ORAL ABSTRACT PRESENTATIONS

S-1.

Evaluation of a Discussion Guide to Promote Understanding of Menopause and Informed Decision Making

Emma Andrews[2], Stacy C. Bailey[1], Candida Halton[3,4], Michael Wolf[1]. [1]Northwestern University, Chicago, IL; [2]Pfizer, New York City, NY; [3]Psychology, University of Westminster, London, United Kingdom; [4]Studio Health Ltd., London, United Kingdom

Objective: Patient-provider communication surrounding menopause is often limited. We developed and evaluated a low-literacy Discussion Guide to educate patients about menopause symptoms and symptom management. **Design:** A two-arm, cross-sectional randomized trial was conducted among 100 English-speaking women, aged 45-60, who had experienced symptoms of perimenopause. Participants were randomly assigned to review either the Discussion Guide or a standard material (n=50 per arm) and to complete a 13-item 'open book' knowledge questionnaire. Participants also completed a health literacy assessment and rated the appearance, quality, and content of both the Discussion Guide and the standard material. Bivariate analyses were conducted to examine women's menopause knowledge and satisfaction by study arm, and then across sociodemographic characteristics. Multivariable linear and logistic regression models were performed to test the effectiveness of the Discussion Guide to improve knowledge scores, and achieve 85% comprehension, compared to the standard. **Results:** Women receiving the Discussion Guide demonstrated significantly higher knowledge scores compared to those who reviewed the standard (Mean (M)=20.0, Standard Deviation (SD)=2.7) vs. M=18.1, SD=2.6; p<0.001); 82.0% of those exposed to the Discussion Guide correctly answered ≥85% of knowledge items compared to 48.0% of those reviewing the standard material (p<0.001). In multivariable analyses, participants who received the Discussion Guide displayed significantly greater knowledge in comparison to those receiving the standard material, regardless of whether knowledge was a score (B=1.9, 95% CI: 0.9-2.9, p<0.001) or a threshold (Odds Ratio: 5.7, 95% CI: 2.0-16.2, p<0.001). Limited health literacy was not independently associated with knowledge. More than two-thirds of women (68%) preferred the Discussion Guide; it was rated highly in terms of content, appearance, and ease-of-use. **Conclusion:** The Discussion Guide improved understanding of menopause symptoms and treatment options in comparison to a current standard and was well-received by a diverse audience. Additional research is needed to evaluate it in actual use.

Sources of Funding: Pfizer, Inc

S-2.

Reproductive period duration and cognitive function in postmenopausal Hispanic/Latina women in the HCHS/SOL

Yamnia I. Cortes, PhD, MPH, FNP-BC[1], Jianwen Cai, PhD[2], Carmen R. Isasi[6], Melissa Lamar, PhD[3], Linda C. Gallo[4], Martha Daviglus, MD, PhD[5], Krista Perreira, PhD[7]. [1]School of Nursing, Univeristy of North Carolina, Chapel Hill, NC; [2]Gillings School of Global Public Health, University of North Carolina, Chapel Hill, NC; [3]Institute for Minority Health Research, College of Medicine, Chicago, IL; [4]Department of Psychiatry and Behavioral Sciences, Rush University Medical Center, Chicago, IL; [5]Department of Psychology, San Diego State University, San Diego, CA; [6]Department of Epidemiology & Population Health, Albert Einstein College of Medicine, Bronx, NY; [7]Department of Social Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC

Objective: Hispanic women (Latinas) have a greater risk of cognitive impairment and dementia than non-Hispanic White women. It is postulated that decreasing levels of estradiol during the menopause transition may be associated with cognitive decline in midlife women. A shorter reproductive period duration (RPD, time from menarche to menopause), a marker of estrogen exposure, has been related to cardiovascular disease and cognitive impairment in women. Yet, these studies focused on older (>65 years) non-Hispanic White women. The primary aim of this analysis is to investigate whether age at menarche, age at menopause, and RPD are related to cognitive function among postmenopausal Latinas. Additionally, we assessed whether associations vary by type of menopause (natural versus surgical) and hormone therapy use. **Design:** A cross-sectional analysis was conducted with 3630 postmenopausal women ages 45-74 years from the Hispanic Community Health Study/Study of Latinos (HCHS/SOL), a multi-center epidemiologic study of the health of Hispanics/Latinos in the United States. Participants completed a reproductive history questionnaire and interviewer administered cognitive tests during the baseline HCHS/SOL examination (2008-2011). For this analysis, we excluded women with neurocognitive disorders or cardiovascular disease (e.g., dementia, Alzheimer's, stroke, myocardial infarction). Independent variables included self-reported age at menarche, age at menopause, and RPD. Cognitive function variables included global cognition, verbal learning, memory, verbal fluency, and processing speed. Associations between each reproductive event and cognitive function were examined using multivariable linear and logistic regression analyses. Models adjusted for HCHS/SOL survey weights and design, socio-demographics (age, Hispanic/Latino background, site, education, income, employment, health insurance), parity, and cardiovascular risk factors (smoking, physical activity, alcohol, overweight/obesity, diabetes, hypertension, dyslipidemia). We additionally assessed whether associations differed by type of menopause and hormone therapy use. **Results:** The study population was on average 59 years old, predominantly Mexican (30%) and Cuban (29%), with a mean RPD of 35 years, 25% reported menopause at age <45 years, and 26% reported a hysterectomy and/or oophorectomy. In fully-adjusted models, older age at menopause and longer RPD were positively related to verbal learning (ß=0.04, SE=0.02; p<0.05) and processing speed (ß=0.16, SE=0.04;p<0.001); associations were more pronounced for women with natural menopause, but not hormone therapy use. Older age at menarche was associated with lower processing speed (ß=-0.62, SE=0.15;p<0.0001). RPD was not related to global cognition. **Conclusion:** Among postmenopausal Latinas, longer RPD was related to more favorable cognitive measures of verbal learning and processing speed. Our findings support the hypothesis that greater lifetime exposure to estrogens may be associated with better cognitive performance. Further understanding of the role of female sex hormones and reproductive events on cognitive function among Latinas could provide an opportunity for earlier risk assessment in this high-risk population.

Sources of Funding: The HCHS/SOL was carried out as a collaborative study supported by contracts from the National Heart, Lung, and Blood Institute (NHLBI, N01-HC65233; N01-HC65235; N01-HC65236; N01-HC65237). The following Institutes/Centers/Offices contribute to the HCHS/SOL through a transfer of funds to the NHLBI: NIMHD, NIDCD, NIDCR, the NIDDK, the NINDS, and the Office of Dietary Supplements.

S-3.

HDL composition and function in relation with calcium density of coronary artery plaque among women transitioning through menopause. The SWAN HDL ancillary study

Samar R. El Khoudary, PhD[1], Alexis Nasr[1], Karen Matthews[1], Jeff Billheimer[2], Dan McConnell[3], Maria Brooks[1], Imke Janssen[4], Trevor Orchard[1], Sybil Crawford[5], Susan Everson-Rose[6], Deb Martin[1], Dan Rader[2]. [1]University of Pittsburgh, Pittsburgh, PA; [2]University of Pennsylvania, Philadelphia, PA; [3]University of Michiga, Ann Arbor, MI; [4]Rush University Medical Center, Chicago, IL; [5]University of Massachusetts, Worcester, MA; [6]University of Minnesota, Minneapolis, MN

Objective: The cardio-protective association of high-density lipoproteins cholesterol (HDL-C) has been questioned in midlife women supporting the need to identify novel metrics of HDL composition and function that better reflect its clinical utility. Greater calcium density in plaques has been associated with lower cardiovascular risk independent of calcium volume score. Associations of novel metrics of HDL with coronary artery calcium (CAC) density in midlife women are unclear and may be modified by menopausal stage. Our objectives were to test associations of HDL particles (HDL-P) and HDL size as measured by nuclear magnetic resonance spectroscopy (NMR), and HDL phospholipids (HDL-PL), HDL triglycerides (HDL-Tg) and cholesterol efflux capacity (CEC) with calcium density and whether these associations vary by menopausal stage. **Design:** We assessed 165 women from the Study of Women's Health Across the Nation (SWAN) HDL ancillary study (at baseline: age 51.9 ± 2.8 years; 45.2% Pre-/Early peri-, 10.8% late peri-, 44.0% post-menopausal) who had NMR HDL subclasses, HDL-PL, HDL-Tg, CEC and CAC density score measured once (N=89 [54%]) or twice (N=76 [46%]) around menopause. Effect modification of menopausal stage on associations of HDL composition and function measures with CAC density over time were tested using linear mixed effect models. Final models were adjusted for study clinical site, race, log-transformed CAC volume score, time varying age, body mass index, physical activity, alcohol use, log-triglycerides, LDL-C, and complement protein C3. **Results:** Although none of the HDL metrics were associated with CAC density in final models, menopausal stage significantly modified the associations of large HDL-P (p=.03) and overall HDL size (p=.02) with CAC density. Consistent suggestions of menopause effect modification on associations of HDL-PL and CEC with CAC density were observed (p=.07, 0.08, respectively) (Table). The estimated associations between concentrations of large HDL-P, and HDL-PL, and overall HDL size, and CEC with CAC density were positive during the late-peri stage and negative during the postmenopausal stage (Table). **Conclusion:** Changes in HDL composition and function during the menopause transition may impact the stability of coronary artery plaque in women, particularly during the late perimenopausal stage. Characterizing associations of HDL composition and function metrics with cardiovascular risk over the menopause transition is critical to better understand the relationship of HDL to coronary disease in midlife women.

Sources of Funding: SWAN HDL ancillary study has grant support from NIA: AG058690. SWAN Heart was supported by NHLBI: HL065581, HL065591. The SWAN has grant support from NIH, DHHS, through NIA, NINR and ORWH: NR004061; AG012505, AG012535, AG012531, AG012539, AG012546, AG012553, AG012554, AG012495. The SWAN Repository: U01AG017719.

Effect modification of menopausal stage on longitudinal associations of HDL metrics with CAC density score

HDL metrics	CAC density score (LOG)			P value for effect modification^
	Menopause Stage			
	Pre/early peri	Late peri	Post	
	β(SE)*	β(SE)*	β(SE)*	
HDL-C	0.0008 (0.005)	0.01 (0.006)+	-0.006 (0.004)	0.04
Total HDL-P	0.0003 (0.008)	0.01 (0.01)	-0.005 (0.007)	0.46
Large HDL-P	-0.005 (0.02)	0.03 (0.02)+	-0.05 (0.02)	0.03
Medium HDL-P	-0.007 (0.008)	-0.0003 (0.01)	-0.01 (0.007)	0.71
Small HDL-P	0.007 (0.007)	0.004 (0.01)	0.01 (0.008)	0.75
HDL Size	0.001 (0.09)	0.22 (0.13)+	-0.21 (0.09)	0.02
HDL-PL	0.002 (0.006)	0.009 (0.007)+	-0.01 (0.005)	0.07
HDL-Tg (Log)	-0.07 (0.23)	-0.81 (0.33)#	-0.46 (0.23)	0.15
HDL-CEC	-0.11 (0.10)	0.17 (0.09)#, +	-0.10 (0.06)	0.08

^Adjusted for study site, race, log-transformed CAC volume score, time varying age, body mass index, physical activity, alcohol use, log-triglycerides, LDL-C, and C3; *β coefficients are per 1-unit increase in an HDL metric; # differs significantly from pre-/early peri; +differs significantly from postmenopause

S-4.

Cholesterol efflux capacity of HDL particles over the menopause transition: The SWAN HDL ancillary study

Samar R. El Khoudary, PhD[1], Xirun Chen[1], Jeff Billheimer[2], Karen Matthews[1], Alexis Nasr[1], Maria Brooks[1], Trevor Orchard[1], Dan McConnell[3], Sybil Crawford[4], Deb Martin[1], Dan Rader[2]. [1]University of Pittsburgh, Pittsburgh, PA; [2]University of Pennsylvania, Philadelphia, PA; [3]University of Michigan, Ann Arbor, MI; [4]University of Massachusetts, Worcester, MA

Objective: Mounting evidence challenges the concept that high-density lipoprotein-cholesterol (HDL-C) is cardio-protective after menopause. Cholesterol efflux capacity (CEC), the only validated measure of the ability of HDL particles (HDL-P) to promote cholesterol efflux from macrophages, might be a better predictor of cardiovascular risk than HDL-C. Changes in CEC as well as its relationship with HDL subclasses have not been characterized over the menopause transition (MT). Our objectives were to characterize trajectories of CEC (crude and per particle [CEC/HDL-P]) relative to time of the final menstrual period (FMP) and evaluate whether associations of HDL-P with CEC vary by time relative to the FMP. **Design:** The Study of Women's Health Across the Nation (SWAN) HDL ancillary study measured CEC and nuclear magnetic resonance spectroscopy of HDL subclasses (total, large, medium and small HDL-P) and total HDL size for a maximum of 5 time points across the MT. LOESS plots were used to characterize changes in CEC measures relative to the FMP. Associations between HDL subclasses and CEC were assessed using mixed effect models and effect modification by time segment relative to FMP (segment 1: >0.5 years before FMP, segment 2: ≤0.5 years before to ≤1.5 years after the FMP, and segment 3: >1.5 years after FMP) was tested. **Results:** We included 471 women (at first visit: mean age ± SD 50.2 ± 2.7 years; 88.9% still menstruating). LOESS plots suggested that crude CEC generally increased over time relative to the FMP while CEC/HDL-P declined up to 4.5 years after the FMP and then increased. Adjusting for study site, race/ethnicity, time varying age, body mass index, and complement protein C3, higher concentrations of total, large, and medium HDL-P and greater HDL size were associated with greater CEC while higher concentrations of small HDL-P was associated with lower CEC, all P values <0.001. Time segment relative to FMP modified adjusted associations of large HDL-P and HDL size with CEC (interaction P values <0.05), such that higher concentrations of large HDL-P and greater HDL size were associated with lower CEC in segment 2 compared to other segments. **Conclusion:** As women transition through menopause, although their crude CEC seems to increase over time, CEC per particle declines. Large HDL-P may be compromised and become less efficient in promoting CEC during the MT. Our results support efforts to identifying novel targets for HDL-based therapies and better HDL biomarkers of CVD risk in women.

Sources of Funding: SWAN HDL ancillary study has grant support from NIA: AG058690. The SWAN has grant support from NIH, DHHS, through NIA, NINR and ORWH: NR004061; AG012505, AG012535, AG012531, AG012539, AG012546, AG012553, AG012554, AG012495. The SWAN Repository: U01AG017719.

S-5.

Fractional CO2 Laser Therapy, a Promising Treatment Alternative for Vulvovaginal Symptoms in Menopause, Breast Cancer and Lichen Sclerosus

Alyssa Gardner, MD[1,2], Sarit Aschkenazi, M.D., M.S.[3]. [1]Obstetrics and Gynecology, UT Health San Antonio, San Antonio, TX; [2]Medical College of Wisconsin, Wauwatosa, WI; [3]Division of Urogynecology, Department of Obstetrics and Gynecology, Prohealth Women's Services, Waukesha, WI

Objective: This study investigated the short term effects of fractional CO2 laser therapy on symptoms of the Genitourinary Syndrome of Menopause using validated questionnaires obtained before and after treatment. **Design:** A retrospective chart review was conducted on 139 patients who underwent fractional CO2 laser therapy from 1/2016 to 12/2019. All women were >18 years old, non-pregnant, and presenting with vulvovaginal atrophy symptoms, where topical estrogen was contraindicated or insufficient. The protocol consisted of 3 vulvovaginal fractional micro-ablative CO2 laser treatments about 6 weeks apart. Patients were surveyed prior to the 1st and 3rd treatments using 2 validated questionnaires, Female Sexual Function Index and Vulvovaginal Symptoms Questionnaire, as well as a visual analog scale. **Results:** The mean age and follow-up time were 62 years and 13.8 weeks, respectively. Concomitant topical estrogen use was reported in 74 women, while 62 stated no hormonal therapy. History of breast cancer was documented in 38 women and lichen sclerosus in 31. All 6 domains and total Female Sexual Function Index scores were significantly improved, (p<.05). The Vulvovaginal Symptom Questionnaire showed 18 of the 21 questions significantly improved, (p<.05). The visual analog scale showed significant improvement in pain, dyspareunia, vaginal itching, burning, and dryness (p<.05). Following the 2 treatments, 19 women who were not previously sexually active became so. No major adverse events were reported. **Conclusion:** Fractional CO2 laser therapy appears to be an effective and safe treatment alternative for symptoms of the Genitourinary Syndrome of Menopause, as well as vulvovaginal atrophy symptoms in women with breast cancer or lichen sclerosus.

Sources of Funding: None

Female Sexual Function Index (FSFI) Results

Variable	Status	N	Mean	Standard Error of the Mean (+/-)	P-Value
Desire	Pre	120	2.508	0.104	<0.000*
	Post	126	2.938	0.0963	
Arousal	Pre	119	2.354	0.159	<0.000*
	Post	126	3.252	0.166	
Lubrication	Pre	119	1.6	0.137	<0.000*
	Post	126	2.983	0.173	
Orgasm	Pre	119	2.261	0.198	<0.000*
	Post	126	3.31	0.199	
Satisfaction	Pre	119	2.503	0.175	<0.000*
	Post	126	3.744	0.173	
Pain	Pre	119	1.348	0.15	<0.000*
	Post	126	2.692	0.193	
Total	Pre	119	12.718	0.768	<0.000*
	Post	124	19.055	0.861	

The mean differences between the pre- and post-treatment scores for the FSFI (domains and total) were compared using a paired t-test. The mean differences for the domains and total FSFI scores are all statistically significant.
***Statistically significant**

Vulvovaginal Symptoms Questionnaire (VSQ) Results

VSQ Item	Pre %	Post %	P-Value
1. Itching	36.5%	20.6%	0.003*
2. Burning or Stinging	41.3%	16.7%	<0.000*
3. Hurting	28.0%	8.7%	<0.000*
4. Being Irritated	54.4%	25.2%	<0.000*
5. Being Dry	72.0%	34.4%	<0.000*
6. Discharge	10.3%	9.6%	1.000
7. Odor	14.3%	7.3%	0.102
8. Worry	31.2%	13.6%	0.001*
9. Appearance	19.8%	6.3%	0.002*
10. Frustration	57.9%	25.2%	<0.000*
11. Embarrassment	32.5%	12.0%	<0.000*
12. Your interaction with others	28.6%	10.2%	<0.000*
13. Your desire to be with people	19.8%	3.1%	<0.000*
14. Making it hard to show affection	46.8%	17.7%	<0.000*
15. Your daily activities	26.0%	7.9%	<0.000*
16. Desire to be intimate	57.3%	19.3%	<0.000*
17. Currently sexually active with a partner?	75.4%	80.2%	0.449
18. Sexual relationships	73.7%	45.0%	<0.000*
19. Pain during sexual activity	76.8%	49.0%	<0.000*
20. Dryness during sexual activity	85.3%	53.5%	<0.000*
21. Bleeding during sexual activity	27.4%	12.0%	0.011*

Pre- and post-treatment proportions of the VSQ were evaluated by the Fisher's Exact Test. All proportions were significantly different except for the following items: (6)Discharge, (7)Odor, and (17)Sexual activity. Each VSQ item is represented in the table by the underlined terms in the questionnaire.
***Statistically significant**

S-6.

Waist to hip ratio predicts cognitive trajectory regardless of hormone therapy use: Analysis from Kronos Early Estrogen Prevention Study's Cognitive and Mood Ancillary Study (KEEPS-Cog)

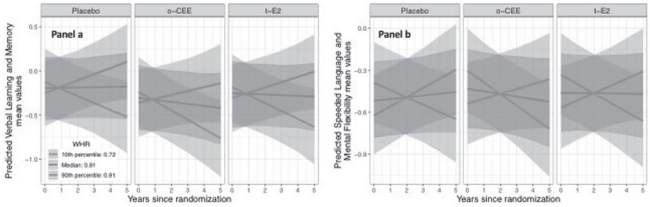
Carey E. Gleason, PhD[4], Taryn James, PhD[4], Carola Ferrer Simó[4], Derek Norton, MS[4,1], N. Maritza Dowling, PhD[5,2], Hector Salazar, BSN[4], Kejal Kantarci, MD[3]. [1]Department of Biostatistics, University of Wisconsin, Madison, WI; [2]Nursing, George Washington University, Washington, DC; [3]Mayo Clinic, Rochester, MN; [4]University of Wisconsin, Madison, WI; [5]George Washington University, Washington, DC

Objective: Data from the Women's Health Initiative Memory Study (WHIMS) suggest that for women over 65, incident cognitive impairment linked to diabetes was exacerbated with use of oral conjugated equine estrogens (o-CEE). Using a surrogate marker for prediabetes – waist-to-hip ratio (WHR), we examined whether this pattern could be observed in younger women. **Design:** Data were from 662 recently menopausal women (mean age 56.2) enrolled in KEEPS, a randomized, controlled trial examining cardiovascular effects of menopausal hormone therapy (MHT). KEEPS-Cog studied cognitive and mood effects of (1) o-CEE; (2) transdermal estradiol; versus (3) placebo. Women with elevated cardiovascular risk were excluded from KEEPS. i.e., women with diabetes, and high fasting glucose levels or body mass index (BMI). Thus, we examined prediabetes using a surrogate marker for insulin resistance –WHR. Cognitive tests were administered at baseline, months 18, 36 and 48 and summarized with factor analysis. Data from 2 derived domain scores were included in models: (1) verbal learning/memory (VLM) and (2) speeded language and mental flexibility (Lang). WHR was measured at screening and months 12, 24, 36, and 48. In linear-mixed models, two longitudinal VLM and Lang factor scores were tested whether WHR moderated factor trajectory generally, and differently by treatment group; follow-up time and WHR were time-varying predictors. Additional predictor variables included baseline age, education and study site. Using Likelihood Ratio Test (LRT), we compared this model structure to one without the three-way interaction. Models without this three-way interaction were examined for the general two-way interaction between follow-up time and WHR. **Results:** Neither factor exhibited significant three-way interactions (p-values > 0.38) – suggesting that WHR may not affect cognitive trajectory differently across treatment groups. Both VLM and Lang models exhibited significant follow-up time by WHR interactions (LRT p-values <0.002) indicating an overall change in cognitive trajectory as WHR changes. In both models,

increasing WHR was associated with worse cognitive trajectory. The Figure illustrates differences in cognitive trajectory by WHR group. **Conclusion:** Previous KEEPS-Cog findings indicated that MHT did not influence cognitive trajectory. WHR, an indicator of early metabolic changes and prediabetes did, however. Women whose WHR increased over time, i.e., those developing central adiposity, evidenced worsening cognitive declines. Unlike older women enrolled in WHIMS, MHT in younger women did not appear to worsen the deleterious effects of metabolic syndrome on cognition.

