function) and considers the contextual factors that are likely influencing these disparities.

Primary Question: Are levels of estradiol (E2) and/or follicle-stimulating hormones (FSH) over the menopause transition associated with an adverse HDL metric profile [lower HDL cholesterol efflux capacity (HDL-CEC), lower concentrations of HDL phospholipids (HDL-PL) and large HDL particles (HDL-P), smaller overall HDL size, and increases in levels of HDL...
triglycerides (HDL-Tg) and small HDL-P? Do these associations vary by time since menopause?

**Summary of Findings:**
Higher levels of estradiol are associated with larger HDL particle size, higher levels of large HDL-P, HDL-CEC and HDL-Tg, but with lower levels of medium HDL-P. The positive association between E2 and HDL-Tg was stronger 2 years after the final menstrual period (FMP) than before. FSH was related to higher total and medium HDL-P, but with smaller HDL particle size, and lower concentrations of large HDL-P, and HDL-CEC per particle. The associations of higher FSH with greater total HDL-P and smaller HDL size were only evident at or after menopause.


**Primary Question:**
**Summary of Findings:**


**Primary Question:** Prior studies have suggested that poor vision in later life is associated with worse cognitive function. We aim to assess whether there is a similar relationship between vision in mid-life and future cognitive function.

**Summary of Findings:** Moderate or worse vision impairment, assessed during mid-life, was associated with lower scores on measures of cognitive function over a 13 year period during which women transitioned from mid-life to later adulthood. Prior studies have suggested a relationship between vision and cognition in older age; this study supports an analogous relationship in mid-life.

Primary Question: Are different metrics of HDL associated with CAC presence or CAC density, and does menopausal stage modify the association of HDL metrics with CAC presence and CAC density?

Summary of Findings: Only medium HDL-particle (HDL-P) concentrations was independently associated with higher odds of CAC presence; none of the HDL metrics were associated with CAC density. However, menopause status modified the associations between HDL metrics and measures of CAC, where higher small HDL-P and smaller overall HDL size were associated with higher odds of CAC presence in the late perimenopausal stage compared to the pre/early perimenopause stage. Lower large HDL-P and smaller overall HDL size were associated with lower CAC density in the late perimenopausal stage.

[WG#1000]


Primary Question: Does the menopause transition (MT) influence regional fat distribution and waist and hip circumferences?

Summary of Findings: The transition from pre- to postmenopause is accompanied by an increase in central fat stores and a decrease in peripheral fat stores. Accelerated gains in visceral, android and gynoid fat mass are associated with the onset of the MT. There are no similar changes in the rates of waist or hip circumference during the MT.

[WG#1017]


Primary Question: Environmental exposure to heavy metals may contribute to increased blood pressure, however, evidence from midlife women who are at greater risk of cardio-metabolic disease, is limited. We evaluated the associations of urinary concentrations of arsenic, cadmium, mercury, and lead with longitudinal changes in blood pressure in the Study of Women's Health Across the Nation Multi-Pollutant Study.

Summary of Findings: After multivariable adjustment, estimated annualized increases (95%CI) in SBP in the highest and lowest tertiles were 0.93 (0.85, 1.01) mmHg and 0.74 (0.66, 0.82) mmHg for arsenic, 0.82 (0.75, 0.90) mmHg and 0.72 (0.65, 0.80) mmHg for mercury, and 0.86 (0.78, 0.93) mmHg and 0.72 (0.64, 0.79) mmHg for lead, respectively. Similar results were observed for associations of arsenic, mercury, lead with DBP. Urinary cadmium was associated with a greater rate of increase in SBP only among never smokers.

**Primary Question:** Perfluoroalkyl and polyfluoroalkyl substances (PFAS) exposure have been associated with obesity and related comorbidities. However, underlying mechanisms are not well understood. Therefore, we determined if serum PFAS concentrations were associated with adipokine profiles in midlife women.

**Summary of Findings:** We found that leptin concentrations and free leptin index (the ratio of leptin to soluble leptin receptor) at a 3-year follow-up were significantly higher in women with higher baseline concentrations of various PFAS compounds. In contrast, PFAS concentrations were not associated with soluble leptin receptor, total adiponectin, or high molecular weight adiponectin.