Sources of Funding: The KEEPS-Cog project was supported by grants from the National Institutes of Health (NIH) R01AG029624, P50AG033514, R01AG031790, 1UL1RR025011 from the Clinical and Translational Science Award (CTSA) program of the NIH National Center for Research Resources and the Wisconsin National Primate Research Center base grant, NIH NCRR000167. KEEPS Continuation is supported by funding from the NIH RF1 AG057547.

Figure: Cognitive trajectories for 2 domains. Women with an increase in WHR demonstrated steepest declines in cognition over time. No statistically significant 3-way interaction (time x treatment group x WHR) was observed. Panel (a) depicts performance *on Verbal Learning and Memory* (VLM) factor over time and Panel (b) shows performance on *Speeded Language and Mental Flexibility* factor (Lang) over time.



Cognition changes by change in WHR.

S-7.

Postmenopausal Dyspareunia – Where Does It Hurt?

Martha F. Goetsch, MD, MPH, Jen Lillemon, MD, Bharti Garg, MBBS, Amanda Clark, MD, MCR, NCMP. ObGyn, Oregon Health & Science University, Portland, OR

Objective: Dyspareunia is one of the most common symptoms of genitourinary syndrome of menopause (GSM), with pain attributed to vulvovaginal atrophy. Estrogen deficiency affects the entire lower genitourinary tract, but resulting dysfunction is inconsistent. Studies to elucidate the precise locations of pain are few. Our objective is to systematically describe the anatomic locations of painful tissues on examination of a cohort of postmenopausal women with moderate/severe dyspareunia likely due to GSM. **Design:** This cross-sectional study reports baseline data of postmenopausal women with dyspareunia screened for a trial of two strengths of topical introital estrogen cream. IRB approval was obtained. Inclusion criteria were: postmenopausal women (age >50 and 1 year of amenorrhea; previous BSO; if no uterus, 2 years after peak vasomotor symptoms), no systemic hormone therapy for 6 months; no local estrogen for 4 weeks; moderate/severe dyspareunia defined as enough discomfort to disrupt preferred intercourse frequency. Exclusion criteria were: mild dyspareunia defined as unpleasant sensation but no change in intercourse frequency; pelvic pain; premenopausal dyspareunia; vulvar dermatoses; an estrogen-sensitive tumor; male sexual partner not able or available. Subjects completed questionnaires and underwent a systematic examination that included a visual assessment, a cotton swab test for vestibular tenderness, a lidocaine test (aqueous 4% applied for 3 minutes to the vestibule followed by a repeat cotton swab test). Tenderness was rated on a 10-point Numerical Rating Scale, with 0=no pain and 10=the worst pain imaginable. Vaginal sensitivity was assessed by stroking each lateral wall with a cotton swab after speculum insertion. Pelvic floor muscles, the bladder, the cervix, uterus and adnexa were palpated for tenderness. **Results:** Between July 2017 and August 2019, screening identified 55 women eligible for enrollment. Mean age was 59.5 ±6.8 years, mean BMI was 25.3 ± 4.7, and 96% were Caucasian. Two thirds of women reported recent vasomotor symptoms, and all reported at least one lower urinary tract symptom. The mean duration of dyspareunia was 6.2 ± 4.3 years, and mean duration of sexual partnerships was 26.9 ± 18.0 years. The mean pain score with intercourse was 7.3 ± 1.8, and pain was most often described as "burning" and "sharp." By visual assessment, the vestibule appeared atrophic in 85%, and 9% had a caruncle. Mean tenderness scores with cotton swab touch at the vestibule were between 1 and 5 in 8 locations. This tenderness was extinguished by topical lidocaine in all women. No patient noted a vaginal discharge, and by speculum, 69% had no visible discharge, 25% had some clinging discharge and 5% had some pooling, usually yellow. Vaginal atrophy was graded as none (1%), mild (20%), moderate (35%), or severe (44%). Mean vaginal pH was 5.6 ± 0.7. Median mid-vaginal tenderness elicited by swab friction was 0 (interquartile range 0,3) with a single outlier score set of 7 & 8. Tense or tender pelvic floor muscles were noted in 14%, and bladder tenderness was noted in 8%. No cervical or uterine tenderness on manipulation was noted in women with an intact uterus (82% of women). No adnexal tenderness was present in the women with intact adnexa (85%). **Conclusion:** All women in this cohort had pain elicited by touch at the anatomic location of the vulvar vestibule. The vaginal walls and upper genital structures were rarely tender despite findings of generalized atrophy. Our findings of localized areas of tenderness in generalized atrophy suggest that treating tenderness may be more important than treating atrophy. GSM treatments might be more effective at the introitus instead of the upper vagina. Future studies utilizing this systematic approach should be conducted in a larger, more generalized cohort of women in order to more precisely characterize the condition of GSM. The ability to extinguish vestibular mucosal tenderness using topical lidocaine suggests that a neurologic mechanism may contribute to menopausal dyspareunia. Better understanding of the underlying mechanisms of GSM is necessary in advancing care of symptomatic women.

Sources of Funding: The Patty Brisbane Foundation and the National Vulvodynia Association

S-8.

A novel, non-hormonal, non-invasive ultrasound device is effective in treating the symptoms of vaginal dryness associated with genitourinary syndrome of menopause (GSM)

Martha Hickey, MD[1], Rodney Baber, MD[2], John Eden, MD[3], Janelle Brennan, MD[4], Deborah Bateson, MD[5], Darlene Dreon, DrPH[6], Holly Rockweiler, MS[6]. [1]Royal Women's Hospital, Melbourne, VIC, Australia; [2]Royal North Shore Hospital, St Leonards, NSW, Australia; [3]Women's Health and Research Institute of Australia, Sydney, NSW, Australia; [4]Goldfields Urology, Bendigo, VIC, Australia; [5]Family Planning New South Wales, Ashfield, NSW, Australia; [6]Madorra, Inc, Portland, OR

Objective: Vaginal dryness is a common symptom of menopause and is a direct result of decreased estrogen stimulation of the vulvovaginal tissues. Given estrogen's effects on vulvovaginal blood flow, augmentation of blood flow with ultrasound energy should reverse some of the effects of GSM. Thus, this pilot study is the first randomized trial to determine whether repeated increases in vaginal temperature (a surrogate marker of vaginal blood flow), initiated by repeated use of therapeutic ultrasound, can improve symptoms of GSM over time. **Design:** This randomized (1:1), double-blind, sham-controlled pilot study assessed the effectiveness of daily, at-home Madorra ultrasound therapy, applied to the vaginal introitus for 8 min/day over the course of 12 weeks, on menopausal vaginal dryness in an ambulatory setting (Clinicaltrials.gov NCT00583-1). After the primary endpoint evaluation at week 12, each participant in both groups received an active device and commenced an open-label period for weeks 12-48. Fifty-nine women with menopause (defined by natural amenorrhea, treatment-induced, or surgical removal of ovaries) were screened between October 2019 and March 2020 in a multi-center study, of which 42 (ages 48-70 years) were randomized. Upon entry, women self-reported vaginal dryness, which was confirmed with a clinical exam. Women were excluded for use of systemic or local estrogen therapy (in the last 6 months) or any other treatment for symptomatic vaginal atrophy (currently or planned use) during the study. Participants self-assessed change (from baseline to week 12) in GSM symptoms (vaginal dryness, soreness, irritation, dyspareunia) measured by the Vaginal Assessment Scale (VAS) with a 4-level response score ranging from none, mild, moderate, to severe. Healthcare providers evaluated change in vaginal tissue response (tissue elasticity, vaginal fluid, pH, mucosa, and vaginal moisture) assessed by the Vaginal Health Index (VHI) giving a numerical score (1-5) for each of the 5 parameters. Vaginal temperature was measured by the healthcare provider before, during, and after therapy using the randomized device at baseline and week 12 clinic visits. **Results:** Interim per protocol results (n=16) after week 12 follow-up showed that participants in both treatment and sham groups reported good adherence to the prescribed therapy, with no significant difference between groups [Mean ± SE (standard error) % were 88.7 ± 6.6% vs. 87.6 ± 4.5%, respectively; p=0.89]. Using an ANCOVA model with baseline value as a covariate, women receiving Madorra ultrasound therapy showed a trend towards reduced symptoms of GSM on the VAS compared to women receiving sham treatment [Adjusted (Least-Square) Means (LSM) ± SE pre- to post-treatment changes were -0.52 ± 0.21 vs. -0.24 ± 0.24, respectively; p=0.40]. Based on clinical exam, women showed improvement in their vaginal health on the VHI with therapeutic ultrasound therapy compared to women receiving sham treatment during the final week of the 12-week treatment period (LSM ± SE pre- to post-treatment changes were 2.03 ± 0.54 vs. 0.25 ± 0.61, respectively; p=0.05). Vaginal temperature during therapy was higher in treatment vs. sham group indicating a thermal effect of the ultrasound treatment. **Conclusion:** For post-menopausal women experiencing symptoms of GSM, daily at-home, self-application of Madorra ultrasound therapy targeting vaginal dryness may improve symptoms and tissue health. Energy is delivered to the vaginal canal to increase temperature, thereby increasing the transudate from the epithelium, and increasing vaginal lubrication. Treatment of GSM with ultrasound therapy could offer a new therapeutic option as it is well tolerated (no serious adverse device effects were recorded) and may relieve symptom severity. This study is continuing to collect safety, efficacy, and adherence data.

Sources of Funding: Madorra, Inc.

S-9.

NT-814, a Non-hormonal Dual NK1,3 Receptor Antagonist Markedly Improves Sleep, Mood and Quality of Life in Post-Menopausal Women; Results of a Randomised, Double-Blind, Placebo-Controlled Study (SWITCH-1)

Hadine Joffe, MD PhD[2,3], Stephen Pawsey[1], Richard Anderson[4], Elizabeth Ballantyne, BSc[1], Mary Kerr, PhD[1], Mary Ann Lumsden, MB BS MD[5], Nicholas Panay, MB BS MRCOG[8], Susan Seymore, BSc[1], James Simon, MD[6,7], Mike Trower, PhD[1]. [1]KaNDy Therapeutics Ltd, Stevenage, United Kingdom; [2]Brigham & Womens Hospital, Boston, MA; [3]Harvard Medical School, Boston, MA; [4]University of Edinburgh, Edinburgh, United Kingdom; [5]University of Glasgow, Glasgow, United Kingdom; [6]George Washington University, Washington, DC; [7]IntimMedicine, Washington, DC; [8]Imperial College, London, United Kingdom

Objective: Disrupted sleep and impaired mood are debilitating symptoms experienced by many women during and after the menopause that contribute, with hot flashes (HF), to reduced quality of life. Hormone therapy can improve sleep but carries risks and may be contraindicated. Clinical evidence shows a role for neurokinin receptor (NKR) antagonists in improving mood and sleep, notably through effects at CNS NK1Rs. NKR antagonists have also been shown to suppress HFs very effectively, with effects being mediated by mechanisms that include blocking NK3Rs on the thermoregulatory pathway controlled by hypothalamic KNDy (kisspeptin, NK, dynorphin) neurons. NT-814 is an oral non-hormonal dual NK1,3R antagonist which showed marked efficacy on HFs in a pilot study in post-menopausal (PM) women. A Phase-2b trial was undertaken to further evaluate efficacy in HF. Data showing efficacy in HF have been reported.

Here we present the a priori analyses of the patient reported outcome (PRO) secondary efficacy endpoints from the study. **Design:** SWITCH-1 was a double-blind, placebo-controlled, adaptive-randomization, dose-finding trial in 199 PM women with HFs. After a 2-week single-blind placebo run-in, women (40 to 65 years) were randomized to 12 weeks once daily treatment with placebo or one of 4 doses of NT-814: 40 mg, 80 mg, 120 mg, 160 mg. PRO assessments were used to assess sleep (Insomnia Severity Index [ISI] and Pittsburgh Sleep Quality Index [PSQI]), mood (Beck Depression Inventory II [BDI]), and quality-of-life (MenQoL) at baseline and Weeks, 4, 8 and 12. Least squares (LS) mean differences vs placebo for Weeks 4 and 12 were analysed using a mixed model repeated measures analysis. **Results:** Dose-related improvement in mean scores for all PRO assessments were observed with NT-814 at all time-points, with a similar magnitude of effect at the 120 and 160 mg doses. Table 1 shows the findings at the end of the treatment period (Week 12) for ISI, BDI and MenQoL. Improvements in all PRO assessments were significant ($p<0.05$) for the 120 and 160 mg doses at both Week 4 and 12. The 40 and 80 mg doses were not consistently significantly different vs placebo. Mean improvements for the 120 mg and 160 mg doses at Week 12 for the ISI (≥6 points), BDI (≥3 points) and MenQoL (≥1 point) were consistent with published clinically relevant improvements. Strikingly, significant improvements were also shown for each domain (Physical, Psychosocial, Vasomotor and Sexual) of the MenQoL. NT-814 was well-tolerated; most AEs were mild or moderate and there were no serious AEs related to treatment. **Conclusion:** In a randomized trial of NT-814 for treatment of HFs in PM women, this non-hormonal NK1,3R antagonist also showed improvement in key secondary endpoints mood, sleep and quality of life at once daily doses of 120 & 160 mg. NT-814 was well tolerated, with a good safety profile. These data demonstrate the potential for the dual NK1R and NK3R antagonism of NT-814 to provide broad benefit on well-being beyond improving HFs.

Sources of Funding: KaNDy Therapeutics Ltd

Table 1. Change from Baseline in PROs at Week 12

	Placebo N=47	40 mg N=31	80 mg N=17	120 mg N=52	160 mg N=52
ISI					
LS mean (95% CI)	-2.13 (-3.61, -0.66)	-3.60 (-5.30, -1.89)	-5.91 (-8.25, -3.57)	-6.41 (-7.74, -5.07)	-6.99 (-8.44, -5.54)
Difference in LS means (95% CI)	-	-1.46 (-3.72, 0.79)	-3.77 (-6.54, -1.01)	-4.27 (-6.26, -2.28)	-4.85 (-6.93, -2.79)
p-value	-	0.2024	0.0078	<0.0001	<0.0001
BDI					
LS mean (95% CI)	-1.38 (-3.51, 0.76)	-3.70 (-6.20, -1.20)	-2.34 (-5.73, 1.06)	-5.12 (-7.06, -3.17)	-5.70 (-7.78, -3.62)
Difference in LS means (95% CI)	-	-2.32 (-5.61, 0.97)	-0.96 (-4.97, 3.05)	-3.74 (-6.63, -0.85)	-4.32 (-7.30, -1.34)
p-value	-	0.1649	0.6373	0.0115	0.0048
MenQoL					
LS mean (95% CI)	-0.80 (-1.12, -0.47)	-0.76 (-1.14, -0.38)	-0.98 (-1.50, -0.46)	-1.60 (-1.90, -1.30)	-1.57 (-1.89, -1.25)
Difference in LS means (95% CI)	-	0.03 (-0.47, 0.53)	-0.18 (-0.79, 0.43)	-0.80 (-1.24, -0.37)	-0.77 (-1.23, -0.32)
p-value	-	0.8971	0.5593	0.0004	0.0009

S-10.

Effect of Vasomotor Symptom Frequency and Comorbidities on Sleep Quality Among Women in Midlife: a Retrospective Analysis of the US SWAN Database

Risa Kagan[1], Aki Shiozawa[2], Andrew Epstein[3], Robert Espinosa[4], Carol Schermer[2]. [1]University of California, San Francisco, and Sutter East Bay Medical Foundation, Berkeley, CA; [2]Astellas Pharma, Inc., Northbrook, IL; [3]Medicus Economics, LLC, Philadelphia, PA; [4]Medicus Economics, LLC, Boston, MA

Objective: Vasomotor symptoms (VMS) associated with menopause can cause sleep interruptions, leading to poor overall sleep. We explored the associations of VMS frequency and comorbid health conditions with sleep problems among US women in midlife. **Design:** In this longitudinal, retrospective cohort study, we extracted data from the Study of Women's Health Across the Nation (SWAN) database from women in midlife (age 42-52 y at enrollment) across the United States. Outcomes included sleep problems (difficulty falling asleep, waking early, and sleep interruptions) ≥3 times per week in the past 2 weeks and overall sleep quality (scale: 1=very good to 4=very bad) in the past month. Sleep data were stratified by the number of days with hot flashes or night sweats during the past 2 weeks (none, 1-5, or ≥6) and presence of comorbidities (diabetes, hypertension, cholesterol, migraines, arthritis, cancer, cardiovascular disease, obesity). Overall sleep quality was evaluated by ordered logistic regression, and sleep problem outcomes were evaluated by binomial logistic regression, controlling for covariates of demographic and household characteristics, vital signs, lifestyle, menopause stage, pregnancy history, hormone therapy use, medical status, medications, and potential stressors. Additional logistic regression models were estimated with interactions between hot flash and night sweat frequencies and comorbid conditions. Statistical significance of interactions was assessed with Wald tests. **Results:** Of 3095 women with 25,487 annual visits recorded in the SWAN database, 3019 (with 21,655 visits) contributed data on sleep problems and 2674 (with 14,488 visits) contributed sleep quality data at follow-up visits 3-10. Mean (SD) age was 50.5 (4.2) years. Greater frequency of hot flashes or night sweats in the prior 2 weeks was associated with greater odds of all three sleep problems and worse quality of sleep (**Table**). Presence of migraine headaches and arthritis also were associated with greater odds of sleep problems and worse quality of sleep (**Table**). There were few statistically significant interactions. Among the comorbidities measured, only three amplified or attenuated the association between VMS frequency and sleep. Likelihood of waking up during the night was higher among women with both hot flashes and diabetes (interaction P=0.004) and lower among women with both hot flashes and hypertension (interaction P=0.006) than women with hot flashes alone. Women with migraines and hot flashes were less likely to have trouble sleeping than women who had hot flashes but no migraines (interaction P=0.028). **Conclusion:** Consistent with prior research, higher VMS frequency was associated with worse sleep outcomes. After controlling for VMS frequency, other comorbidities, and a range of covariates, women with migraines or arthritis were at higher risk of worse sleep. Some comorbidities amplify or attenuate the association between VMS frequency and sleep and warrant further investigation.

Sources of Funding: Astellas Pharma, Inc.

Effects of VMS Frequency and Comorbidities on Sleep					
			Association with Sleep: OR (95% CI)		
	Number (%) of Visits (21,665 Visits Total)	Trouble Sleeping(a)	Waking Early(a)	Sleep Interruptions(a)	Sleep Quality in Past Month(b)
Days with HFs in past 2 wk					
0	12,291 (57)	Reference	Reference	Reference	Reference
1–5(c)	5595 (26)	1.26 (1.10-1.45)‡	1.05 (0.92-1.19)	1.07 (0.97-1.18)	1.21 (1.09-1.34)‡
≥6(c)	3769 (17)	1.60 (1.34-1.92)§	1.39 (1.16-1.65)‡	1.64 (1.44-1.87)§	1.50 (1.31-1.72)§
Days with night sweats in past 2 wk					
0	13,997 (65)	Reference	Reference	Reference	Reference
1–5(c)	5252 (24)	1.23 (1.06-1.41)†	1.41 (1.23-1.60)§	1.36 (1.23-1.51)§	1.31 (1.18-1.45)§
≥6(c)	2406 (11)	2.14 (1.77-2.58)§	2.26 (1.90-2.70)§	2.87 (2.49-3.31)§	2.28 (1.94-2.67)§
Comorbidities					
Diabetes	1290 (6)	0.76 (0.52-1.11)	0.80 (0.59-1.09)	1.04 (0.77-1.42)	0.87 (0.63-1.19)
Hypertension	4599 (21)	1.08 (0.87-1.35)	1.09 (0.91-1.31)	0.97 (0.82-1.13)	1.12 (0.94-1.34)
Cholesterol	3952 (18)	0.95 (0.81-1.12)	1.05 (0.91-1.21)	1.02 (0.90-1.15)	1.06 (0.93-1.20)
Migraines	1469 (7)	1.54 (1.25-1.89)‡	1.24 (1.02-1.51)*	1.34 (1.13-1.59)‡	1.52 (1.26-1.85)§
Arthritis	3513 (16)	1.17 (1.01-1.37)*	1.17 (1.02-1.35)*	1.20 (1.07-1.35)†	1.24 (1.09-1.41)†
Cancer	220 (1)	1.10 (0.73-1.65)	1.04 (0.65-1.67)	1.13 (0.79-1.62)	0.58 (0.39-0.87)†
Cardiovascular disease(d)	260 (1)	0.97 (0.61-1.53)	1.16 (0.81-1.66)	1.01 (0.72-1.42)	1.07 (0.69-1.63)
Obesity (BMI ≥30 kg/m2)	7577 (35)	1.13 (0.90-1.42)	1.06 (0.87-1.28)	0.96 (0.81-1.14)	1.07 (0.89-1.27)
(a)Considered positive for women who reported experiencing that sleep problem ≥3 times per week during past 2 weeks. (b)Based on 4-point rating scale of 1=good to 4=very bad. (c)Relative to 0 events in past 2 wk. (d)Cardiovascular disease category includes stroke, myocardial infarction, and angina. *P<0.05; †P<0.01; ‡P<0.001; §P<0.0001. BMI, body mass index; CI, confidence interval; HFs, hot flashes; OR, odds ratio.					

S-11.

Higher Blood Pressure is Associated with Loss of White Matter Integrity and Higher Alzheimer's Tau Biomarkers in Postmenopausal Women of the KEEPS Continuation Study

Firat Kara, PhD[1], val J. Lowe[1], Robert I. Reid[1], Christopher G. Schwarz[1], Nirubol Tosakulwong[1], Timothy G. Lesnick[1], Samantha M. Zuk[1], June Kendall-Thomas[1], Kaely B. Thostenson[1], Denise A. Reyes[1], Julie A. Fields[1], Matthew M. Senjem[1], Hoon-Ki Min[1], Clifford R. Jack Jr.[1], Kent R. Bailey[1], Taryn James, PhD[2], Rogerio A. Lobo[3], JoAnn E. Manson[4], Lubna Pal[5], Dustin B. Hammers[6], Michael Malek-Ahmadi[7], Marcelle Cedars[8], Frederick Naftolin[10], Virginia M. Miller[1], Sherman M. Harman[9], N. Maritza Dowling, PhD[11], Carey E. Gleason, PhD[2], Kejal Kantarci, MD[1]. [1]Mayo Clinic, Rochester, MN; [2]University of Wisconsin-Madison, Madison, WI; [3]Columbia University, New York, NY; [4]Brigham and Women's Hospital, Boston, MA; [5]Yale University, New Haven, CT; [6]University of Utah, Salt Lake City, UT; [7]Banner Alzheimer Institute, Phoenix, AZ; [8]University of California, San Francisco, CA; [9]Phoenix VA Health Care System, Phoenix, AZ; [10]New York University, New York, NY; [11]George Washington University, Washington, DC

Objective: Elevated blood pressure (BP) is a risk factor for white matter injury associated with cerebrovascular disease, cognitive decline, and dementia. White matter hyperintensities (WMH) on MRI, a marker of white matter injury, increases with aging and are more common in women than in men after the age of 60. We examined BP in relation to WMH volume, diffusion MRI biomarkers of white matter microstructure and PET biomarkers of Alzheimer's disease (AD) in postmenopausal women. **Design:** Women (mean age 67 ± 2, n=75), who had previously enrolled in the multi-site Kronos Early Estrogen Prevention Study (KEEPS), were invited to participate in the present KEEPS Continuation Study. BP, MRI, and PET data were collected 9 years after the end of KEEPS menopausal hormone therapies. White matter integrity was assessed with WMH volume measurements on structural MRI and with measures of white matter microstructure on diffusion MRI. AD biomarkers were measured by

Florbetapir amyloid-β PET and Flortaucipir tau PET which were performed in a subset of participants from the Mayo Clinic site (n=25). Multiple linear regression analysis was used to assess the association between imaging measures and measured BP. All models were adjusted for age and $p<0.05$ was considered statistically significant. **Results:** Higher systolic BP (SBP) and diastolic BP (DBP) were associated with higher brain WMH volumes ($p=0.0002$ and $p=0.0016$, respectively). Regionally, higher SBP and DBP were associated with lower fractional anisotropy and higher mean diffusivity in the association (e.g. frontal, temporal, occipital, and angular WM), projection (e.g. posterior thalamic radiation, fronto-occipital fasciculus, sagittal stratum) and commissural (corpus callosum) white matter tracts ($p<0.05$). Higher SBP was associated with higher tau standard uptake value ratio (SUVR) in the calcarine ($p=0.0281$), cuneus ($p=0.0456$), inferior occipital ($p=0.0346$), and lingual cortices ($p=0.0417$). Similarly, increased DBP was associated with increased tau SUVR in the angular ($p=0.0443$), inferior parietal ($p=0.0212$), and occipital cortex ($p=0.0295$). No association between regional amyloid-β SUVR and BP was observed. **Conclusion:** These data, together with previously published studies of KEEPS [1], confirm that elevated BP is associated with higher WMH volumes in postmenopausal women. Diffusion MRI further demonstrates that higher BP is associated with greater microstructural injury in the white matter, which may contribute to cognitive decline in the long-term. We observed elevated AD-related tau deposition in the parietal and occipital cortices with higher BP in a subset of postmenopausal women. However, a similar relationship between higher BP and amyloid-β deposition did not exist, which requires further investigation in a larger sample. Blood pressure control in post-menopausal women may reduce the risk for white matter injury and possibly AD-related tau pathology. [1] Barnet et al., Journal of Neurology, 2017.

Sources of Funding: National Institutes of Health RF1 AG57547, American Federation of Aging Research, research support from Avid Radiopharmaceuticals, Eli Lilly.

S-12.

Effect of estradiol therapy on markers of inflammation: Results from the Early vs Late Intervention Trial with Estradiol (ELITE)

Roksana Karim, Phd, MBBS[1,2], Xiaofu Dai, MS[1], Naoko Kono[1,2], Howard N. Hodis[1,2], Wendy J. Mack[1,2], Frank Z. Stanczyk[3]. [1]Preventive Medicine, University of Southern California, La Crescenta, CA; [2]Atherosclerosis Research Unit, University of Southern California, Los Angeles, CA; [3]Department of Obstetrics and Gynecology, University of Southern California, Los Angeles, CA

Objective: Atherosclerosis is a chronic inflammatory process of blood vessels that is central to most of cardiovascular disease (CVD). CVD is the leading cause of death in women in the US and the risk of CVD in women rapidly increases after menopause. Hormone therapy (HT) reduced progression of atherosclerosis in relatively younger, healthy postmenopausal women in the Early versus Late Intervention Trial with Estradiol (ELITE). We evaluated the effect of HT on biomarkers of inflammation in postmenopausal women randomized to ELITE. **Design:** In ELITE, 643 healthy postmenopausal women (248 early (within 6 years) and 348 late (≥10 years postmenopause) were randomized to either oral 17β-estradiol (1 mg per day) or to placebo for an average 5 years. A panel of 14 inflammatory biomarkers were measured from stored serum samples from 535 women who had baseline, 12 months and 36 months of trial follow-up. Mixed effects linear regression models were used to evaluate the effect of HT on circulating concentrations of these 12 inflammatory biomarkers. **Results:** In the total sample, average ontrial levels of E-selectin, ICAM-1, IFNγ and IL-8 were significantly lower in the HT group compared with placebo-treated women (all p-values <0.035). Stratified by time-since-menopause, women within 6 years of menopause when randomized to HT showed significantly lower levels of E-selectin, ICAM-1 and IL-8 compared with placebo; only E-selectin was significantly lower among women randomized to HT 10 or more years since menopause compared with placebo. **Conclusion:** HT significantly reduced circulating serum concentrations of E-selectin, ICAM-1, IFNγ and IL-8 compared with placebo. Women <6 years from menopause showed a greater anti-inflammatory benefit from HT compared with women 10 or more years after menopause when randomized to HT. These results suggest that the atheroprotective effects of HT in ELITE may partially be explained by HT-induced reduction of multiple biomarkers of inflammation.

Sources of Funding: The National Institute on Aging, National Institutes of Health (R01-AG024154 and R01-AG059690)

Effect of hormone therapy on biomarkers of inflammation in postmenopausal women

	All women (n = 535)		Early postmenopausal (n = 227)		Late postmenopausal (n = 308)	
Inflammatory biomarkers	Difference (SE) ‡	p-value†	Difference (SE) ‡	P-value†	Difference (SE) ‡	p-value†
E-Selectin, ng/mL	-0.131 (0.035)	0.002	-0.135 (0.054)	0.01	-0.126 (0.046)	0.006
P-Selectin, ng/mL	0.009 (0.013)	0.052	0.021(0.021)	0.32	0.005 (0.039)	0.89
ICAM-1, ng/mL	-0.037 (0.017)	0.03	-0.07 (0.026)	0.008	-0.012 (0.022)	0.57
VCAM-1,ng/mL	-0.004 (0.020)	0.86	-0.031(0.033)	0.35	0.018 (0.025)	0.48
MIP-1α, pg/mL	-0.095 (0.087)	0.28	-0.04 (0.023)	0.08	-0.0005 (0.119)	0.99
INFγ, pg/mL	-0.144 (0.066)	0.03	-0.17 (0.103)	0.10	-0.123 (0.087)	0.16
MCP-1, pg/mL	-0.002 (0.027)	0.94	0.066 (0.041)	0.11	-0.047 (0.036)	0.19
TNF-α, pg/mL	-0.027 (0.024)	0.26	-0.037 (0.039)	0.35	-0.018 (0.03)	0.55
VEGF-A, pg/mL	0.042 (0.054)	0.43	0.028 (0.078)	0.72	0.057 (0.073)	0.43
IL-6, pg/mL	-0.110 (0.060	0.067	-0.145 (0.099)	0.14	-0.081 (0.075)	0.28
IL-8, pg/mL	-0.249 (0.116)	0.03	-0.487 (0.169)	0.004	-0.061 (0.157)	0.69
IL-10, pg/mL	-0.084 (0.117)	0.47	-0.306 (0.175)	0.08	0.083 (0.156)	0.59

*** Treatment group comparisons on log-transformed biomarkers.**
† P-values for (log) mean comparisons between the treatment groups.
‡ Differences are the (log) mean circulating level in the estradiol group minus that in the placebo group.
§ Baseline value adjustment was performed for P-selectin.

S-13.

A clinical study to evaluate Elismetrep (TRPM8 antagonist), a non-hormonal drug for the treatment of vasomotor symptoms in postmenopausal women

Sheryl Kingsberg, PhD[4], Fuyuhiko Marubayashi[1], Steven Goldstein, MD[2], Tommaso Simoncini, MD[3], Nobuhiro Nakanishi[5], Akihito Ogasawara, PhD[5], Bunpei Kakinoki, PhD[5], Samina Khan, MD[1]. [1]Medical Science, Mitsubishi Tanabe Pharma Development America Inc., Jersey City, NJ; [2]Obstetrics and Gynecology, New York University School of Medicine, New York, NY; [3]Clinical and Experimental Medicine, University of Pisa, Pisa, Italy; [4]Department of OB/GYN, University Hospitals Cleveland Medical Center, Cleveland, OH; [5]Mitsubishi Tanabe Pharma Corporation, Tokyo, Japan

Objective: Elismetrep is a selective transient receptor potential melastatin 8 (TRPM8) channel antagonist, which is being developed as a nonhormonal treatment of vasomotor symptoms (VMS) associated with menopause. TRPM8 is a member of the TRP cation channel family, which plays a key role in the sensation of environmental cold. VMS are triggered by elevations in core body temperature (Tc) within a reduced thermoneutral zone. We hypothesized that a TRPM8 antagonist reduces VMS by using the body's natural methods of passive cooling to prevent an increase in Tc. **Design:** This was a phase 2 randomized, double-blind, placebo-controlled, dose-ranging study to evaluate the efficacy and safety of elismetrep in postmenopausal women with VMS (Clinicaltrials.gov NCT03291067). Coprimary efficacy endpoints were changes from baseline in both the frequency and severity of VMS at Weeks 4 and 12. The study design included screening, 2-week placebo run-in, and 12-week double-blind placebo-controlled treatment periods. Postmenopausal women who had 7 or more per day, or 50 or more moderate-to-severe VMS per week during the screening period were eligible. **Results:** A total of 375 subjects were randomized into the study (94, 94, 93, and 94 subjects to the placebo, 1-, 5-, and 10-mg groups, respectively). In the planned primary efficacy analysis, the 1-, 5-, and 10-mg groups failed to demonstrate clinical or statistical significance in VMS frequency or severity at Weeks 4 or 12 vs. placebo. Pharmacokinetic data showed that at 8 of the total 51 sites, majority of the subjects had elismetrep plasma concentration below the level of quantification throughout the study, confirming significant noncompliance to the study medication. In a post-hoc analysis (Table 1), after the exclusion of these 8 sites, the 5-mg group produced both a clinically and statistically significant decrease in VMS frequency and severity at Weeks 4 and 12. The incidence of adverse events (AEs) was similar across all groups. There were no safety or tolerability concerns in the 5-mg group. One serious adverse event of a transient ischemic attack was observed in the 5-mg group. There was a higher rate of withdrawal associated with AEs in the 10-mg group (22.6%), and paraesthesia was the most frequently (4.3%) reported AE leading to discontinuation. **Conclusion:** Elismetrep, a selective TRPM-8 antagonist, with a novel, non-hormonal mechanism of action, demonstrated efficacy in the treatment of VMS in postmenopausal women. Future studies will be conducted to confirm the efficacy and safety of elismetrep for VMS treatment in postmenopausal women.

Sources of Funding: None

Post-hoc Primary Efficacy

Time point	Statistic	Placebo (N=54)	1 mg Elismetrep (N=58)	5 mg Elismetrep (N=59)	10 mg Elismetrep (N=58)
VMS frequency					
Baseline	Mean (SD)	11.18 (8.064)	8.92 (3.457)	9.74 (5.403)	9.40 (4.826)
Change from baseline at Week 4	LSMean (SE)	-0.87 (0.523)	-1.65 (0.500)	-3.43 (0.497)	-2.53 (0.511)
	LSMD vs Placebo (SE)	-	-0.79 (0.727)	-2.56 (0.723)	-1.66 (0.733)
	P-value	-	0.282	<0.001	0.024
Change from baseline at Week 12	LSMean (SE)	-1.73 (0.656)	-2.90 (0.623)	-4.08 (0.622)	-3.09 (0.658)
	LSMD vs Placebo (SE)	-	-1.18 (0.910)	-2.36 (0.906)	-1.36 (0.931)
	P-value	-	0.198	0.010	0.145
VMS Severity					
Baseline	Mean (SD)	2.444 (0.2728)	2.519 (0.2618)	2.545 (0.2148)	2.466 (0.2555)
Change from baseline at Week 4	LSMean (SE)	-0.192 (0.0586)	-0.342 (0.0561)	-0.372 (0.0562)	-0.379 (0.0578)
	LSMD vs Placebo (SE)	-	-0.150 (0.0813)	-0.180 (0.0816)	-0.187 (0.0821)
	P-value	-	0.067	0.029	0.024
Change from baseline at Week 12	LSMean (SE)	-0.201 (0.0828)	-0.403 (0.0786)	-0.465 (0.0794)	-0.485 (0.0855)
	LSMD vs Placebo (SE)	-	-0.202 (0.1144)	-0.264 (0.1152)	-0.285 (0.1187)
	P-value	-	0.079	0.023	0.017

Abbreviations: LSMD = Least Square Mean Difference.
P values were calculated (vs. Placebo) based on the Mixed-effects model for repeated measures.

S-14.

Anti-Müllerian hormone (AMH) and markers of oxidative stress, inflammation, and endothelial dysfunction

Melissa Wellons[2], James Terry[2], James Slaughter[2], David R. Jacobs[3], Nisha Parikh[4], Duke Appiah[5], Benjamin Leader[6], Molly B. Moravek[1], Catherine Kim[1]. [1]University of Michigan, Ann Arbor, MI; [2]Vanderbilt University Medical Center, Nashville, TN; [3]University of Minnesota, Minneapolis, MN; [4]University of California, San Francisco, CA; [5]Texas Tech University, Lubbock, TX; [6]ReproSource, Woburn, MA

Objective: Our objective was to examine whether adverse systemic markers were associated with ovarian aging in a population-based study of black and white women. **Design:** We conducted a cross-sectional analysis using data from the Coronary Artery Risk Development in Young Adults (CARDIA) study. The main outcome was plasma

AMH; lower levels indicate lower ovarian reserve or older ovarian age. AMH was measured at exam year 15 (mean age 40 years) and markers were measured at years 5, 7, 10, and 15. Markers (Table) included F2-isoprostanes, super-oxide dismutase, paraoxonase activity, phospholipase A2 activity, oxidized low-density lipoprotein, carotenoids; CRP (C-reactive protein), fibrinogen, and uric acid; ICAM-1 (intercellular adhesion molecule-1), P-selectin, and VCAM (vascular cell adhesion molecule-1). Linear regression models were used to examine associations with log-transformed AMH, before and after adjustment for age, use of cigarettes and oral contraceptives (OCPs), and body mass index (BMI) in 830 women. **Results:** After adjustment for age, higher concentrations of year 15 F2-isoprostanes (-0.0015, p=0.001), CRP (-0.009, p=0.022), and P-selection (-0.004, p=0.029) were associated with lower AMH. After additional adjustment for smoking status, OCP use, and BMI, only the association between F2-isoprostanes and AMH remained significant (-0.0013, p=0.008). **Conclusion:** Higher systemic oxidative stress, indicated by F2-isoprostanes, is associated with lower ovarian reserve.

Sources of Funding: CARDIA is supported by the NHLBI in collaboration with the University of Alabama (HHSN268201800005I & HHSN268201800007I), Northwestern University (HHSN268201800003I), University of Minnesota (HHSN268201800006I), and Kaiser Foundation Research Institute (HHSN268201800004I). NHLBI supported the CARDIA Women's Study (R01HL065611), AMH measurement (K23HL87114, R03HL135453), and oxidative stress measures (R01HL05356016)

Table. The association between markers of oxidative stress, inflammation, endothelial dysfunction with anti-Müllerian hormone (AMH) concentrations at year 15, before and after adjustment for age, smoking status, oral contraceptive (OCP) use, and body mass index (BMI). β –coefficients (95% confidence intervals) and p-values are shown. AMH concentrations are log-transformed (lnAMH + 1).

	β -coefficient (95% CI), p-value Unadjusted for age	β -coefficient (95% CI), p-value Adjusted for age	β -coefficient (95% CI), p-value Adjusted for age, smoking status, OCP use, and BMI
Oxidative stress markers			
F2-isoprostane	-0.001 (-0.002, 0.002) p=0.10	**-0.0015 (-0.002, -0.0006), p= 0.001**	**-0.0013 (-0.002, -0.0003) p=0.008**
Super-oxide dismutase	0.006 (-0.012, 0.024) p=0.49	0.006 (-0.009, 0.021) p=0.42	0.006 (-0.009, 0.021) p=0.44
Paraoxonase activity	0.0005 (-0.0002, 0.0013) p=0.16	-0.00001(-0.001, 0.001) p=0.97	0.0001 (-0.001, 0.0007) p=0.82
Phospholipase A2 activity	-0.001 (-0.005, 0.003) p=0.65	0.003(-0.0005, 0.006, p=0.09	0.003 (-0.001, 0.006) p=0.09
Oxidized LDL	0.0004 (-0.0012, 0.0021) p=0.64	0.0002(-0.0012, 0.0016) p=0.75	0.0008 (-0.0007, 0.002) p=0.29
Carotenoids	-0.0004 (-0.001, 0.001) p=0.45	0.0004(-0.0005, 0.0013) p=0.37	-0.0002 (-0.001, 0.001) p=0.62
Inflammatory markers			
Y7 CRP	0.0002(-0.007, 0.007) p=0.95	-0.004 (-0.010, 0.002) p=0.17	-0.003 (-0.009, 0.003) p=0.36
Y15 CRP	-0.004 (-0.013, 0.006) p=0.44	**-0.009 (-0.017, -0.001) p=0.022**	-0.008 (-0.017, 0.002) p=0.12
Change Y15-Y7	-0.002 (-0.009, 0.005) p=0.53	-0.001 (-0.007, 0.005) p=0.78	-0.0001 (-0.006, 0.006) p=0.96
Y5 fibrinogen	-0.0004 (-0.001, 0.0004) p=0.32	-0.0004 (-0.001, 0.0002) p=0.18	-0.0003 (-0.001, 0.0004) p=0.46
Y7 fibrinogen	-0.0001 (-0.001, 0.0004) p=0.64	-0.0003 (-0.001, 0.0002) p=0.19	-0.0002 (-0.001, 0.0003) p=0.35
Change Y7-Y5	-0.0004 (-0.001, 0.0006) p=0.90	-0.0001 (-0.001, 0.0005) p=0.68	-0.0001 (-0.001, 0.0004) p=0.64
Y10 UA	0.011 (-0.034, 0.056) p=0.64	0.005 (-0.033, 0.042) p=0.80	0.024 (-0.02, 0.65) p=0.24
Y15 UA	0.018 (-0.020, 0.055) p=0.36	0.008 (-0.025, 0.040) p=0.65	0.031 (-0.006, 0.068) p=0.10
Change in UA Y15-Y10	0.014 (-0.040, 0.067) p=0.62	0.007 (-0.037, 0.052) p=0.75	0.17 (-0.03, 0.06) p=0.48
Endothelial dysfunction markers			
Y7 ICAM-1	-0.003(-0.002, 0.002) p=0.75	-0.001 (-0.002, 0.001) p=0.33	-0.0002 (-0.002, 0.001) p=0.81
Y15 ICAM-1	0.001 (-0.0003, 0.002) p=0.18	0.0004 (-0.0005, 0.001) p=0.33	0.0008 (-0.0002, 0.002) p=0.11
Change Y15-Y7	0.001 (-0.0001, 0.002) p=0.08	0.001 (-0.0001, 0.002) p=0.08	0.001 (-0.0001, 0.002) p=0.07

S-15.