**Primary Question:** Do physical activity behavior and physical functioning influence fall risk among older adult women?

**Summary of Findings:** Women with low physical activity and poor physical functioning are more likely to fall compared to women with high physical activity and good physical functioning. Women who experience declining physical functioning over time are more likely to fall, but women who increase physical activity over time are not more likely to fall. Women can be physically active to the extend they are able without increasing fall risk, even among those with physical functioning limitations.


**Primary Question:** We aimed to examine associations of serum PFAS concentrations with longitudinal changes in weight, waist circumference (WC), fat mass, and proportion fat in midlife women.

**Summary of Findings:** PFOS, PFOA, EtFOSAA and MeFOSAA serum concentrations during midlife were positively associated with large body size and body fat in midlife women. Higher PFOS, PFHxS, EtFOSAA and MeFOSAA at baseline were also associated with accelerated increases in measures of adiposity over time. PFAS may be an underappreciated
contributing factor to women’s obesity risk.

[ WG#877MS7 ]


Primary Question: Epidemiologic studies on associations between metals and adipokines have been limited and results are mixed. We examined the associations of 15 urinary metal concentrations with prospectively-assessed serum levels of adipokines including HMW adiponectin, leptin, and soluble leptin receptor (sOB-R).

Summary of Findings: In multivariable adjusted adaptive elastic-net models, urinary molybdenum was associated with a 5.54% higher level (95% CI: 1.36%, 9.90%), whereas cadmium was associated with a 4.53% lower level (95% CI: -8.17%, -0.76%) of HMW-adiponectin. Urinary molybdenum was also associated with a 5.95% lower level (95% CI: -10.15%, -1.56%) and a 2.98% (95% CI: 0.69%, 5.32%) higher sOB-R level. Urinary cesium and lead were associated with a 3.58% (95% CI: -6.06%, -1.03%) and a 2.53% (95% CI: -4.80%, -0.21%) lower level of sOB-R, respectively.

[ WG#877MS8 ]

29 Yi Y, El Khoudary SR, Buchanich JM, Miller RG, Rubinstein D, Matthews K, Orchard TJ, Costacou T Women with Type 1 diabetes (T1D) experience a shorter reproductive period compared with nondiabetic women: the Pittsburgh Epidemiology of Diabetes Complications (EDC) study and the Study of Women’s Health Across the Nation (SWAN). Menopause 2021 Mar;28(6):634-641. doi: 10.1097/GME.0000000000001758. PMID: 33651743

Primary Question: Whether the length of reproductive period, age at menarche, and age at natural menopause differ in women with type 1 diabetes, compared to women without diabetes.

Summary of Findings: Women with type 1 diabetes onset before menarche have a shorter reproductive period compared with non-diabetic women, exhibiting delayed menarche and earlier natural menopause.

[ WG#1015 ]


Primary Question: Do higher amounts of physical activity during middle age slow cognitive aging?

Summary of Findings: We did not find evidence that greater physical activity was related to either better cognitive scores at the beginning of the study, when women were in their 50’s, or less cognitive decline during up to 13 years of follow up.

[ WG#951MS ]

Primary Question: Summary of Findings:

[WG#1007PUD]


Primary Question: Summary of Findings:

[WG#1041MS]

Wang X, Ding N, Harlow SD, Randolph JF Jr, Mukherjee B, Gold EB, Park SK. Urinary metals and metal mixtures and timing of natural menopause in midlife women: The Study of Women’s Health Across the Nation.

Primary Question: Limited data have reported the possible effects of various metals on the timing of natural menopause. In this study, we examined if women with higher urinary concentrations of metals and metal mixtures experienced natural menopause earlier using data from a prospective cohort of midlife women, the Study of Women’s Health Across the Nation, from 1999 to 2018.

Summary of Findings: We found that women with higher urinary concentrations of arsenic, mercury, and lead reached natural menopause earlier. Women whose combined exposure to metals above the top 25 percentile had a 69% higher risk of reaching natural menopause than women in the bottom 25 percentile, which is equivalent to a 1 year earlier median time to natural menopause.