Global Prospective Survey of Women with Vasomotor Symptoms Associated with Menopause: US Findings

Robin Kroll[1], Rossella E. Nappi[2], Emad Siddiqui[3], Boyka Stoykova[4], Carol Rea[5], Eric Gemmen[6], Neil M. Schultz[7]. [1]Seattle Women's: Health, Research, Gynecology, Seattle, WA; [2]Research Center for Reproductive Medicine, Gynecological Endocrinology and Menopause, IRCCS San Matteo Foundation, Department of Clinical, Surgical, Diagnostic and Pediatric Sciences, University of Pavia, Pavia, Italy; [3]Astellas Pharma, Chertsey, United Kingdom; [4](At time of research) Astellas Pharma, Chertsey, United Kingdom; [5]IQVIA, London, United Kingdom; [6]IQVIA, Real World Solutions, Falls Church, VA; [7]Astellas Pharma, Northbrook, IL

Objective: To determine the prevalence of moderate-to-severe vasomotor symptoms (VMS) associated with menopause and understand Health-Related Quality of Life (HRQoL) in postmenopausal women 40–65 years from the US, France, Germany, Italy, Spain, UK, and Japan. **Design:** This was a cross-sectional online survey of postmenopausal women currently experiencing moderate-to-severe VMS, or who reported having symptoms in the prior 12 months. A screening survey was sent by global consumer panels to a random sample of women aged 40–65 years; the full questionnaire was sent to those who completed the screening survey and met inclusion criteria. Women with successfully treated VMS were, by default, not eligible for the full questionnaire. Women with breast cancer or on hormonal treatment for any cancer or medical condition were excluded. The menopause-specific QoL (MENQOL) and work productivity and activity impairment (WPAI) questionnaires were included in the survey. Information on costs associated with menopause-related symptoms were collected. Analyses of US women are reported. **Results:** Of 25,161 women screened, 11,771 were postmenopausal and 3459 met inclusion criteria, receiving the full questionnaire. European countries reported the highest prevalence of women with moderate-to-severe VMS (40%), followed by the US (34%) and Japan (16%). The majority of women were 51–60 years of age. For US respondents (n=675), mean age was 57 years, 48% were employed. Most common concurrent medical conditions (>30%) were high cholesterol or triglycerides (37%) and hypertension (34%). Women with both hot flashes and night sweats (n=458) experienced a mean of 2.7 hot flashes and 2.0 night sweats a day, of which 1.8 and 1.5, respectively, were moderate/severe; the average duration was 13 and 29 minutes per episode, respectively. Overall, most women (61%) reported sleep disturbances. Only 7% were currently receiving hormone therapy, 4% were receiving non-hormonal prescription drugs, and 15% were taking non-prescription medications/supplements for menopause-related symptoms. Based on the MENQOL, the most bothersome symptoms of menopause were (scale: 0–6; 0=not bothersome/6=extremely bothersome): weight gain (mean score 4.80); difficulty sleeping (4.32); and "accomplishing less than I used to" (4.27). Night sweats (mean score 3.72) and hot flashes (3.57) were considered moderately bothersome. Most common menopause-related symptoms experienced in the last week were: feeling tired or worn out (75%); aching in muscles/joints (68%); hot flashes (68%); night sweats (67%); and sweating (67%). In the past 12 months, 47% had contacted an HCP to discuss hot flashes/night sweats. Based on the WPAI questionnaire (perceived impact scale 0–10; 0=no impact/10=completely prevented from working/activities), hot flashes and night sweats had a numerically higher impact on daily activities (mean score 1.99) than working activities (1.14); however, generally the perceived impact was low. Average recalled monthly costs associated with menopause-related symptoms included: $35.50 on prescription drugs, $24.30 on over-the-counter medications, $36.90 on supplements/alternative medications, $34.80 on doctor consultations and $33.80 on tests. Most women (60%) reported that they needed to keep an eye on prices when making purchases. **Conclusion:** The results from this global survey demonstrate that a high proportion of postmenopausal women experience moderate-to-severe VMS and have associated sleep disturbance. Menopause is associated with significant humanistic burden; many women report feeling tired and worn out, and experience other highly bothersome symptoms such as weight gain. There is a high economic burden of menopause-related symptoms in terms of healthcare resource utilization and out-of-pocket costs. These findings support the need for developing newer treatments for menopause-related symptoms.

Sources of Funding: Astellas Pharma Global Development, Inc.

S-16.

Real-life impact of menopause on midlife women's health and well-being: A comprehensive survey of U.S. women's health choices, behaviors and experiences during various stages of menopause.

Monica P. Mallampalli, PhD[1], Christina Louie[2], John Whyte, MD, MPH[2], Elizabeth Battaglino, RN[1]. [1]HealthyWomen, Red Bank, NJ; [2]WebMD, New York, NY

Objective: Women are living longer than before but many in their 40s-60s do not receive the health care they need. The changing health care needs while transitioning through menopause combined with the lack of information can lead to confusion and misinformation among women about screening for specific at-risk conditions and availability of effective therapies. This survey served as a vehicle to directly hear from women on the issues that concern them most during menopausal transition and the impact these issues have on their quality of life. **Design:** U.S. women (total 3,197) aged 18 and older, were randomly surveyed through on WebMD.com between September 10-October 24, 2019. The women were grouped into premenopause, perimenopause, menopause, and postmenopause stages. During analysis, the data was segmented by race/ethnicity, menopausal life stage, socioeconomic factors and geography. Majority of respondents self-reported as White, Hispanic and Black. There were insufficient responses from women of Asian, American Indian/Native Alaskan and Native Hawaiian/Pacific Islander descent. The effect size difference between subgroups was examined by applying a statistical significance test at the 95% confidence level. **Results:** This survey revealed important factors that have a real-life impact on women's health choices, behaviors and experiences as they transition from pre- to postmenopause. Race/ethnicity and socioeconomic factors played an important role in shaping the knowledge, attitudes and beliefs regarding menopause. Overall, menopause seemed to have a significant impact on a woman's physical health (41%) and sexual health (41%) compared to their mental health (36%). Only 1/3rd of respondents rated their **physical health** as excellent/very good. Menopausal Black women (47%) rated their physical health much higher compared to White women (28%), but Hispanic women (39%) rated their physical health as fair/poor compared to Black women. Women rated their **mental health** as excellent/very good (44%) compared to their physical health (32%). Mental health seemed to improve as women progressed through stages of menopause with 60% postmenopausal women rating their mental health as excellent/very good. Sixty percent of menopausal Black women also rated their mental health as very good/excellent compared to White women (38%). **Sexual health** satisfaction decreased with age with twice as many post-menopausal women rating it as fair/poor as compared to pre-menopausal women. No statistically significant differences were noted between women of different racial/ethnic backgrounds when it came to sexual health. A majority of women (59% of menopausal and postmenopausal women) proactively discussed their **overall health concerns** with their providers as they aged. Hispanic women are least likely to discuss about health risks with their providers unless they are experiencing symptoms. Pre- and peri-menopausal women were more concerned with cancer whereas menopausal and postmenopausal women were concerned with dementia. Despite concerns, only a small percentage of menopausal (3%) and postmenopausal women (5%) had recent discussions with their health care providers about dementia. Women are more likely to make lifestyle changes

(45%) or use vitamin supplements (37%) to manage symptoms. Although, more than half of all women surveyed were aware of prescription treatments such as menopausal hormonal therapy (MHT) and vaginal estrogen therapy, only 10% or less were currently using these methods. This suggests either lack of awareness or need for more education around the efficacy of these treatment options. Among the women who have tried MHT previously, 1/3rd have indicated that their healthcare provider recommended them to stop taking It and others cited fear of getting cancer or increasing their risk for heart attack or stroke. **Conclusion:** Understanding midlife women's needs will allow us to promote a national dialogue among patients, their health care providers, and policy makers to address knowledge gaps in screenings, care, and educational resources to ensure women live a healthy physical and emotional life.

Sources of Funding: This program was supported by Amgen, Astellas, Pfizer and TherapeuticsMD

S-17.

Associations of abdominal and intrathoracic fat depots with high-density lipoprotein metrics in midlife women: The SWAN Study

Alexis Nasr[1], Karen Matthews[1], Maria Brooks[1], Trevor Orchard[1], Dan McConnell[2], Jeff Billheimer[3], Emma Barinas-Mitchell[1], Norman Wang[1], Imke Janssen[4], Samar R. El Khoudary, PhD[1]. [1]University of Pittsburgh, Pittsburgh, PA; [2]University of Michigan, Ann Arbor, MI; [3]University of Pennsylvania, Philadelphia, PA; [4]Rush University Medical Center, Chicago, IL

Objective: Low high-density lipoprotein cholesterol (HDL-C) concentrations have been documented in individuals with visceral fat accumulation suggesting a contribution of visceral fat deposition to HDL metabolism. Postmenopausal women experience an alteration in body fat distribution of several ectopic adipose depots including the abdomen, the heart and the vasculature, compared to premenopausal women. The quality of HDL molecules may also be compromised during the menopause transition. Whether visceral abdominal and cardiovascular fat depositions at midlife are related to HDL quality measures, including HDL subclasses and contents of triglycerides and phospholipids or HDL function is not known. We aimed to assess whether visceral abdominal and cardiovascular fat depots are associated with HDL metrics in midlife women, and whether these associations differ by obesity status. We hypothesized that higher volumes of visceral abdominal and cardiovascular [epicardial fat (EAT), the fat within the pericardium; paracardial fat (PAT), the fat outside the pericardium; and perivascular aortic fat (PVAT)] fat depots are associated with a worse HDL profile [lower levels of HDL cholesterol efflux capacity (HDL-CEC), phospholipids (HDL-PL), and large HDL particles (HDL-P), higher levels of HDL- triglycerides (HDL-Tg), small HDL-P, and smaller overall HDL size] in midlife women. These associations will be more pronounced in obese women. **Design:** We evaluated 297 women (age: 51.1± 2.8 years, 67% White) with at least one fat assessment (visceral fat, EAT, PAT or PVAT) by computerized tomography and one HDL metric at a later visit in the Study of Women's Health Across the Nation (SWAN) HDL ancillary study [median time elapsed 1.95 (1.80, 2.12) years]. Multivariable generalized linear models were used to test the relationship of each fat depot with HDL metrics, separately. Effect modification of obesity [BMI <30 vs ≥30 kg/m^2] on the relationships between visceral fat depots and HDL metrics were tested in final models. **Results:** In the final models **(Table),** higher abdominal visceral fat, PAT and PVAT volumes were associated with lower levels of large HDL-P; higher abdominal and PAT volumes were associated with higher levels of small HDL-P and smaller overall HDL size, while higher abdominal and PVAT volumes were associated with lower HDL-C and HDL-PL. PVAT was the only ectopic fat to negatively associate with HDL-CEC. The associations between higher abdominal visceral adiposity with more small HDL-P levels, and higher PVAT with lower HDL-PL and large HDL-P levels were limited to non-obese women (p-value of interactions <0.05) **Conclusion:** Ectopic fat accumulation, particularly PVAT, may be linked to a dysfunction in HDL, which could relate to higher CVD in midlife women. Moreover, our results indicate that the relation between visceral fat and HDL metrics in women may differ by obesity status, such that fat deposition in certain locations may be associated with a worse HDL profile only in non-obese women.

Sources of Funding: SWAN HDL study has grant support from NIA (AG058690). SWAN has grant support from the NIH, DHHS, through the NIA, NINR and NIH ORWH (Grants NR004061; AG012505, AG012535, AG012531, AG012539, AG012546, AG012553, AG012554, AG012495). The SWAN Repository (U01AG017719). SWAN Heart has support from the NHLBI (grants HL065581, HL065591). SWAN Cardiovascular Fat Ancillary Study was supported by an award from the AHA Great River Affiliation Clinical Research Program: 12CRP11900031.

Multivariable associations visceral fat depots and each HDL metric[1,2]

	HDL-CEC (%)	Log HDL-Tg (mg/dL)	HDL-PL (mg/dL)	HDL-P(μmol/L)				HDL size (nm)	HDL-C (mg/dL)
				Total	Large (log)	Medium (log)	Small		
Abdominal Fat	-0.08 (0.04)	0.01 (0.02)	-1.70 (0.67)*	-0.05 (0.46)	-0.13 (0.03)*	-0.004 (0.06)	1.31 (0.49)*	-0.14 (0.03)*	-2.68 (0.84)*
EAT	-0.07 (0.04)	0.03 (0.02)	-0.26 (0.67)	0.13 (0.45)	-0.04 (0.03)	-0.03 (0.05)	0.94 (0.49)	-0.05 (0.03)	-0.76 (0.85)
PAT	-0.06 (0.05)	-0.0001 (0.02)	-0.88 (0.68)	0.14 (0.46)	-0.08 (0.03)*	-0.01 (0.05)	1.16 (0.50)*	-0.10 (0.03)*	-1.44 (0.85)
PVAT[3]	-0.10 (0.04)*	0.001 (0.02)	-1.30 (0.66)*	-0.47 (0.45)	-0.07 (0.03)*	0.08 (0.05)	0.29 (0.48)	-0.06 (0.03)	-1.94 (0.85)*

[1] β(SE) per standard deviation of log-visceral fat volume.
[2] Models adjusted for age, site, race, time elapsed between measures, economic hardship, physical activity, alcohol use, menopause status and log-triglycerides.
[3]Additionally adjusted for aortic length.
*** p<0.05**

S-18.

The Severity of Vasomotor Symptoms and Number of Menopausal Symptoms in Postmenopausal Women and Select Clinical Health Outcomes in the Women's Health Initiative Calcium and Vitamin D Randomized Clinical Trial

Matthew S. Nudy, MD[1], Xuezhi Jiang, MD, PhD[2,3], Aaron Aragaki[4], Andrew J. Foy[1], Jonathan Beurger[2], Anita Kelsey[5], Erin S. LeBlanc[6], Aladdin H. Shadyab[7], Robert A. Wild[8], Jean Wactawski-Wende[9], JoAnn E. Manson[10], Marcia L. Stefanick[11], John A. Robbins[12], Peter F. Schnatz[2,3]. [1]Cardiology, Penn State Hershey Medical Center, Hershey, PA; [2]ObGyn, Reading Hospital/Tower Health; Reading, PA., Reading, PA; [3]ObGyn, Sidney Kimmel Medical College, Philadelphia, PA; [4]Public Health Sciences, Fred Hutchinson Cancer Research Center, Seattle, WA; [5]Cardiology, Duke University, Durham, NC; [6]Center for Health Research, Kaiser Pemanente, Portland, OR; [7]Family Medicine and Public Health, University of California San Diego, San Diego, CA; [8]Colleges of Medicine and Public Health, University of Oklahoma Health Sciences Center, Oklahoma City, OK; [9]Social and Preventive Medicine, State University of New York at Buffalo, Buffalo, NY; [10]Preventive Medicine, Brigham and Women's Hospital/ Harvard Medical School, Boston, MA; [11]Stanford University School of Medicine, Palo Alto, CA; [12]UC Davis Medical Center, Davis, CA

Objective: The objective of this study was to evaluate whether vasomotor symptom (VMS) severity (none; mild; moderate or severe) and/or number of moderate/severe menopausal symptoms (nMS; none; 1 symptom; or ≥ 2 symptoms) were associated with clinical health outcomes, and whether calcium and vitamin D (CaD) supplementation modified the associated risks. **Design:** The Women's Health Initiative (WHI)-Calcium and Vitamin D (CaD) trial was a double blind, randomized, placebo-controlled study designed to test the effects of 400 IU of 25-hydroxyvitamin-D and 1000 mg of elemental calcium per day on incident hip fracture and other health outcomes in women aged 50-79 years. The outcomes of interest for this secondary analysis included hip fracture, colorectal cancer, invasive breast cancer, all-cause mortality, CaD global index (composite endpoint of the aforementioned events), coronary heart disease, stroke, cardiovascular death, and total cardiovascular disease. This study included 20,050 women with a median follow-up of 7 years. The MS included: hot flashes, night sweats, dizziness, heart racing or skipping beats, tremors, feeling restless or fidgety, feeling tired, difficulty concentrating, forgetfulness, mood swings, vaginal dryness, breast tenderness, headache or migraine, and waking up several times at night. Severity was measured with a questionnaire at trial baseline. Multivariable Cox proportional hazards regression tested the associations between VMS severity and number of menopausal symptoms (nMS) with health outcomes. Whether CaD supplementation modified any associations was assessed. An exploratory analysis examined the association between the severity of each individual MS and total CVD events. **Results:** We found no association between VMS (hot flashes and night sweats) severity and any health outcome. In contrast, nMS was significantly associated with risk for stroke (HR 1.41 95% confidence interval (CI) 1.04-1.91 for ≥ 2 MS vs. none; HR 1.19 95% confidence interval (CI) 0.88- 1.61 for 1 MS vs. none, p-trend=0.02) and total CVD (HR 1.37, 95% CI, 1.20-1.56 for ≥ 2 MS vs. none; HR 1.00, 95%CI, 0.87-1.15 for 1 MS vs. none p-trend < 0.001). When stratified by randomization status, CaD did not influence any association. The severities of many individual MS (i.e. night sweats, restless and fidgety, difficulty concentrating, dizziness; heart racing or skipping beats; feeling tired; forgetfulness) were associated with higher total CVD. **Conclusion:** Severity of VMS was not associated with any clinical event. However, having 2 or more moderate or severe MS was associated with increased risk for CVD and stroke events, but not other outcomes examined. Supplementation with calcium and vitamin D did not influence these findings. The number or type of moderate or severe MS, but not VMS alone, may be a marker for a higher risk of CVD.

Sources of Funding: The research on which this abstract is based was supported by R01 HL083326 (to Dr. Mackey) from the National Heart, Lung, & Blood Institute. The Women's Health Initiative (WHI) program is funded by the National Heart, Lung, and Blood Institute, National Institutes of Health, U.S. Department of Health and Human Services through contracts HHSN268201600018C, HHSN268201600001C, HHSN268201600002C, HHSN268201600003C, and HHSN268201600004C.

S-19.

Female Sexual Function and Urinary Incontinence: Six Month Follow-up after High-Intensity Focused Electromagnetic Procedure

Julene B. Samuels[1], Kimberly Evans, Dr[2]. [1]Julene B. Samuels, Prospect, KY; [2]Hillcroft Medical Clinic, Sugar Land, TX

Objective: Strong pelvic floor muscles (PFM) are essential for the correct functioning of the female genital and lower urinary system, since they support pelvic organs and help to facilitate sensation and arousal during intercourse. Nonetheless, due to menopause and other physiological changes, the PFM may become under-active because of decreasing strength. Weakness of PFM leads to pelvic floor dysfunctions such as loss of bladder control and impaired sexual function, which considerably influence women's physical and mental health. Fortunately, targeted PFM strengthening by the High-Intensity Focused Electromagnetic (HIFEM) procedure is able to effectively reverse loss of muscle strength. The aim of this study is to document long-term treatment response to non-invasive HIFEM-induced PFM strengthening for reduction of urinary incontinence (UI) and improvement in female sexual function. **Design:** This is a prospective multi-center open-label single-arm study. Thirty-one females of average age 49.8±9.9 years, who showed decreased interest in sexual activity accompanied with UI due to the PFM weakening, were recruited. Subjects received six 28-minute HIFEM treatments of the pelvic floor scheduled twice a week for three weeks. HIFEM intensity was increased up to 100% of the device's maximum output (2.5 Tesla) with regard to the patient's feedback. Primary outcomes were to assess favorable change in a score of standardized

questionnaires designed to evaluate UI and sexual function: International Consultation on Incontinence Questionnaire – Urinary Incontinence Short Form (ICIQ-UI SF); Female Sexual Function Index (FSFI); Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire short form (PISQ-12). Three follow-up visits were performed at 1, 3 and 6 months after the last treatment. Therapy comfort was assessed by the 7-point Likert scale, and adverse events were monitored during the entire study. Results were statistically analyzed by Freidman test followed by post-hoc Conover's comparisons (α=0.05). **Results:** Therapy was safe and patients found it comfortable. Out of 31 recruited subjects, 23 finished 1- and 3-month follow-up and 17 finished 6-month follow-up thus far. Results showed that UI symptoms and sexual function were both significantly improved when compared to the baseline. Initial ICIQ score decreased from 11.3±5.1 points to 4.5±3.1; 4.3±3.6; 5.0±4.4 at 1, 3 and 6 months respectively (P<0.001), while reaching an improvement rate of 56-62%. Subjects also reported considerably lower frequency of urine leakage when exercising or coughing. Average FSFI score of 22.1±6.8 points at baseline indicated female sexual dysfunction (inclusion threshold of 26.55 points), nevertheless it significantly (P<0.001) improved to 29.5±4.5; 30.0±4.1; 28.4±5.8 at 1, 3 and 6 months. The greatest improvement was seen in the domains lubrication, arousal and orgasm. The PISQ score also showed significant (P<0.001) increase from 31.9±6.8 points to 39.2±6.2; 40.3±5.3; 39.5±5.6 at 1, 3 and 6 months. Subjects improved most in emotive domain of PISQ questionnaire, meaning they in general reported more frequent orgasms, as well as increased sexual desire and excitement. Fluctuations of score between the follow-up visits were insignificant in all examined questionnaires. **Conclusion:** The present study confirms that the HIFEM procedure significantly improved quality of life of enrolled patients who were suffering from urinary incontinence as well as sexual dysfunction. Achieved results were seen to be sustained over time with slight, but clinically insignificant decline at 6-month follow-up. The relevance of this trend, as well as the necessity and specific interval of the re-treatment period in order to preserve treatment outcomes, is expected to be verified by upcoming 9-month and 12-month follow-up data.