[WG#877MS12]

Lee S, Karvonen-Gutierrez C, Mukherjee B, Herman WH, Harlow SD, Park SK. Urinary concentrations of phenols and parabens and incident diabetes in midlife women: The Study of Women’s Health Across the Nation

Primary Question: Although environmental exposure to personal care and product chemicals may play a role in the pathogenesis of diabetes, only a few phenols, most notably bisphenol A, have been studied with limited data. We examined associations between personal care and consumer product chemicals, assessed in urine at two time-points, and incident diabetes in the Study of Women’s Health Across the Nation (SWAN), a multi-ethnic prospective cohort of midlife women.

Summary of Findings: We observed consistent inverse associations between parabens and incident diabetes at the Multi-pollutant study (MPS) baseline (1999-2000) and three-year later (2002-2003). Triclocarban with the 3-year exposure later baseline, dichotomized (yes/no) due to low detection rates (<15%), was positively associated with incident diabetes. Positive associations were found for 2,4-dichlorophenol only with the MPS baseline and for bisphenol-A only with the 3-year exposure later baseline. No significant associations were observed for the overall joint effect of phenol and paraben mixture at either time-points.

[WG#877MS9]


Primary Question:

Summary of Findings:


Primary Question:

Summary of Findings:


Primary Question: Epidemiologic studies on associations between metals and insulin resistance and β-cell dysfunction have been cross-sectional and focused on individual metals. We assessed the association between exposure to metal mixtures, based on assessment of 15 urinary metals, and longitudinal changes in homeostatic model assessments for insulin resistance (HOMA-IR) and β-cell function (HOMA-β).

Summary of Findings: In multivariable adjusted adaptive elastic-net models, urinary copper, lead, and zinc were associated with higher HOMA-IR at baseline, whereas molybdenum was associated with lower HOMA-IR at baseline. The estimated changes in baseline HOMA-IR for one standard deviation increase in log-transformed urinary metal concentrations were 1.57% (-1.09%, 4.29%) for copper, 0.70% (-1.59%, 3.05%) for lead, 5.76% (3.05%, 8.55%) for zinc, and -3.25% (-5.45%, -1.00%) for molybdenum, respectively. Urinary zinc was also positively associated with a faster rate of increase in HOMA-IR. Urinary arsenic and zinc were associated with lower baseline HOMA-β, whereas cobalt was associated with higher baseline HOMA-β. Arsenic was also associated with a faster rate of decline in HOMA-β.


Primary Question: Can VALENCIA (VAginaL community state typE Nearest Centroid clAssifier), a tool developed to classify vaginal samples into community state types (CSTs) developed from over 13,000 reference vaginal samples from mostly reproductive age women.
in the U.S. be used for assignment of samples to CSTs from other data sets, including postmenopausal women and women from other regions of the world?

**Summary of Findings:** VALENCIA provides a much-needed solution for the robust and reproducible assignment of vaginal CSTs, including for postmenopausal women. This will allow unbiased analysis of both small and large vaginal microbiota datasets, comparisons between datasets and meta-analyses that combine multiple datasets.

[WG#977MS2]


**Primary Question:** We examined the associations between PFAS exposures and incidence of natural menopause in the multi-racial/ethnic sample of women who were premenopausal at baseline from a prospective cohort, i.e., the Study of Women's Health Across the Nation (SWAN), with standard approximately annual clinic visits from 1999-2017, and assessed whether the relationship differed by racial/ethnic groups. We next identified subgroups exposed to different patterns of PFAS using the k-means clustering method and evaluated the combined effects of PFAS mixtures on natural menopause.

**Summary of Findings:**

[WG#877MS5]


**Primary Question:** Is melatonin, a hormone that controls sleep-wake cycles in humans, also involved in the control of the menstrual cycle?

Do melatonin levels go down when women become postmenopausal?

**Summary of Findings:** We found a rise in aMT6s, a melatonin metabolite that appears in the urine, at the end of the menstrual cycle (just before menses occurs). We believe that melatonin helps to regulate the menstrual cycle. After menopause, the amount of melatonin in the urine declines, suggesting that a drop in melatonin may be partly responsible for some of the symptoms of menopause.

[WG#1026]


**Primary Question:**

**Summary of Findings:**

[WG#1003PUD]

Primary Question:  1) Is child maltreatment associated with lower health-related quality of life (HRQoL) and quality-adjusted life years (QALY) and the rate of change in these measures over a 9-year follow-up?  2) Are these associations explained by adulthood psychosocial mediators over time?

Summary of Findings:  Any CM was associated with both reduced midlife mental and physical HRQoL over 9 years. Compared to women without CM, women who experienced multiple CM types reported 5 and 4 points lower in MCS and PCS, respectively, and 28 fewer healthy days per year for QALY. But the rate of change over time in these measures was similar between women with and without CM. In longitudinal mediation analyses, low levels of optimism, sleep problems, and low social support each explained >10% of the relationship between multiple CM types and HRQoL and QALY.


Primary Question:  This study examined temporal variations in serum concentrations of per- and polyfluoroalkyl substances (PFAS), a family of synthetic compounds widely used in a variety of industrial applications and consumer products, such as non-stick cookware, carpeting, apparels, food packaging, and firefighting forms, in midlife women. Specifically, we explored how patterns of exposure differ by race/ethnicity and reproductive characteristics.

Summary of Findings:  Serum concentrations of legacy compounds (e.g. perfluorooctanoic acid, PFOA, and perfluorooctane sulfonic acid, PFOS) decreased significantly; whereas their replacements (e.g. perfluorononanoic acid, PFNA) increased from 1999-2011. Temporal variations varied significantly by race/ethnicity. For example, Chinese women tended to have consistently higher PFNA concentrations at each follow-up visit, compared to white and black women. Menstruating women also had lower concentrations over time. Parity was associated with lower concentrations at baseline but the differences between nulliparous and parous women narrowed during the follow-up visits.


Primary Question:  Summary of Findings:  [WG#877_MS2]

Primary Question:
Summary of Findings: In this pooled study that included 21,312 midlife women from eight observational studies, we observed a prospective bi-directional relationship between VMS and depressed mood. Baseline sleep difficulties largely affected the relationship between VMS and subsequent depressed mood over three years, but it had little impact on the relationship between depressed mood and subsequent VMS.


Primary Question:
Summary of Findings: Current evidence on the association between body mass index (BMI) and age at menopause remains unclear. We investigated the relationship between BMI and age at menopause using data from 11 prospective studies. A total of 24,196 women who experienced menopause after recruitment was included. Baseline BMI was categorised according to the WHO criteria. Age at menopause, confirmed by natural cessation of menses for ≥ 12 months, was categorised as: 45 years (early menopause), 45–49, 50–51 (reference category), 52–53, 54–55, and ≥ 56 years (late age at menopause). We used multinomial logistic regression models to estimate multivariable relative risk ratios (RRRs) and 95% confidence intervals (CI) for the associations between BMI and age at menopause. The mean (standard deviation) age at menopause was 51.4 (3.3) years, with 2.5% of the women having early and 8.1% late menopause. Compared with those with normal BMI (18.5–24.9 kg/m2), underweight women were at a higher risk of early menopause (RRR 2.15, 95% CI 1.50–3.06), while overweight (1.52, 1.31–1.77) and obese women (1.54, 1.18–2.01) were at increased risk of late menopause. Overweight and obesity were also significantly associated with around 20% increased risk of menopause at ages 52–53 and 54–55 years. We observed no association between underweight and late menopause. The risk of early menopause was higher among obese women albeit not significant (1.23, 0.89–1.71). Underweight women had over twice the risk of experiencing early menopause, while overweight and obese women had over 50% higher risk of experiencing late menopause.

Primary Question:

Summary of Findings: Overall, 76% of the women were Caucasian, 22% Japanese, and other ethnicity (of 300 or more participants) included Hispanic/Latin American (0.2%), Chinese (0.2%), Middle Eastern (0.3%), African/black (0.5%), and Other (1.0%). The median age at baseline was 47 years (Inter-quartile range (IQR): 41-53), and that at the last follow-up was 56 years (IQR: 48-64). Regarding reproductive characteristics, half of the women (49.8%) had their first menstruation (menarche) at 12-13 years of age. The distribution of menopausal status and the prevalence of chronic disease varied considerably among studies. At baseline, most women (57%) were pre- or peri-menopausal, 20% reported a natural menopause (range 0.8-55.6%), and remaining had surgery or were taking hormones. By the end of follow-up, the prevalence of CVD and diabetes were 7.2% (range 0.9-24.6%) and 4.7% (range 1.3-13.2%), respectively.