Sources of Funding: This study is sponsored by BTL Industries Ltd. Registered trial on ClinicalTrials.gov (NCT03942484).

S-20.

Bioenergetic Markers and Cognition in Peri- and Postmenopausal Women

Rachel A. Schroeder, BS[1], Rebecca C. Thurston, PhD[2], Sruti Shiva, PhD[3], Garrett A. Williams, BA[1], Pauline M. Maki, PhD[4]. [1]Psychology, University of Illinois at Chicago, Chicago, IL; [2]Psychiatry, University of Pittsburgh, Pittsburgh, PA; [3]Pharmacology and Chemical Biology, University of Pittsburgh, Pittsburgh, PA; [4]Psychiatry, Psychology and OB/GYN, University of Illinois at Chicago, Chicago, IL

Objective: Complaints of forgetfulness increase and memory test performance decline from the premenopause to the perimenopause. Declines in memory after oophorectomy and during the natural menopause transition occur independently of chronological age. The factors contributing to these menopause-related changes in memory include sex steroid hormones and menopausal symptoms. At a cellular level, menopause-related changes in mitochondrial function are thought to play a role in these memory changes, although most evidence comes from rodent studies. One neuroimaging study in midlife women showed a decline in one aspect of mitochondrial function, platelet mitochondrial cytochrome oxidase (COX) activity, across the menopause in a small sample of women. They also found associations between COX activity, verbal memory performance, and brain hypometabolism in prefrontal and temporal cortices. Here we examine the association between a more extensive array of mitochondrial biomarkers and cognitive test performance in a larger sample of peri- and postmenopausal women. **Design:** Participants were enrolled in MsBrain, a cohort study of peri- and postmenopausal women (n=110, mean age 58.56 +/- 4.38 years, 77.3% White). Women completed a cognitive test battery including tests of verbal learning and memory (California Verbal Learning Test-2, CVLT), spatial reasoning (Card Rotations), working memory (Symbol Digit Modalities Test, Letter-Number Sequencing subtest of the WAIS), verbal recall (Verbal Fluency), and global cognition (Montreal Cognitive Assessment, MOCA). Seahorse extracellular flux analysis was used to obtain measures of non-mitochondrial oxygen consumption, baseline respiratory rate, maximal respiratory capacity, basal glycolytic rate, proton leak, mitochondrial oxidation production, and ATP-linked respiration in circulating platelets. Linear regression models were used to evaluate the correlation of mitochondrial functional markers on cognition with covariates age, education, race, and body mass index (BMI). **Results:** Higher non-mitochondrial oxygen consumption, baseline respiratory rate, maximal respiratory capacity, basal glycolytic rate, proton leak, ATP-linked respiration in circulating platelets, and mitochondrial oxidant production were each associated with better performance on a range of cognitive test scores, including verbal learning (Total CVLT, β=.14, SE=.05, p<.01), organizational strategies to enhance learning (CVLT Total Cluster Weighted β=17, SE=.18, p<.05; CVLT Short Delay β=.04, SE=.02, p<.05; LNS, β =.04, SE=.02, p<.05; Card Rotations, β=.44, SE=.18, p<.05) and memory (MOCA, β=.03, SE=.01, p<.05). **Conclusion:** In peri- and postmenopausal women, markers of mitochondrial function were associated with cognitive performance on measures of verbal learning, verbal memory, organizational strategies that support verbal learning and memory, verbal fluency, and spatial ability. Higher mitochondrial function was most consistently associated with the use of executive, prefrontal-dependent strategies. The pattern and direction of findings across mitochondrial markers suggests a compensatory shift in mitochondrial function to non-mitochondrial function to support cognitive function as women age.

Sources of Funding: Supported by NIH RF1AG053504 (Thurston & Maki) and the National Science Foundation Graduate Research Fellowship Program 1842398 (Schroeder)

S-21.

NT-814, a Non-Hormonal Dual Neurokinin 1,3 Receptor Antagonist Markedly Improves Hot Flashes in Post-Menopausal Women; Results of a Randomised, Double-Blind, Placebo-Controlled Study

James Simon, MD[3,4], Richard Anderson[2], Elizabeth Ballantyne, BSc[1], Hadine Joffe, MD PhD[5,6], Mary Kerr, PhD[1], Mary Ann Lumsden, MB BS MD[7], Nicholas Panay, MB BS MRCOG[8], Susan Seymore, BSc[1], Mike Trower, PhD[1], Stephen Pawsey[1]. [1]KaNDy Therapeutics Ltd, Stevenage, United Kingdom; [2]University of Edinburgh, Edinburgh, United Kingdom; [3]George Washington University, Washington, DC; [4]IntimMedicine, Washington, DC; [5]Brigham and Womens Hospital, Boston, MA; [6]Harvard Medical School, Boston, MA; [7]University of Glasgow, Glasgow, United Kingdom; [8]Imperial College, London, United Kingdom

Objective: Hot flashes (HF), caused by declining estrogen in menopausal women, are common and debilitating. Hormone therapy is effective but carries risks and may be contraindicated. Biological and clinical evidence shows a modulatory role for neurokinin (NK) receptor antagonists acting primarily via hypothalamic KNDy (kisspeptin, NK, dynorphin) neurons on HF. NT-814 is an oral non-hormonal dual NK1,3 receptor antagonist which showed marked efficacy on HFs in a pilot study in post-menopausal (PM) women. This Phase-2b trial (SWITCH-1) was undertaken to further evaluate efficacy and safety and to establish the optimum dose for Phase 3 studies. **Design:** SWITCH-1 was a double-blind, placebo-controlled, adaptive-randomization, dose-finding trial in 199 PM women. After a 2-week single-blind placebo run-in to establish symptom stability, women (40 to 65 years) with ≥7 moderate and/or severe HF/day were randomized to 12 weeks of once daily treatment with placebo or one of 4 doses of NT-814: 40 mg, 80 mg, 120 mg, 160 mg. Frequency and severity of HF were recorded in electronic diaries twice daily. Data were analysed using a mixed model repeated measures analysis, with treatment, baseline frequency and region as covariates; supportive non-parametric analyses (Wilcoxon) were undertaken to account for outliers. Adverse events (AEs), vital signs, hematology and clinical chemistry tests and ECGs were recorded periodically. **Results:** HF frequency was reduced in all treatment groups, including placebo. HF reductions were significantly greater than placebo with the two higher NT-814 doses at most time-points, as soon as week 1 of treatment, with benefit maintained for the full 12 weeks. The 40 and 80 mg doses were not significantly different from placebo. Least squares (LS) mean reductions from baseline in moderate/severe HF per day for Weeks 1, 4 and 12 are shown in Table 1. The significant difference for the 160 mg dose at Week 12 in the non-parametric (Wilcoxon) analysis shows the effect of a high outlier on the mean in this group. Average HF severity also improved in a dose-related manner, with greater reductions vs placebo in the 2 higher NT-814 doses. Similarly, the hot flash score (frequency x severity) was significantly improved for the 120 and 160 mg doses at each assessment time, showing a reduction in overall hot flash burden. NT-814 was well-tolerated; most AEs were mild or moderate and there were no serious AEs related to treatment. Possible treatment related AEs at the higher doses were fatigue and somnolence which were both reported infrequently. There were no NT-814-related increases in liver enzymes. **Conclusion:** NT-814, a once daily non-hormonal dual NK 1,3 antagonist, at doses of 120 & 160 mg reduced the frequency and severity of HF and significantly reduced overall hot flash burden in PM women. NT-814 was well tolerated, with a safety profile that supports further evaluation in Phase 3 trials.

Sources of Funding: kaNDy Therapeutics Ltd

Table 1. Change from Baseline in Moderate and Severe HF Frequency

	Placebo N=47	40 mg N=31	80 mg N=17	120 mg N=52	160 mg N=52
Week 1					
LS mean (95% CI)	-1.4 (-2.4, -0.4)	-1.7 (-2.9, -0.6)	-1.4 (-3.01, 0.17)	-3.2 (-4.1, -2.3)	-3.1 (-4.0, -2.2)
LS mean difference (95% CI)	-	-0.35 (-1.86, 1.17)	-0.03 (-1.89, 1.84)	-1.80 (-3.12, -0.48)	-1.69 (-3.01, -0.37)
p-value	-	0.6494	0.9779	0.0079	0.0125
Wilcoxon p-value	-	0.5233	0.2639	0.0009	0.0003
Week 4					
LS mean (95% CI)	-2.8 (-4.3, -1.3)	-4.3 (-6.1, -2.5)	-4.1 (-6.5, -1.7)	-6.7 (-8.1, -5.4)	-5.4 (-6.8, -4.0)
LS mean difference (95% CI)	-	-1.52 (-3.83, 0.78)	-1.29 (-4.11, 1.53)	-3.93 (-5.94, -1.92)	-2.63 (-4.66, -0.59)
p-value	-	0.1946	0.3682	0.0002	0.0115
Wilcoxon p-value	-	0.1677	0.0164	<0.0001	<0.0001
Week 12					
LS mean (95% CI)	-4.8 (-6.48, -3.15)	-6.5 (-8.49, -4.46)	-5.6 (-8.32, -2.85)	-7.8 (-9.31, -6.21)	-6.6 (-8.24, -4.95)
LS mean difference (95% CI)	-	-1.67 (-4.28, -0.95)	-0.77 (-3.97, 2.44)	-2.95 (-5.22, -0.67)	-1.78 (-4.12, 0.56)
p-value	-	0.2097	0.6369	0.0116	0.1346
Wilcoxon p-value	-	0.3084	0.1756	0.0043	0.0023

S-22.

Effect of hormone therapy on lipoprotein subfractions in early and late postmenopausal women

Intira Sriprasert[1], Stephanie Kim[1], Naoko Kono[1,2], Roksana Karim[1,2], Howard N. Hodis[1,2], Hooman Allayee[1], Ronald Krauss[3], Wendy J. Mack[1,2]. [1]Department of Preventive Medicine, University of Southern California, Los Angeles, CA; [2]Atherosclerosis Research Unit, University of Southern California, Los Angeles, CA; [3]Department of Pediatrics, University of San Francisco, San Francisco, CA

Objective: Specific lipoprotein particle subfractions (LPs) have been associated with atherosclerosis risk. In the Early versus Late Intervention Trial with Estradiol (ELITE), atherosclerosis progression was reduced among women randomized to hormone therapy (HT) <6-years from menopause (early-postmenopause) but not in women ≥10-years past

menopause (late-postmenopause). We tested HT compared with placebo effects on LPs overall and by time-since-menopause. **Design:** Standard lipids (total triglycerides (TG), LDL-cholesterol (C) and HDL-C) and 21 LPs including various size subfractions of low-density lipoproteins (LDL), intermediate-density lipoproteins (IDL), very-low-density lipoproteins (VLDL) and high-density lipoproteins (HDL) were measured using ion mobility in fasting blood samples from ELITE participants every 6-months over a median follow-up of 4.8-years. Mixed effects linear regression with a participant-level random intercept evaluated HT effects on lipids and LPs compared with placebo adjusted for baseline levels. Analyses were conducted among total, early and late postmenopausal strata. Least square mean differences were compared between HT and placebo. **Results:** 564 women (242 early, 323 late postmenopause) with on-trial standard lipids and LPs contributed 4989 visits to this analysis. Compared with placebo, HT significantly increased TG, HDL-C, small LDL, and large HDL, whereas HT significantly decreased LDL-C, small VLDL, large IDL, large and very small LDL, and LDL peak diameter. HT initiated in early- and late-postmenopause showed consistent effects in reducing LDL-C, small VLDL, large LDL, and LDL peak diameter, while increasing TG, HDL-C and large HDL particles. Uniquely, HT initiated in early-postmenopause increased small LDL particles. **Conclusion:** HT and timing of initiation relative to menopause have complex effects on LPs that are not reflected by standard lipid levels. Whether these contribute to the differing effect of HT on subclinical atherosclerosis progression according to time of initiation remains to be determined.

Sources of Funding: NIH (R01-AG024154, R01-AG059690); Quest Diagnostics provided ion mobility measurements.

Mean difference in standard lipids and lipoprotein subfractions between postmenopausal women using hormone therapy compared with placebo among total sample and by time-since-menopause.

	Total		Early postmenopause		Late postmenopause	
	Mean difference (95%CI)	p	Mean difference (95%CI)	p	Mean difference (95%CI)	p
TG	5.50 (1.78,9.21)	0.0009	6.49 (0.42,12.55)	0.03	4.81 (0.17,9.44)	0.01
LDL-C	-6.69 (-9.74,-3.65)	<.0001	-6.90 (-11.50,-2.30)	0.003	-6.46 (-10.53,-2.39)	0.002
HDL-C	2.56 (1.38,3.73)	<.0001	2.24 (0.50,3.98)	0.01	2.77 (1.18,4.36)	<.0001
Small VLDL	-3.43 (-5.15,-1.72)	<.0001	-2.93 (-5.56,-0.30)	0.03	-3.74 (-6.01,-1.47)	0.0009
Large IDL	-4.13 (-8.06,-0.21)	0.03	-4.01 (-10.02,2.00)	0.19	-4.23 (-9.48,1.03)	0.07
Large LDL	-25.79 (-37.93,-13.64)	<.0001	-33.82 (-52.28,-15.35)	0.0003	-19.28 (-35.50,-3.05)	0.01
Small LDL	11.66 (1.46,21.86)	0.01	18.97 (2.42,35.52)	0.008	6.22 (-6.49,18.92)	0.30
Very small LDL	-2.52 (6.2,1.18)	0.03	-3.36 (-8.75,2.04)	0.18	-1.8 (-6.90,3.3)	0.08
Large HDL	239.82 (112.26,367.37)	<.0001	279.48 (95.83,463.14)	0.0008	204.68 (28.62,380.75)	0.02
LDL peak size	-0.86 (-1.28,-0.44)	<.0001	-1.14 (-1.79,-0.48)	0.0003	-0.66 (-1.21,-0.11)	0.02

Table displays statistically significant treatment group differences (10 of 21 lipoprotein subfractions measured). *Least square mean difference (hormone therapy minus placebo) with 95% confidence interval; p-value from linear mixed effects model testing hormone therapy effect on each lipoprotein subfraction. TG=total triglyceride; LDL-C = low density lipoprotein cholesterol; HDL-C = high density lipoprotein cholesterol; VLDL=very low density lipoprotein; IDL=intermediate density lipoprotein; Large LDL 224-250Å; Small LDL = 204.9-214.1Å; Very small LDL = 180-199Å

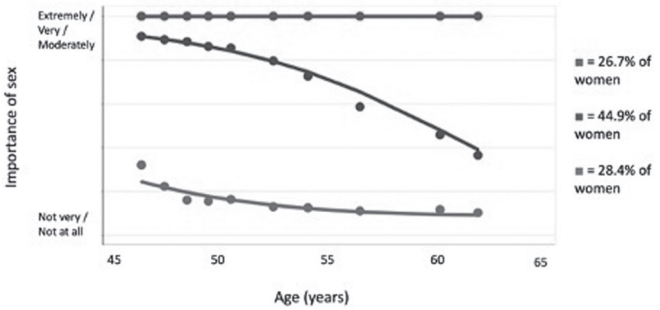
S-23.

How important is sex to women during midlife?

Holly N. Thomas, MD[1], Nancy E. Avis, PhD[2], Rachel Hess, MD MS[3], Rebecca C. Thurston, PhD[4]. [1]Department of Medicine, University of Pittsburgh, Pittsburgh, PA; [2]Social Sciences and Health Policy, Wake Forest University, Winston-Salem, NC; [3]Health Systems Innovation and Research, University of Utah, Salt Lake City, UT; [4]Psychiatry, University of Pittsburgh, Pittsburgh, PA

Objective: Importance of sex is highly correlated with sexual function among midlife women. Longitudinal studies allow us to examine how importance of sex changes as women age. In a large longitudinal cohort study, we evaluated whether women followed distinct trajectories in importance of sex throughout midlife. We also defined factors that predicted which trajectory women followed. **Design:** The Study of Women's Health Across the Nation (SWAN) recruited pre- and perimenopausal women from different racial and ethnic backgrounds to complete 14 visits involving interviews, questionnaires, blood draws, and biometric measures. The primary outcome in this analysis was importance of sex, dichotomized importance of sex as not at all / not very versus moderately / quite / extremely. We used trajectory analysis to identify distinct patterns in importance of sex over time. Then we used multinomial logistic regression to identify baseline factors related to membership in each trajectory (race/ethnicity, education, partner status, BMI, blood pressure, menopause status, hormones, depression symptoms, perceived stress, antidepressant use, sexual orientation, sexual satisfaction, pelvic pain, vaginal dryness, hot flashes). Factors significant at $p<0.10$ were included in a multivariable analysis, in which alpha was set at <0.01 to adjust for multiple comparisons. **Results:** Among 3257 women, we identified 3 distinct trajectories in importance of sex with aging (Figure). For half of women (45%), sex was important early in midlife and became less so over time. For a quarter of women (27%), sex remained highly important to them throughout midlife, and for another quarter (28%), sex was of low importance throughout midlife. Factors that predicted membership in these groups included race/ethnicity, education, depression, and sexual satisfaction. Specifically, Black women were more likely to rate sex as important for the duration of midlife, while Chinese and Japanese women were more likely to rate sex as not important or to see drops in importance. Women with depression symptoms were more likely to have low importance or see drops in importance of sex. Better sexual satisfaction was associated with maintained high levels of importance of sex over time. Finally, higher educational attainment was associated with sustained high importance of sex throughout midlife. **Conclusion:** In constrast to prior literature reporting that importance of sex decreases as women move through midlife, we found that for a quarter of women, sex remains highly important to them throughout midlife. Women with fewer depression symptoms, higher education, higher sexual satisfaction, and Black race are more likely to report high importance of sex.

Sources of Funding: Supported by NIH, DHHS, NIA, NINR and NIH Office of Research on Women's Health (ORWH) (Grants U01NR004061; U01AG012505, U01AG012535, U01AG012531, U01AG012539, U01AG012546, U01AG012553, U01AG012554, U01AG012495). Content is solely the responsibility of the authors and does not necessarily represent the official views of NIA, NINR, ORWH or NIH.



Trajectories in importance of sex across midlife

POSTER PRESENTATIONS

P-1.

The Effect of Early Menopause on the Development of Osteoporosis in the Canadian Longitudinal Study on Aging.

Alice Buwembo, MD, MSc[1], Alexandra Mayhew, PhD[2], Nazmul Sohel, PhD[3], Lauren Griffith, PhD[2,3], Parminder Raina, PhD[2,3], Alison Shea, MD, PhD, FRCSC, NCMP[1]. [1]Obstetrics & Gynecology, McMaster University, Hamilton, ON, Canada; [2]Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, ON, Canada; [3]Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, ON, Canada

Objective: The objective of this study is to describe the effect of premature and early menopause on bone mineral density (BMD) in a large representative cohort of women living in Canada. **Design:** Cross-sectional baseline data from the Canadian Longitudinal Study on Aging (CLSA) was used. Female participants of the CLSA were aged 45-85 at time of recruitment (Sept 2011 – Dec 2015, N=12339). The goal of this study was to describe the BMD profiles (T-score for hip) among women with premature ovarian insufficiency ([POI], final menstrual period (FMP) occurring before age 40 years, N=374) and early menopause (FMP age 40-45, N=1396), as compared to women with a normal age of menopause (N=8067) and those having undergone hysterectomy (N=2502). Additional bio-psycho-social characteristics that may mediate bone health and the development of osteoporosis were explored. **Results:** The average age of women at the time of baseline assessment was 65 years. Compared to those who experienced menopause at a normal age, women with POI had a lower rate of secondary school and post-secondary graduation (60.28% vs. 76.64%) and were more likely to earn less than CDN $20,000 annually (14.44% vs. 6.09%). Women in the POI group were more likely to be obese (39.78% vs. 26.68%), have decreased physical activity (24.88% vs. 19.22%), and were more likely to be current smokers (14.16% vs. 6.12%). Although there was no difference in hip BMD between groups, women in the POI group were more likely to have used osteoporosis drugs (11.39% vs. 7.63%) and have a higher rate of self-reported osteoporosis (21.91% vs. 16.65%). After adjustment for confounding, POI was found to increase the likelihood of developing osteoporosis (OR 1.59). Other significant factors were insufficient calcium intake (OR 1.47) and current smoking (OR 1.63). Protective factors against development of osteoporosis included obesity (OR 0.41) and current HRT use (OR 0.65), but not duration of HRT use. **Conclusion:** These results confirm findings from smaller cohorts illustrating that POI is a significant risk factor for the development osteoporosis. Our findings also suggest associations between social determinants of health and an earlier age at menopause, including education, income, diet, obesity, and smoking. Increasing understanding of the sequelae associated with an earlier loss of ovarian function will aid in targeting earlier screening and intervention strategies for women in Canada and abroad.

Sources of Funding: Canadian Institutes of Health Research (CIHR)

P-2.

A MsFLASH Investigation of Self-reported Menopausal Palpitations Distress

Janet S. Carpenter, PhD, RN, FAAN[1], James E. Tisdale, PharmD, FCCP, FAPhA, FNAP, FAHA, FACC[2,1], Chen X. Chen, PhD, RN[1], Richard Kovacs, MD[1], Joseph Larson, MS[3], Katherine Guthrie, PhD[3], Kristine E. Ensrud, MD, MPH[4,5], Katherine M. Newton, PhD[6], Andrea Z. LaCroix, PhD[7]. [1]Indiana University, Indianapolis, IN; [2]College of Pharmacy, Purdue University, Indianapolis, IN; [3]Fred Hutchinson Cancer Research Center, Seattle, WA; [4]University of Minnesota, Minneapolis, MN; [5]Minneapolis VAHCS, Minneapolis, MN; [6]Kaiser Permanente Washington Health Research Institute, Seattle, WA; [7]University of California, San Diego, La Jolla, CA

Objective: To describe the degree of menopausal palpitations distress and its demographic, clinical, symptom, and quality of life (QOL) correlates. Palpitations are reported by 29% to 50% of peri- and postmenopausal women. Little is known about palpitations distress or its correlates. **Design:** Analysis of existing, baseline, data from peri- and post-menopausal women, aged 42 to 62, who participated in the Menopause Strategies – Finding Lasting Answers for Symptoms and Health (MsFLASH) clinical trials 1, 2, and 3 testing interventions for vasomotor symptoms (n=759). Degree of distress from "heart racing or pounding" was self-reported over the past two weeks as "not at all", "a little bit", "moderately", "quite a bit", or "extremely". Other measures included self-report forms, clinic-verified body mass index, vasomotor symptom diaries, and validated symptom and QOL tools. **Results:** The percentage who reported palpitations distress was 19.6% to 33.5% in the three trials or 25.0% overall. Distress from palpitations was rated "a little bit" by 15.7% to 25.0% in the three trials (18.6% overall), "moderately" by 3.6% to 6.8% (5.0% overall), and "quite a bit" or "extremely" by 0.4% to 2.3% (1.5% overall). Multivariate analysis showed the odds of reporting palpitations distress was lower in past and current smokers relative to never-smokers, lower with every 5 kg/m^2 higher body mass index, and higher with every 5 point worse insomnia, 5 point worse depression, 5 point worse perceived stress, and 1 point worse menopausal QOL. **Conclusion:** Among symptomatic menopause women, palpitations distress is common and associated with demographic, clinical, symptom, and QOL factors. These findings can be used for screening purposes as well as to test therapeutic interventions in groups of women reporting palpitations distress.

Sources of Funding: This research was made possible, in part, with support from the Indiana Clinical and Translational Sciences Institute funded, in part by Grant Number UL1TR002529 and KL2 TR002530 from the National Institutes of Health, National Center for Advancing Translational Sciences, Clinical and Translational Sciences Award. The MsFLASH studies were funded by the National Institutes of Health as a cooperative agreement issued by the National Institute on Aging (NIA), the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), the National Center for Complementary and Alternative Medicine (NCCAM), the Office of Research on Women's Health (ORWH), and grants U01AG032656, U01AG032659, U01AG032669, U01AG032682, U01AG032699, and U01AG032700 from the NIA. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

P-3.

The effect of menopause on metabolic syndrome: Cross-sectional results from the Canadian Longitudinal Study on Aging

Marie K. Christakis, MD, MPH[1,2], Haroon Hasan, BSc, MPH[3], Leanne De Souza, PhD[1,2], Lindsay Shirreff, MD, MSc(HQ)[4,2]. [1]Obstetrics & Gynecology, St. Michael's Hospital, Toronto, ON, Canada; [2]Obstetrics & Gynecology, University of Toronto, Toronto, ON, Canada; [3]Epi Methods Consulting, Toronto, ON, Canada; [4]Obstetrics & Gynecology, Mount Sinai Hospital, Toronto, ON, Canada

Objective: We examined data on women surveyed in the Canadian Longitudinal Study on Aging (CLSA) to evaluate whether menopause is an independent risk factor for the development of metabolic syndrome (MetS) or its components, including hypertension, central obesity, dyslipidemia or elevated glycated hemoglobin. **Design:** We conducted a cross-sectional analysis on women aged 45-85 years old that participated in the baseline data of the CLSA Comprehensive Cohort collected from 2012 to 2015. We used modified Poisson regression with robust error variance to estimate the crude and adjusted relative risks of MetS in postmenopausal women compared to premenopausal women. **Results:** Among 12,611 women analyzed, 10,035 (79.6%) had undergone menopause and 2,576 (20.4%) were premenopausal. Postmenopausal women were more likely to meet criteria for MetS compared to premenopausal women (32.6% vs. 20.5%, $p<0.001$). Using the MetS criteria with a lower waist circumference threshold, the prevalence of MetS was higher at 38.2% among postmenopausal women and 23.2% among premenopausal women ($p<0.001$). After adjusting for age, Body Mass Index and other covariates, the occurrence of menopause was not associated with a significantly higher relative risk of MetS, using the unified criteria for MetS (aRR 1.09 [95% CI: 0.99 to 1.19]). However, women with menopause had a significantly higher relative risk of MetS when using criteria with a lower waist circumference (aRR 1.10 [95% CI: 1.01 to 1.19]). Menopause was also associated with a higher risk of impaired glucose tolerance (aRR 1.42 [95%CI: 1.26-1.59]), elevated blood pressure (aRR 1.12 [95%CI: 1.03-1.21]) and elevated triglycerides (aRR 1.17 [95%CI: 1.08-1.26]). **Conclusion:** Menopause is associated with an increased risk of MetS, independent of age. Lifestyle-interventions targeted at women with MetS are known to prevent type 2 diabetes mellitus and cardiovascular risk. Perimenopause may be an important preventative care opportunity to assess metabolic risk factors and improve health and longevity of Canadian women.

Sources of Funding: This work was funded by a New Investigator Grant provided to Marie Christakis by the St. Michael's Hospital Department of Obstetrics & Gynaecology

P-4.

Resident Physician Impressions of Menopause Core Content Delivered by Podcast

Amanda Clark[1,2], Tovi Anderson[2], Neon Brooks[1], Melanie Francisco[1], Kimberly Vesco, MD, MPH[1,2]. [1]Kaiser Permanente Center for Health Research, Portland, OR; [2]Kaiser Permanente Northwest, Portland, OR

Objective: Currently, there is a dearth of resident training about management of menopause symptoms, leading to undertreatment of symptomatic patients. Using a flipped classroom design, we created a curriculum consisting of a 6-episode podcast and a case-based classroom session containing practical, evidence-based content to provide internal medicine (IM), family medicine (FM) and obstetrics and gynecology (OBGYN) residents with the knowledge needed to counsel women and prescribe therapy for menopausal symptoms. Elsewhere, we reported on the success of this curriculum at improving resident knowledge and comfort in managing menopause. Here, we report on residents' assessment of the usefulness of a podcast to deliver evidence-based content. **Design:** We developed 6 podcast episodes, 13-21 minutes in length, that could be streamed from a dedicated website which also provided transcripts with topic outlines and references. The podcast, entitled *Practice Pearls: Menopause*, was also available through Apple and Google Podcasts. The content was based on clinical practice guidelines. Topics included counseling women and prescribing hormone therapy (HT) and non-HT therapy for vasomotor and genitourinary symptoms, stopping HT, and abnormal vaginal bleeding. The 2-hour cased-based classroom session provided visual content, such as charts and photographs of vulvar changes, and an opportunity for case discussion. Target learners were 49 IM residents, 48 FM residents and 28 OBGYN residents at Oregon Health & Science University in the 2019-2020 academic year. The residency program directors approved the curriculum and integrated it into regularly-scheduled didactic sessions. Residents were assigned podcast listening 4-6 weeks before a classroom session. At the end of the classroom session, residents were asked to complete an electronic survey, administered via REDCap, that assessed their use of the podcast and their impressions of the convenience and effectiveness of the curriculum. No incentives were provided for survey completion. Per IRB review, informed consent was not required. **Results:** The survey was completed by 66 (52.8%) of the eligible residents. Fifty-seven (86.4%) of these attended a case-based session. Of the 6 podcast episodes, 53.0% listened to the 1st episode; fewer listened to subsequent episodes. Overall, 25.8% reported listening to all episodes, 39.4% to some but not all, and 34.8% to none of the episodes. The devices used for listening to the podcast were mobile phones (74.4%), computers (30.2%), and tablets (4.7%). The platforms for podcast streaming were the website (65.1%), Apple (30.2%) and Google Podcasts (0.0%), and other (4.7%). Of the 43 residents who listened to some of or all episodes, two-thirds reported that the podcast was a convenient way to learn the content and was more convenient than an equivalent amount of reading (Table). Slightly fewer agreed that the podcast was an effective method for learning. Most respondents approved of the length and detail of the podcast content. The most common locations for listening were at home (60.5%), work (14.0%) and while commuting (55.8%). Many residents listened while performing another activity; 9.3% listened while exercising, 44.2% while driving, 34.9% while doing other computer-based work and other (14.0%). **Conclusion:** For some residents, podcasts may be a convenient and effective way to gain knowledge. While a podcast provides ubiquitous and mobile access to important information, one-third of residents in our cohort did not listen to any of the podcast episodes. It is unclear if this was due to competing demands for their time, lack of interest, or lack of comfort with the modality.

Sources of Funding: Pfizer Independent Grant for Learning and Change #42360015

Resident Podcast Feedback

	Agree	Neutral	Disagree
The podcast format was:			
A convenient way to learn this content	65.1%	25.6%	9.3%
An effective way to learn this content	53.5%	34.9%	11.6%
Learning via podcast was:			
More convenient than equivalent amount of reading	69.5%	14.0%	16.3%
More effective than equivalent amount of reading	55.8%	30.2%	14.0%
	Too detailed	Just right	Insufficient
Overall podcast content judged as:	25.6%	74.4%	0
	Too long	Just right	Too short
Individual episode duration judged as:	48.8%	51.2%	0

P-5.

A Novel Consumer Based Product for Vasomotor Symptoms (VMS) of Menopause; *Prototype Trial*.

Alyssa Dweck, MS MD FACOG[1,2]. [1]Gynecology, CareMount Medical, Scarsdale, NY; [2]OB/GYN, New York Medical College, Valhalla, NY

Objective: A user experience trial was conducted from a single site office based gynecology practice to assess a novel and newly patented, over the counter (OTC) and direct to consumer (DTC) genital device to manage troublesome VMS during the peri and menopausal period. Professionally manufactured (in USA) prototypes were used to assess effectiveness, comfort, ease of use, and general user experience. The purpose of this trial was to provide feedback to modify and implement any improvements for the prototype prior to commercialization **Design:** Ten female volunteers were invited participated. Participants consisted of all comers with self-reported moderate to severe VMS. Each was provided with identical written/pictorial product usage instructions. After X uses, participants were asked to complete a post-use questionnaire. The patented device is an inverted heart shaped vulvar pad measuring approximately 2.25″ in longest dimension. It is composed of a water based polymer in clear gel sandwiched/encased in

micro porous polyethylene. The pad is placed in the user's undergarment /panty with a thin adhesive strip (similar to a pantiliner) to abut the clitoris and labia while specifically avoiding the urethra. The well-established mechanism of action involves evaporation of water from the gel polymer upon touching the warm vulva, creating an overwhelming sensation of cool for the wearer. The user's body/skin temperature is not affected. Users were instructed to use the device as often as they needed, day and/or night. Multiple devices were provided to each participant. Each device was packaged in a foil pouch, disposable and required no refrigeration or special preparation. Users were compensated for participation but were unaware of compensation offering until after participation. All data was HIPPA compliant. **Results:** Female participants ranged in age from 43-57. 100% of users found the device easy to use, comfortable and/or unnoticeable in the panty, and cool immediately on contact. The sensation of cooling was noted immediately on contact by 10/10 users. The 10th user claimed no cooling on sensation but noted that in retrospect, she had a systemic fever unrelated to VMS. The duration of cooling lasted up to 5-6 hours per pad. 80% (8/10) users claimed VMS improved notably during sleep when the device was placed prior to bed. 2/10 users claimed VMS improved notably during the day. All users were willing to retry the product in future and all noted the concept and design of the device was acceptable. 100% of participants were satisfied with their product experience. There were no adverse experience reports as a result of device use. No participants had a negative criticism of the prototype on exit interview and discussion **Conclusion:** This OTC and DTC product offers a novel, safe, easy to use, disposable and discreet option for women to manage VMS. This device satisfies an unmet need for women to manage VMS and provides both consumers and health care professionals a novel nonsystemic, non-hormonal offering for symptom management. It is appropriate for use in women with breast and other hormone sensitive cancers and is safe to use in conjunction with medication, hormones, herbal products and lifestyle modification. This trial provided the necessary information for the inventors to modify and perfect the prototype with the manufacturer, confirm the novelty and positive consumer acceptance of such a device, market DTC appropriately and to launch expeditiously and in a streamline fashion.
Sources of Funding: This project is not supported by the pharmaceutical or device industry.

P-6.

Qualitative Study of the Burden of Vasomotor Symptoms Associated With Menopause and Content Validity of Two PROMIS Sleep Measures in Menopausal Women

Marci English[1], Boyka Stoykova[2], Christina Slota[3], Lynda Doward[4], Emad Siddiqui[5], Rebecca Crawford[4], Dana DiBenedetti[3]. [1]Astellas Pharma Inc., Northbrook, IL; [2]Astellas Pharma Inc, Surrey, United Kingdom; [3]RTI Health Solutions, Research Triangle Park, NC; [4]RTI Health Solutions, Manchester, United Kingdom; [5]Astellas Pharma Inc, Leiden, Netherlands

Objective: Vasomotor symptoms (VMS) associated with menopause (hot flashes, night sweats) negatively impact quality of life and sleep. Patient-Reported Outcomes Measurement Information System (PROMIS) sleep measures have been validated in the general population and those with sleep issues but not in women with menopause-associated VMS. We sought to evaluate the impact of VMS, especially on sleep patterns, and establish content validity of PROMIS Short Form Sleep-Related Impairment 8a and Sleep Disturbance 8b measures in menopausal women with moderate/severe VMS. **Design:** Cross-sectional, in-person, 60-min, qualitative interviews were conducted in the US (Dallas, TX; Chicago, IL) and EU (Manchester, UK; Paris, France) with women aged 40-64 years experiencing moderate/severe VMS (≥35/wk). The main outcome measures were patient-reported impact of VMS based on concept elicitation and content validity of PROMIS 8a/8b via cognitive debriefing. **Results:** Thirty-two women (16 US; 16 EU) participated. A majority (US 93.8%; EU 93.8%) said VMS affected their sleep; specifically, they had sleep interrupted by physical discomfort (eg, sweating, overheating) and difficulty returning to sleep. Sleep disturbance was the most bothersome aspect of VMS (US 75%; EU 50%). Menopause-associated VMS led women to lift bed covers on/off and to change clothes, wash bedding, shower, and apply deodorant/perfume more often. VMS also affected next-day work productivity, mood, relationships, daily activities, concentration, social activities, and physical health. Participants found PROMIS sleep measures easy to understand and answer and relevant to evaluating their sleep pattern. On PROMIS 8a (sleep-related impairment), ≥50% of US respondents said VMS had an impact ranging from a little bit to very much on alertness, tiredness, daytime problems due to poor sleep, and daytime sleepiness; 50% of EU respondents said VMS at least somewhat affected alertness, concentration, irritability, and ability to get things done because of daytime sleepiness. PROMIS 8b (sleep disturbance) items most affected by VMS were "trouble staying asleep" and "sleep quality was restless." **Conclusion:** VMS associated with menopause significantly interfere with sleep and next-day functioning (eg, work productivity), supporting assessment of sleep outcomes in studies evaluating treatment of VMS. Women with VMS found that the PROMIS short form sleep measures 8a/8b assessed constructs important to management of menopause-associated VMS.
Sources of Funding: Interviews were conducted and analyzed by RTI Health Solutions (Research Triangle Park, NC), and medical writing and editorial support were provided by Lauren A. Cerruto and Diane M. Sloan, PharmD, of Echelon Brand Communications, LLC (Parsippany, NJ), an OPEN Health company. Both were funded by Astellas Pharma, Inc.

P-7.

Perception of Menopause in South America

Vivian L. Ernst - Baez, MD, Gloria Bachmann, Sonal Grover, MD. Women's Health Institute, Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ

Objective: Despite social media connecting global citizens and unifying many beliefs and norms, cultural and regional customs and expectations still remain in many areas, including those that pertain to the menopause. This review sought to identify the evidence found in PubMed to understand the cultural perception about menopause in women in South American (SA) countries. **Design:** This abstract only considered studies found on the PubMed website in independent countries of SA during May 2020. All territories on this continent were excluded from the search. The inclusion criteria other than the name of the country included "Menopause", and "Menopause" associated with: "Perception", "Attitude", "Culture", "Social" and "Psychology." For example: "Argentina menopause perception". The studies were not differentiated by text availability, article attribute, article type, publication date, language, or journal. **Results:** The PubMed website search was made by country and there were 285 studies in total with the inclusive criteria; 177 of them being relevant to the investigation. Based on the relevant ones, almost 40% of the studies were repeated or shared between countries or categories, showing similar data for different cultures without consideration of country cultural differences. The average age of publication for the studies was 10 years old (2010), underlining the lack of up-to-date information available to women. One difference noted during the search itself was the plethora of medical articles in the English literature. It appeared that many countries in SA do not have as robust a quantity of literature on this topic, considering the population combined for SA is nearly 100 million more than the USA. The PubMed search suggested that the USA has over 6 times the quantity of information compared to the SA citations combined. Our research highlighted that women's perception around menopause is influenced by multiple factors such as, religion (for example, God determining the function of the body), naturalistic view (the menopause as a natural phenomenon) and patriarchal connotations (the menses characterize a woman and defining her role for the society) (1). In some parts of SA menopause is also perceived as a loss of health and youth and in extreme cases means to "stop being a woman"; (1) (2) while in other areas it is comprehended as a life crisis laden with opportunities, bringing new self-accomplishment and greater autonomy (3). The perception that associates beauty and youth with healthy characteristics, and the inexorable aging process with the menopausal woman's deterioration of health, despite being a normal physiologic process, was also noted (1) (4). Over 90% of patients in menopause complain of one symptom, and 25% consider it severe. (5) (6) A common thread in SA literature as in most literature is the lack of knowledge about the symptoms and the reluctance to talk about it was identified as the barrier in seeking professional help and treatment. (1) (7) (8) (9) Further, menopausal women perceived their health more poorly compared to non-menopausal women, although this is related to the health and aging process (10) (11). The Menopause rating scale (MRS) score, which is a marker for quality of life (QoL), was also found to be high in most of the SA countries. (10) (12) (13) The perception of menopause being associated with a decrease in QoL appeared to be related to alternative therapies attempted, presence of chronic diseases or psychiatric diseases, living at high altitude and having a partner with sexual dysfunction. A more optimistic QoL appeared to be related to women who lived in a country with a lower income, had higher education levels and participated in healthy habits, such as exercise. (10) (13 - 18). **Conclusion:** In this era of technology where any information is available "at one's fingertips", women in the SA region do not enjoy that luxury. This review suggests that there are many cultural characteristics that define menopause, and they can be a barrier to optimal health care if they are ignored or skipped in any healthcare setting. More specific and detailed information is needed to assess the common cultural idiosyncrasies that a country may display. Addressing the common cultural idiosyncrasies that women of a country may display while respecting the patient history will contribute to best practice.
Sources of Funding: None

P-8.

Examining the Long-Term Brain Effects of Menopausal Hormone Therapy: KEEPS Continuation Study

Carola Ferrer Simó, MPH[1], Taryn James, PhD[1], N. Maritza Dowling, PhD[2], Hector Salazar, BSN[1], S. Mitchell Harman[3], Kejal Kantarci, MD[4], Carey E. Gleason, PhD[1]. [1]University of Wisconsin, Madison, WI; [2]George Washington University, Washington, DC, DC; [3]Kronos Longevity Research Institute, Phoenix, AZ; [4]Mayo Clinic, Rochester, MN

Objective: Previous studies reported contradictory findings on the effects of hormone therapy (HT) treatment on cognitive health. The Women's Health Initiative Memory Study (WHIMS) revealed that women ≥65 years (yrs) were at increased risk for mild cognitive impairment (MCI) and dementia after ~4 yrs of HT treatment. The Kronos Early Estrogen Prevention Study (KEEPS) and its ancillary Cognitive and Affective Study (KEEPS-Cog) hypothesized that the timing of the administration of HT treatment could influence the cardiovascular and cognitive effects of HT. In particular, if HT was started proximal to the menopausal transition (menopausal HT; MHT) women may benefit. However, KEEPS-Cog found that cognitive factor scores of women on two forms of MHT were similar to those from women on placebo after 4 yrs of MHT. The objective of the KEEPS Continuation (KEEPS-Cont) study is to understand the long-term brain effects of MHT in KEEPS-Cog study participants ~12-14 years after randomization. **Design:** The aims of KEEPS-Cont are to measure the long-term effect of MHT on: (1) an AD imaging biomarker (amyloid Positron Emission Tomography (PET)), (2)long-term cognition and mood effects, and (3)associations between the AD biomarker status and cognitive and mood outcomes in women enrolled in KEEPS. In KEEPS, a double-

blind trial, women were randomized to 4 yrs of treatment with one of two formulations of MHT: oral conjugated equine estrogens (o-CEE) + progestin, transdermal estradiol (t-E2) + progestin, or placebos. At enrollment (2005-2008), all women were within 36 months of their last menstrual period. Participants are eligible to participate in KEEPS-Cont if they were randomized to MHT or placebo in KEEPS, had baseline data, and at least one post-baseline visit. Recruitment is ongoing and done via letters or phone call. After providing consent to participate, women are asked to return to a study site for data collection, including the following: medical history, blood draw, brain Magnetic Resonance Imaging (MRI) and Amyloid PET scan, and neurocognitive studies, among others. **Results:** Demographic data and baseline characteristics from KEEPS-Cog and KEEPS-Cont are listed, but not compared, as data collection is on-going (Table 1). At present, follow up has been completed with 94 women of a planned enrollment of 482. Women in KEEPS-Cont are on average 67 yrs old, predominantly White, and well-educated. Initial results from the Modified Mini-Mental State Exam (3MSE) revealed that participants' scores were generally comparable to the average baseline visit of the KEEPS-Cog total sample (97.26, SD 3.12 vs 96.61, SD 4.47, respectively). **Conclusion:** KEEPS-Cont. aims to understand the long-term effects of MHT on cognition and an AD biomarker. Although KEEPS-Cog revealed MHT had no short-term changes in cognitive health, data from the KEEPS-Cont will add to our understanding of the relationship between HT and cognitive health, further informing women's decisions around MHT treatment.

Sources of Funding: KEEPS-Cont is supported by funding from NIH RF1 AG057547.

Baseline Characteristics in KEEPS-Cog vs KEEPS-Cont.

	KEEPS-Cog Baseline	KEEPS-Cont. Baseline
N	660	94
Age (mean (SD))	52.64 (2.59)	67.09 (3.26)
Race / Ethnicity (%)		
White	515 (78.0)	66 (71.0)
Black	48 (7.3)	6 (6.5)
Asian	21 (3.2)	1 (1.1)
Hispanic	41 (6.2)	5 (5.4)
Declined to answer	35 (5.3)	15 (16.1)
Education level (%)		
High School degree or less	49 (7.4)	7 (7.4)
Some college/vocational to College graduate	388 (58.8)	48 (51.1)
Some graduate to Graduate degree	217 (32.9)	39 (41.5)
Not answered	6 (0.9)	0 (0.0)
Modified Mini-Mental State Exam (3MSE) (mean (SD))	96.61 (4.27)	97.26 (3.12)
BMI (mean (SD))	26.36 (4.33)	27.04 (4.86)
WHR (mean (SD))	0.82 (0.08)	0.84 (0.06)
Treatment (%)		
Placebo	250 (37.9)	31 (36.0)
o-CEE	208 (31.5)	26 (30.2)
t-E2	202 (30.6)	29 (33.7)
APOE e4 = Positive (%)	139 (25.2)	19 (25.3)

P-9.

Dyspareunia and the resulting impairment of daily life improves over time in equal measure when using a hormone-free moisturizing vaginal cream or a standard estriol cream

Petra Stute, Prof.[2], Susana Garcia de Arriba[1], Manuel Häuser, Dr.[1], Simone Thum, Dr.[1], Clarissa Masur, Dr.[1], Christoph Abels, Prof.[1]. [1]Medical Affairs, Dr. August Wolff GmbH & Co. KG - Arzneimittel, Bielefeld, Germany; [2]Department of Obstetrics and Gynecology, Faculty of Medicine, University of Bern, Bern, Switzerland

Objective: Dyspareunia, or pain during sex, is one of the most common disabling symptoms reported by postmenopausal women due to Genitourinary Syndrome of Menopause (GSM). Therefore, it has a significant impact on the quality of life of affected women. The decrease in circulating estrogen is directly associated with the occurrence of vaginal dryness, which in turn is largely responsible for the appearance of dyspareunia. Previous clinical results have shown that a hormone-free vaginal cream (oil-in-water emulsion) is able to improve vaginal dryness as effectively as an estriol vaginal cream (0.1 %). In this case, we have evaluated the effect of both treatments on the relief of dyspareunia und the resulting impairment of daily life. **Design:** In a six-week, prospective, open-label, randomized, controlled trial 106 out of 171 post-menopausal women suffering from vaginal dryness were sexually active. 96% of them suffered from the clinical symptom dyspareunia which was rated by affected women on a severity scale from 0 (absent) to 4 (very severe). **Results:** From Day 1 to Day 43, the mean **severity** for dyspareunia decreased from 2.6 ± 0.1 to 0.9 ± 0.1 for the hormone-free treatment group and from 2.7 ± 0.2 to 0.5 ± 0.1 for the estriol treatment group, respectively. No significant difference between both treatment groups was detected for the severity scoring for dyspareunia (p=0.398). The percentage of women suffering from at least severe dyspareunia on Day 1 was 59.4 % in the hormone-free treatment group and 59.5 % in the estriol treatment group which decreased until Day 43 to 10.5 % (hormone-free cream) and 2.6 % (estriol cream), respectively. An improvement of dyspareunia until Day 43 was reported by 84.2 % of the hormone-free-treated women and 86.8 % of the estriol treated women. In addition to the improvement of the clinical symptom dyspareunia, the impact on **Quality of Life** was assessed as impairment of daily life due to dyspareunia. From Day 1 to Day 43, the mean impairment of daily life due to dyspareunia decreased by 77% for the hormone-free treatment group and 90% for the estriol treatment group, respectively. An improvement of daily life until Day 43 was reported by 98.2 % of the hormone-free treated women and 86.8 % of the estriol-treated women. When comparing the AUCs the difference between the results was statistically not significant. **Conclusion:** Treatment of GSM with a hormone-free cream (oil-in-water emulsion) acting as an emollient reduced the severity of dyspareunia and significantly improved Quality of Life over time without statistical significance compared to an estriol vaginal cream (0.1 %).

Sources of Funding: This study was sponsored by Dr. August Wolff GmbH & Co. KG Arzneimittel (Bielefeld, Germany).

P-10.

Cannabis use for menopause symptom management among midlife women Veterans

Carolyn Gibson, PhD, MPH[1,2], Alison Huang, MD, MAS[2], Shira Maguen[1,2], Sabra Inslicht[1,2], Amy Byers[1,2], Karen Seal, MD, MPH[1,2]. [1]San Francisco VA Health Care System, San Francisco, CA; [2]University of California, San Francisco, San Francisco, CA

Objective: Laws and regulations prohibiting cannabis use have relaxed dramatically over the past decade in the United States, with medical or recreational use now legalized in the majority of states. Mainstream use of cannabis for the management of chronic health conditions and mood symptoms has been increasingly reported over this period. Although little research has been conducted in this area, anecdotal evidence suggests a high rate of interest in use for menopause symptom management among midlife and older women. We examined patterns of self-reported cannabis use for menopause symptom management in a sample of midlife women Veterans. **Design:** Cross-sectional data were drawn from the Midlife Women Veterans Health Survey, an observational study of women Veterans aged 45-64 enrolled in Department of Veterans Affairs (VA) health care in Northern California. Data were collected between March 2019-May 2020. Participants reported previous or current methods of menopause symptom management, including cannabis use in any form, as well as current health, mental health, and menopause symptoms in structured-item questionnaires. Descriptive analyses were used to describe the sample, and key demographic and clinical characteristics of women with and without cannabis use for menopause symptom management were compared with chi-square (categorical variables) and ANOVA (continuous variables). **Results:** In this sample of 232 midlife women Veterans (mean age 55.95 years, SD 5.13), over half reported current bothersome menopause symptoms, including hot flashes and night sweats (54%), insomnia (27%), and genitourinary symptoms (69%). Current or ever use of cannabis for menopause symptom management was reported by 27% of all participants, while an additional 10% expressed interest in future use. In contrast, only 19% reported traditional forms of menopause symptom management, including menopausal hormone therapy. In bivariate analyses, women who did and did not report cannabis use for menopause symptom management did not differ by age, race/ethnicity, socioeconomic status, or mental health conditions. Cannabis use was more commonly reported among women reporting hot flashes (67% vs. 50%, p=.03) and night sweats (68% vs. 47%, p<.01) in the past two weeks, with no differences observed for other menopause symptoms. **Conclusion:** Use of cannabis for menopause symptom management was common in this sample midlife women Veterans in Northern California. This study raises questions about the generalizability of these findings in other regions with differing legal and cultural attitudes toward cannabis use, the degree to which women disclose cannabis use to health care providers when discussing menopause management, and the specific symptoms targeted by women using cannabis for menopause symptom management. These findings also highlight the importance of understanding the potential risks, benefits, and effectiveness of cannabis for this indication.

Sources of Funding: This research was supported in part by VA Health Services Research & Development Career Development Award (IK2 HX002402; CJG). The content is solely the responsibility of the authors and does not necessarily represent the official views of the Department of Veterans Affairs.

P-11.

The Effects of a 17β-estradiol, Softgel, Vaginal Insert on Vulvar and Vaginal Atrophy (VVA), Including Moderate to Severe Dyspareunia and Vaginal Dryness in Postmenopausal Women > 60 Years of Age

Steven R. Goldstein[1], David F. Archer, MD[2], Shelli Graham, PhD[3], Brian Bernick, MD[3], Sebastian Mirkin, MD[3]. [1]New York University School of Medicine, New York, NY; [2]Eastern Virginia Medical School, Norfolk, VA; [3]TherapeuticsMD, Boca Raton, FL

Objective: An estimated 32 million women in the US suffer from symptoms of vulvar and vaginal atrophy (VVA), a chronic and progressive medical condition. Due to aging of the population and increasing longevity, this burden may last for over one-third of their lives. The 17β-estradiol (E2), softgel, vaginal insert (TX-004HR) significantly estrogenized the vaginal tissue, improved symptoms of dyspareunia and vaginal dryness vs placebo and was shown to be safe and well-tolerated in menopausal women with moderate to severe dyspareunia in the 12-week, phase 3 REJOICE trial. The 4- and 10-μg E2 doses were approved by the FDA in May 2018 as IMVEXXY® [(estradiol vaginal inserts) TherapeuticsMD, Boca Raton, FL], for the treatment of moderate to severe dyspareunia, a symptom of VVA, due to menopause. The effect of therapies for VVA on women > 60 is not well studied. One agent showed a lower magnitude of effect on dyspareunia in women > 55 compared to women < 55. The objective of this analysis was to evaluate the efficacy of TX-004HR in women > 60 years of age who participated in the REJOICE trial. **Design:** Menopausal women (40-75 years) with VVA and moderate to severe dyspareunia received 4 μg, 10 μg, or 25 μg E2, or placebo vaginal inserts for 12 weeks. Percentages of superficial and parabasal cells, vaginal pH, severity of dyspareunia and vaginal dryness as well as visual assessments (vaginal color, secretions, epithelial integrity and surface thickness) were analyzed in women > 60 years of age. **Results:** Of 764 enrolled in REJOICE, 295 were age > 60 years. TX-004HR, when compared

with placebo, statistically significantly increased the percentage of superficial cells ($p<0.05$), decreased the percentage of parabasal cells and vaginal pH ($p<0.0001$, both) from baseline to weeks 2, 6, 8 and 12 in all treatment groups. Severity of dyspareunia showed statistically significant improvement beginning at week 8 ($p<0.05$, all groups) as well as the TX-004HR 4 μg group with severity of vaginal dryness at weeks 6 and 12 ($p<0.05$, both). All visual assessments were statistically significantly improved for all doses at all timepoints ($p<0.05$). **Conclusion:** In menopausal women > age 60, TX-004HR statistically significantly improved the objective measures of VVA, including vaginal pH and cytology. Corresponding symptom relief was observed for dyspareunia at week 8 (all doses) and weeks 6 and 12 for vaginal dryness (4 μg dose). TX-004HR was well tolerated with an acceptable safety profile.
Sources of Funding: TherapeuticsMD

P-12.
SJX-653 Demonstrates Potent NK3 Antagonism Across Nonclinical and Clinical Studies

Philip Graham, PhD[1], Jennifer Cormier[1], David Turnquist, MS[1], Søren Møller Nielsen, PhD[2], Björn Steiniger-Brach, PhD[2], Christoffer Bundgaard, PhD[2], Karsten Juhl[2], Malcolm Boyce[3], Frans van den Berg, MD[3], Daniel Grau[1], Ruth Thieroff-Ekerdt, MD[1]. [1]Sojournix, Boston, MA; [2]H. Lundbeck A/S, Copenhagen, Denmark; [3]Hammersmith Medicines Research, London, United Kingdom

Objective: Background: NK3 antagonism is a clinically validated mechanism of action for treating menopausal vasomotor symptoms ("hot flashes"). SJX-653 is a novel and selective small-molecule NK3 receptor antagonist in clinical development for the treatment of moderate-to-severe vasomotor symptoms due to menopause. **Objective:** To assess the pharmacology of SJX-653 and determine the relationship between SJX-653 concentration and activity on pharmacodynamic (PD) markers of NK3 receptor antagonism across in vitro, in vivo and clinical studies. **Design: Methods:** Selectivity and binding of SJX-653 to the NK3 receptor were assessed through in vitro radioligand displacement studies. NK3 receptor activity was evaluated using used calcium flux induced by neurokinin B in cell lines expressing NK3 receptors. Plasma protein binding was assessed by ultrafiltration or equilibrium membrane dialysis. Receptor occupancy was assessed by displacement of a radiolabeled NK3 ligand in guinea pigs and correlated with efficacy in an amphetamine-induced hyperactivity model (AIH). Brain/plasma ratio was assessed in rats and guinea pigs. The effect of SJX-653 on established PD markers of NK3 receptor engagement was assessed after single doses in male dogs (testosterone, T), single doses in men (T and luteinizing hormone, LH), and single and multiple doses in postmenopausal women (PMW) (LH). **Results: Results:** SJX-653 is a competitive antagonist with an in vitro affinity for the human, guinea pig and dog NK3 receptor of 4.3, 2.0 and 4.2 nM and corresponding IC50 for functional antagonism of 9.0, 9.6 and 4.9 nM, respectively. Affinity for the human NK2 and NK1 receptors was >100 and >1000 fold lower than for NK3. Plasma protein binding was 87%, 96% and 81% for human, guinea pig and dog, respectively. Brain/plasma ratio in rats and guinea pigs was 0.5. 50% receptor occupancy (RO) in guinea pigs was achieved at a plasma concentration of 6 ng/mL which corresponded to efficacy in the guinea pig AIH model. In male dogs reversible reduction of T was evident at a plasma concentration of 10 ng/mL. In healthy men, statistically significant dose-dependent decreases of LH and T were observed with near maximal effect after a single 15 mg dose corresponding to plasma levels of ~30 ng/mL. In PMW a statistically significant 20% LH reduction occurred after a single 4.5 mg dose with corresponding plasma levels of ~10 ng/mL. SJX-653 demonstrated a plasma $t_{1/2}$ of 13-14 h, peak trough ratio of 3:1 and dose-linear PK. **Conclusion: Conclusions:** SJX-653 demonstrates NK3 receptor antagonism at low nanomolar concentrations. This high potency has been shown to translate across in vitro, in vivo, and clinical studies and reflects the low IC50 for NK3 receptor inhibition, moderate protein binding, and good brain penetration of SJX-653. In summary, SJX-653 is a potent and selective NK3 receptor antagonist with a PK profile supportive of once-daily (QD) administration.
Sources of Funding: Nonclinical studies were funded by H. Lundbeck A/S Clinical studies were funded by Sojournix Inc.

P-13.
Metabolic Risk Factors and Cognitive Function in Midlife Women from Sub-Saharan Africa

Nicole G. Jaff, PhD[4,5], Marketa Toman, PhD[4], Tracy Snyman, MSc(Med)[4], Shane A. Norris, PhD[3], Pauline M. Maki, PhD[1,2], Nigel J. Crowther, PhD[4]. [1]Department of Psychiatry, University of Illinois at Chicago, Chicago, IL; [2]Department of Psychology, University of Illinois at Chicago, Chicago, IL; [3]SAMRC/Developmental Pathways for Health Research Unit, University of the Witwatersrand, Chris Hani Baragwanath Hospital, Johannesburg, South Africa; [4]Department of Chemical Pathology, National Health Laboratory Service and University of the Witwatersrand Faculty of Health Sciences, Johannesburg, South Africa; [5]The Aurum Institute, Johannesburg, South Africa

Objective: Obesity is associated with reductions in cognitive function. It has been suggested that these associations are mediated by insulin resistance, adipokines, inflammation and/or vascular damage. The aim of the current study was therefore to investigate the relationship of adiposity measures, adipokines and insulin resistance with cognition in a large cohort of middle-aged sub-Saharan African women. **Design:** Fasting serum levels of adiponectin, leptin and insulin resistance (HOMA) and socio-demographic variables, and body fat measures were assessed in 608 black, urban, midlife women aged 40-60 years and participating in the Study of Women Entering and in Endocrine Transition(SWEET). Menopausal stage was determined using the Stages of Reproductive Aging Workshop +10 criteria. For cognitive function, processing speed and incidental recall were measured using the symbol-digit modalities test and used as dependent variables in separate multivariable regression models. The relationship of incidental recall with insulin resistance was analysed by comparing incidental recall across HOMA tertiles. **Results:** The mean BMI of this population was 33.4±7.35. The main determinants of processing speed were age ($\beta=-0.19$, $p<0.0001$), education level ($\beta=0.42$, $p<0.0001$), employment status ($\beta=0.12$, $p=0.0006$), visceral fat ($\beta=-0.08$ $p=0.049$) and adiponectin ($\beta=-0.10$, $p=0.006$), whilst for incidental recall the determinants were education ($\beta=0.20$, $p<0.0001$), visceral fat ($\beta=-0.10$, $p=0.018$) and insulin resistance ($\beta=0.09$, $p=0.043$). Neither diabetes nor menopausal stage were associated with processing speed or incidental recall in the final regression models. The incidental recall levels for HOMA tertiles 1, 2 and 3 were as follows: 4.35±3.42, 5.25±3.85 and 4.98±3.54, respectively ($p=0.036$ by ANOVA). **Conclusion:** These data suggest that visceral fat has a weak, negative effect on both processing speed and incidental recall independently of adipokines or insulin resistance, whilst adiponectin specifically attenuates processing speed. Furthermore, incidental recall increases with rising levels of insulin resistance, but plateaus at high HOMA levels.
Sources of Funding: Medical Research Council of South Africa (MRC); National Health Laboratory Service (NHLS) Research Trust; University of the Witwatersrand Iris Ellen Hodges Cardiovascular Research Trust; National Research Foundation (NRF) of South Africa. S.A.N. is supported by the DST-NRF Centre of Excellence in Human Development at the University of the Witwatersrand, Johannesburg, South Africa.

P-14.
Trauma and Sleep Problems Over Midlife in Women

Karen P. Jakubowski, PhD[1], Pauline M. Maki, PhD[2], Yuefang Chang, PhD[1], Rebecca C. Thurston, PhD[1]. [1]University of Pittsburgh, Pittsburgh, PA; [2]University of Illinois at Chicago, Chicago, IL

Objective: Trauma is a risk factor for poor sleep. Prior work is limited by a reliance on self-reported sleep outcomes measured at one timepoint and a lack of study into the effect of trauma timing on sleep in midlife. We tested whether trauma exposure during childhood and/or midlife was related to persistently poor objectively- and subjectively-assessed sleep over midlife. **Design:** 296 women aged 40-60 were assessed at baseline; 166 were assessed 5 years later. At baseline and follow-up, women reported adult trauma (Brief Trauma Questionnaire), demographics, depressive symptoms, and sleep (quality [Pittsburgh Sleep Quality Index; PSQI], apnea); provided physical measures of height/weight; and had a 3-day objective sleep assessment via actigraphy (duration and wake after sleep onset [WASO]). At baseline, women reported childhood trauma (Child Trauma Questionnaire). Relations of childhood trauma (any/none) and adult trauma (any/none) at baseline with persistently poor sleep [duration (<7 hrs), WASO (≥31 min), PSQI (>5)] across visits were assessed in logistic regression models, adjusted for age, race, education, body mass index, sleep medications, nightshift work, apnea, and depressive symptoms. **Results:** At baseline, the 296 women (72% White, 28% Black) were on average 54 years old; 44% and 60% of women reported childhood or adult trauma, respectively. Persistently poor sleep duration, WASO, and sleep quality was seen in 61%, 60%, and 33% of women, respectively. Childhood trauma was related to persistently poor WASO [OR (95%CI)=2.32 (1.11-4.84), p=.025, Figure]. Adult trauma was related to persistently poor sleep quality [OR (95%CI)=2.13 (1.01-4.52), p=.048]. Trauma was unrelated to persistently poor sleep duration. **Conclusion:** Poor sleep was prevalent in midlife women. Childhood and adult trauma are related to poor objective sleep continuity and subjective sleep quality, independent of sleep risk factors and depressive symptoms. Findings highlight the adverse sleep sequelae of trauma exposure among midlife women.
Sources of Funding: R01HL105647, RF1AG053504, 2K24HL123565, T32MH018269

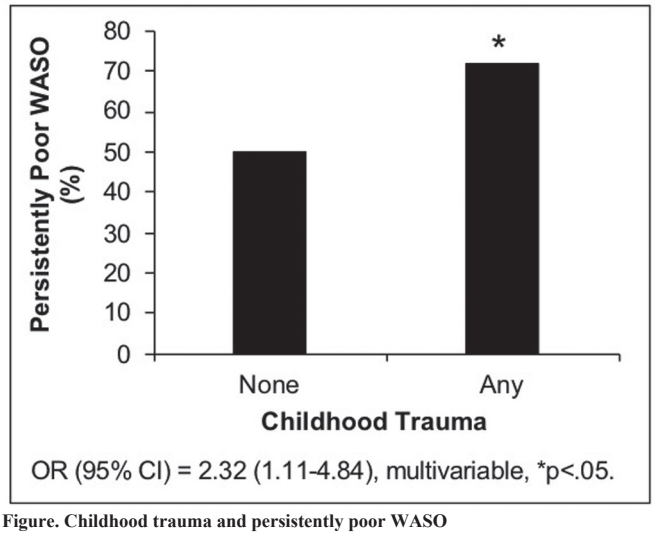


Figure. Childhood trauma and persistently poor WASO

P-15.

Lifetime History of Intimate Partner Violence and Current Clinical Insomnia Among Midlife Women Veterans

Karen P. Jakubowski, PhD[1], Alison Huang, MD, MAS[2], Karen Seal, MD, MPH[2,3], Shira Maguen[2,3], Sabra Inslicht[2,3], Amy Byers[2,3], Connie Fee, BA[3], Carolyn Gibson, PhD, MPH[2,3]. [1]University of Pittsburgh, Pittsburgh, PA; [2]University of California, San Francisco, San Francisco, CA; [3]San Francisco VA Health Care System, San Francisco, CA

Objective: Over a third of women in the United States report intimate partner violence, making this one of the most common forms of trauma in women. Intimate partner violence includes a variety of exposures, including physical and sexual violence and emotional abuse by a current or former partner. Although a recent review found that intimate partner violence is related to poor subjective sleep, the majority of studies involved reproductive-aged women, even though sleep disturbance is more common among midlife women. We examined the relationship between history of intimate partner violence and current clinical insomnia in a sample of midlife women Veterans. **Design:** Cross-sectional data were drawn from the Midlife Women Veterans Health Survey, an observational study of women Veterans aged 45-64 enrolled in Department of Veterans Affairs (VA) health care in Northern California. Data were collected between March 2019-May 2020. Participants completed validated, structured-item questionnaires, including an adapted Extended-Hurt, Insult, Threaten, Scream (E-HITS) to assess lifetime history of intimate partner violence (screening threshold score and any physical, sexual, and emotional intimate partner violence), the Insomnia Severity Index to assess current insomnia, the Patient Health Questionnaire-9 (PHQ-9) to assess current clinically significant depressive symptoms, and the PTSD Checklist for DSM-5 (PCL-5) to assess current probable posttraumatic stress disorder. Multivariable logistic regression analyses were used to examine associations between intimate partner violence and moderate-severe clinical insomnia, adjusting for age, race, education, menopause status, and body mass index. Separate secondary models further adjusted for depressive symptoms and posttraumatic stress disorder (PTSD). **Results:** In this sample of 232 midlife women Veterans (mean age 55.95, SD 5.13), 63% met standardized screening criteria for lifetime intimate partner violence. In response to individual items, 35% reported a history of any physical intimate partner violence, 27% reported a history of any sexual intimate partner violence, and 78% reported a history of any emotional intimate partner violence. Moderate-severe clinical insomnia was observed in 36% of participants. In multivariable analyses, lifetime history of intimate partner violence was associated with two- to four-fold odds of current clinical insomnia, including overall intimate partner violence (OR 3.09, 95% CI 1.49-6.39), physical intimate partner violence (OR 1.96, 95% CI 1.06-3.62), emotional intimate partner violence (OR 4.15, 95% CI 1.74-9.88), and sexual intimate partner violence (OR 2.05, 95% CI 1.05-4.02). After further adjustment for depressive symptoms or PTSD, results were attenuated but remained significant for overall (with depressive symptoms OR 2.73, 95% CI 1.24-6.00; with PTSD OR 2.89, 95% CI 1.37-6.08) and emotional intimate partner violence (with depressive symptoms OR 3.08, 95% CI 1.23-7.74; with PTSD OR 3.76, 95% CI 1.55-9.10), but were no longer statistically significant for physical and sexual intimate partner violence. **Conclusion:** Lifetime history of intimate partner violence is common among midlife women Veterans and may contribute to clinical insomnia during midlife. Emotional intimate partner violence appears particularly detrimental to sleep. Findings highlight the importance of screening midlife women for intimate partner violence and recognizing the role of this traumatic exposure on women's health.

Sources of Funding: This research was supported in part by NIMH T32MH018269 (KPJ) and a VA Health Services Research & Development Career Development Award (IK2 HX002402; CJG). The content is solely the responsibility of the authors and does not necessarily represent the official views of the Department of Veterans Affairs.

P-16.

Implementation of Standardized Practice Guideline May Allow Stabilization of Serum Hormone Levels and Impact the Incidence of Side Effects in Women Taking Custom-Compounded Hormone Therapy

Xuezhi Jiang, MD, PhD[1,2], Anna Roble[1,3], Tara Lamb[1,3], Anna Bossert[1], Kirthik N. Parthasarathy, MD[1], Kristine Leaman, MD[1], Shahab S. Minassian, MD[1], Peter F. Schnatz[1,2], Mark B. Woodland, MD[1,3]. [1]OBGYN, Reading Hospital, Tower Health, Reading, PA; [2]OBGYN, Thomas Jefferson University, Philadelphia, PA; [3]Drexel School of Medicine, Philadelphia, PA

Objective: Custom-compounded hormone therapy (CHT) was found to be associated with a higher incidence of side effects compared with FDA-approved hormone therapy. To reduce the incidence of side effects, we established strict department guidelines on use of CHT including dose and duration of treatment. We aim to compare dosage, blood serum levels, duration of treatment and the incidence of side effects in women on CHT before and after implementation of a departmental practice guideline. **Design:** A standardized guideline for CHT, to allow uniform practice patterns, was established and implemented in Sep. 2017. A before-and-after study was designed to compare a group of postmenopausal women who were on pellet, a subcutaneous form of CHT, both before and after the guideline was implemented. In June 2020, the patient data were retrieved from the Electronic Medical Records at Reading Hospital, including demographics, treatment duration, dosage of CHT, side effects, serum estradiol (E2), total testosterone (TT), and free testosterone (FT) levels, and frequency of laboratory follow-up. Data were categorized into Before and After groups. Paired t-test and McNemar test were applied to compare continuous data and categorical data, respectively. **Results:** A group of 106 postmenopausal women were identified with mean (SD) age and body mass index (BMI) on first contact of 56.4 (7.5) years and 28.9 (4.0) kg/m2, respectively. Mean (SD) treatment duration was significantly shorter in the After than the Before group (1.6[0.2] vs. 5.1[2.1] years, p<.0001). The number of E2 (2.7[0.9] vs. 1.1[0.4], p<.0001) and T (2.3[1.0] vs. 0.9 [0.4], p<.0001) measurement per year were significantly higher in After than Before, respectively. In the After group, compared to the before, the degree of serum hormone level fluctuation represented by the difference between the peak and nadir was significantly lower in E2 (81.5 [65.6] vs. 200.8[126.8] pg/mL, p<.0001), TT (73.0[59.2] vs. 105.6[70.0] ng/dL, p=.001), and FT (6.7[6.9] vs. 11.3[20.7] pg/mL, p=.027). There were no significant differences in the mean (SD) highest E2 and T dosages between Before and After. The peak serum levels of E2(193.4[91.9] vs. 289.4[134.3] pg/mL, p<.0001), TT(130.9[50.8] vs. 195.0[72.7] ng/dL, p<.0001), and FT(11.4[7.8] vs. 15.7[21.8] pg/mL, p=0.048) were significantly lower in After than Before. Both the incidence (58 [54.7%] vs. 77[72.6%], p=0.011) and total number (0.9[1.0] vs. 1.8[1.6], p<.0001) of overall side effects were significantly lower in the After group; however, the total number of side effects per year in After was significantly higher than Before (0.6[0.6] vs.0.4[0.4], p=0.015]). **Conclusion:** Implementation of department practice guidelines markedly increased the frequency of laboratory follow-up during the treatment which significantly reduced the peak and fluctuation of serum hormone levels as well as the incidence and total number of side effects. While considering the length of treatment duration, however, the total number of side effects per year in women on CHT was not significantly reduced after implementation of a standardized practice guideline.

Sources of Funding: None

P-17.

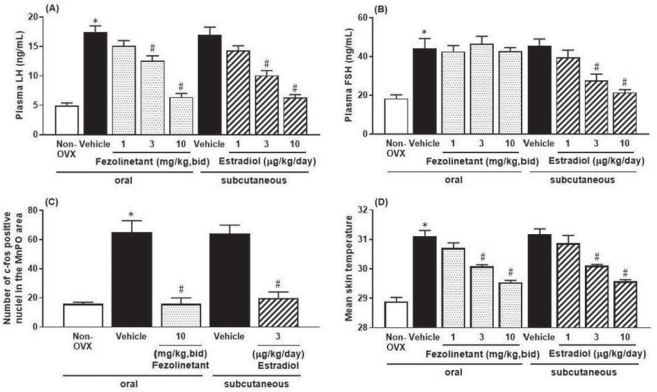
Fezolinetant Attenuates Hot Flash-like Symptoms via Inhibition of Neuronal Activity in the Median Preoptic Nucleus in Ovariectomized Rats

Atsuo Tahara[1], Keiko Tanaka-Amino[2], Akiyoshi Ohtake[1], Hajime Takamatsu[1], Seiji Kaku[1]. [1]Astellas Pharma, Inc., Tsukuba, Ibaraki, Japan; [2]Astellas Pharma, Inc., Chuo-City, Tokyo, Japan

Objective: In a pair of preclinical studies, we investigated the effects of repeated administration of fezolinetant, a neurokinin 3 receptor antagonist, on sex hormone and gonadotrophin levels, activity of hypothalamic neurons, and hot flash-like symptoms in female ovariectomized (OVX) rats. **Design:** Four weeks after ovariectomy, fezolinetant (1, 3, or 10 mg/kg BID PO), estradiol (1, 3, or 10 μg/kg/d SC), or vehicle (PO or SC) was administered to OVX rats for 1 week; a non-OVX control group received vehicle PO. We measured body weight, food intake, plasma sex hormone and gonadotrophin levels, c-fos expression (an indirect marker of neuronal activation) in median preoptic nucleus (MnPO) neurons, and hot flash-like symptoms based on changes in core and tail skin temperature. **Results:** OVX rats exhibited several typical menopausal signs/symptoms including hyperphagia, obesity (determined by body weight), significant decreases in plasma estradiol levels, increases in luteinizing hormone (LH) and follicle-stimulating hormone (FSH) levels, and hot flash-like symptoms (increased tail skin temperature). These menopausal symptoms were accompanied by increased c-fos expression in MnPO neurons. Repeated administration of fezolinetant significantly reduced plasma LH levels (**Figure A**) without affecting estradiol and FSH levels (**Figure B**), inhibited activation of MnPO neurons (**Figure C**), and attenuated hot flash-like symptoms (**Figure D**) without affecting core temperature. In addition, fezolinetant significantly attenuated hyperphagia and obesity. These pharmacologic effects of fezolinetant were almost equivalent to those observed with estradiol, except for the effects on plasma estradiol and FSH levels. **Conclusion:** These results suggest that fezolinetant attenuates hot flash-like symptoms via inhibition of neuronal activity in the MnPO in OVX rats. Fezolinetant is currently being evaluated in phase 3 clinical studies as a potential therapeutic option for treatment of vasomotor symptoms associated with menopause.

Sources of Funding: Astellas Pharma, Inc.

Effects of fezolinetant on plasma (A) LH and (B) FSH levels, (C) c-fos expression in MnPO neurons, and (D) skin temperature in OVX rats.



MnPO: median preoptic nucleus, OVX: ovariectomized. Data are expressed as the mean ± SEM for 6-8 animals. *P<0.05 vs. Non-OVX group, #P<0.05 vs. vehicle group.

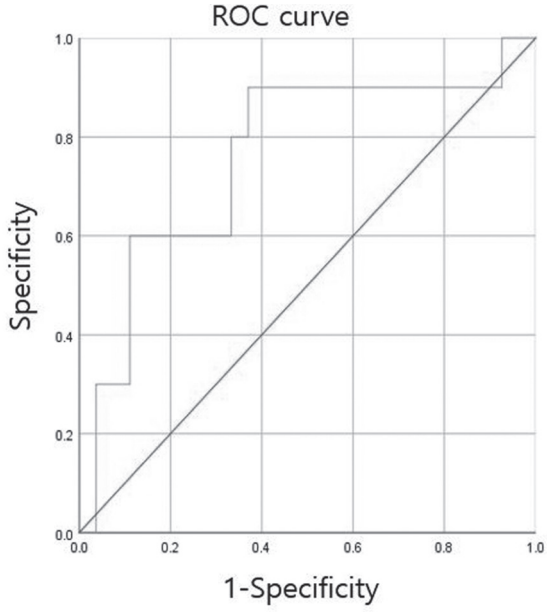
P-18.

Postchemotherapy serum FSH as a predictor of ovarian function recovery in young cancer patients

Hye Kyeong Kim, medicine, Sejin Kim, M.D., Jiyeon Han, Medicine, Soojin Han, M.D., Sung Woo Kim, Medicine, Hoon Kim, Medicine, Seung-Yup Ku, M.D. PhD., Chang Suk Suh, M.D. PhD., Seok Hyun Kim, M.D. PhD.. Obstetrics and Gynecology, Seoul National University Hospital, Seoul, Korea (the Republic of)

Objective: There are several studies regarding the prediction of ovarian function after chemotherapy. Anti-mullerian hormone (AMH) is the only widely accepted marker to forecast ovarian function before and after chemotherapy. However, the application of a low AMH to predict menopause is more sensitive in late reproductive age than in young. Also, the value of AMH for prediction of amenorrhea after chemotherapy are mainly based on the data of breast cancer. The objective of the study was to investigate markers representing ovarian function recovery in young cancer patients. **Design:** A retrospective cohort study **Results:** All patients diagnosed with malignancy and received first chemotherapy from July 2012 to March 2017 were reviewed for potential inclusion. Among them, patients who underwent only GnRH agonist treatment and were under 25 years old on the first day of chemotherapy were selected. Finally, a total of 50 patients was included. 10 out of 50 patients were excluded due to follow-up loss or death. 40 out of 50 patients were included. Serum AMH, FSH, and estradiol (E2) were measured on 6-month, 1-year, 2-year, 3-year after chemotherapy. 11 patients (group 1) recovered menstrual cycle within three years after chemotherapy, while 29 patients (group 2) did not recover menstruation. Mann-Whitney U test, chi-square test, and receiver operating characteristic (ROC) curve were used for analysis. FSH level in group 2 is significantly higher than in group 1 at 6-month (median: 15.0 [2.4-21.0]), 1-year (28.0 [1.9-160.0]), 2-year (9.7 [3.7-42.7]), and 3-year after chemotherapy (7.10 [5.5-14.1]). In particular, cut-off value of FSH at 6-month after chemotherapy measured by ROC curve was 18.0 (AUC 0.759, p=0.017). AMH level in group 2 was low in all period but there was no statistical significance. **Conclusion:** This study presents the possible value of FSH as a predictor of ovarian function recovery especially in young cancer patients. Serum FSH level higher than 18.0 at 6-months after chemotherapy may forecast amenorrhea.

Sources of Funding: None



ROC curve of serum FSH level at 6-months after chemotherapy

AUC 0.759, p=0.017

FSH cut-off value 18.0

P-19.

KAP (knowledge, attitude and practice) survey on THM in the Santiago (Chile) population.

Alejandra M. Lavín, Physician[1,3], Pablo A. Lavín, MD, MPH, MSc[1,4], Pablo A. Lavín, Physician[1,2]. [1]SIAPMED, Santiago, Chile; [2]UDP, Santiago, Chile; [3]Medicina, CESFAM Dr Alejandro Gutiérrez, Coyhaique, Chile; [4]OBGYN, Universidad de Chiel - Hospital Barros Luco-Trudeau, Santiago, Chile

Objective: Asses the knowledge, attitude and practices of the Santiago (Chile) menopuasal population about Menopausal Hormonal Therapy. **Design:** In 2018 using the 3,600 UDD panelists, male and women over 18 years old, [Socio-Economic Groups: ABC_1 9.7%, C_2 22%; C_3 36.1% and D + E 32.2%, and Ages: 18-30 29%; 31-40 19%; 41-50 17%; 51-60% 16%; 61+ 19%] distributed in 52 counties of the Metropolitan Region {selection of houses by simple random sampling} who voluntarily agreed to participate in online surveys, using the cell phone as a push bottom board. With a very simple questionnaire, the population was asked about the degree of knowledge they have on issues related to climacteric and menopause; if they know the symptoms; on hormonal treatment for menopause (THM), and its association with cancer. Also if they are menopausal, what degree of use do they have of THM and if they do not use it, would they use it? and why not? **Results: Knowledge about:** -Menopause: 99% of the male and female respondents (of all ages) declare that they know about menopause and 67% declare that they have someone close or familiar at this stage of life. -THM: the lowest level of knowledge is evident in men, reaching 28%. The greatest knowledge occurs in women >45 years of age, where 56% state that they know about it with an increment with age, 45-50 = 46% (CI 95% 37,8-54,2); 51-60 = 57% (CI 95% 51,1-62,9); 61+ = 64% (CI 95% 59,0-69,0) that is not statistical significant at p = 0.05. The knowledge that there are treatments to alleviate symptom is higher in the highest socioeconomic groups ABC_1 and C_2 with more than 80% and in older age groups 45-50 =73%; 51-60 = 80%; 61+ = 80%. -When asked if they would use it, 64% of women between 45 and 50 declared that they would. The proportion decreases with age, 53% in 51-60, reaching 50% in those over 61 years of age. The main reason for using the treatment is to avoid the bothersome symptoms of menopause. **THM**: -THM use: to less knowledge greater acceptance of use is related, reaching 70% in men who believe that women should use THM to decrease symptoms. Only 11% (CI 95% 8,8-13,2) of the 760 women older than 44 years declare using any treatment to combat symptoms, 45-50 = 9% (CI 95% = 4,3-13,7); 51-60 = 14% (CI 95% = 9,8-18,2); 61+ = 12% (CI 95% = 8,6-15,4). Only 47% uses in Group C_2: and in them it is observed to a greater extent (23%) the presence of fear for the potential "side effects" of hormones and 22% do not want to have "chemicals in their body". -Non-use: 35% of the 1,040 women surveyed (280 of <45 years and 760 of> 44 years) say that "I would not use THM" because: -I do not need it; -I don't like chemicals or I prefer natural treatments (exercise, diet changes, homeopathy, etc.); -It has adverse side effects; -I am not informed about it; -They can cause cancer; -I cannot take hormones (they refer to diseases or conditions that do not allow it, such as cysts, liver problems, etc.); -I mistrust on them; -It has not been prescribed for me. **Conclusion:** After a peak THM use of around 30% before the first WHI publication in 2002, the Santiago (Chile) population is still are aware of menopause symptoms and THM for controlling them (58%), but few women (11%) are using the therapy, with no differences in the women age as shown in an electronic (digital) questionnaire.

Sources of Funding: Grünethal Pharma

Menopausal Hormonal Teatment

Women Age Group	Menopausal Hormonal Treatment					
	N°	%	Knows about		Uses	
Years			N°	%	N°	%
45-50	143	100%	66	46%	13	9%
51-60	268	100%	153	57%	38	14%
61(+)	349	100%	223	64%	42	12%
All	760	100%	442	58%	93	11%

Reason to Never use Menopause Hormonal Treatment

Total women interviewed	Reason to Never use Menopause Hormonal Treatment								
1,040	TOTAL Never Users	do not need it	do not like chemicals	not informed	collateral effects	fear of cancer	afraid of hormones	I cannot use them	not been prescribed
N° Women	377 (36%)	124	64	64	41	26	23	23	11
%	100%	33%	17%	17%	11%	7%	6%	6%	3%

P-20.

Nutrient Gaps for Women of Menopausal Transition Age in the United States

LeeCole Legette, PhD[1], Prasad Devarshi, PhD[1], Kelly Higgins, PhD[2], Ryan Grant, PhD[1], Susan Hazels Mitmesser, PhD[1]. [1]Science & Technology, Pharmavite, West Hills, CA; [2]Center for Chemical Regulation and Food Safety, Exponent, Inc., Washington, DC

Objective: Nutrition is an integral component of wellness with inadequate diets serving as major contributory factor in chronic disease risk. The objective of this study is to determine usual nutrient intakes (from food and food + supplements) and to compare these to the corresponding Estimated Average Requirement (EAR) or Adequate Intake (AI), and Upper Limit (UL) in women of menopausal transition age (40-65 years). **Design:** Usual intake of nutrients from food and food + supplements were estimated using the National Cancer Institute method among 3,438 women aged 40-65 years (further grouped into 40-50 and 51-65 years) in NHANES 2011-16, a cross-sectional nationally representative health examination survey. **Results:** The mean age was 52.4 ± 0.2 and majority of the sample in the analysis was non-Hispanic white (66.8%). Majority (70.7%) of the sample was high income (Poverty Income Ratio >1.85). The percentage of women that had total usual intake from food less than the EAR was as follows (percentage for 40-50 years, percentage for 51-65 years): vitamin D (>97%, >97%), vitamin E (88% ± 1.6%, 86% ± 1.8%), magnesium (50% ± 2.0%, 49% ± 1.8%), calcium (48% ± 1.7%, 74% ± 1.5%), vitamin A (44% ± 2.7%, 37% ± 2.1%), vitamin C (44% ± 2.5%, 41% ± 1.7%), and vitamin B_6 (11% ± 1.3%, 21% ± 1.8%). The approximate percentage of women that had total usual intake that did not meet the AI was as follows (percentage for 40-50 years, percentage for 51-65 years): vitamin K (40%, 37%), choline (95%, 94%), potassium (66%, 62%), dietary fiber (93%, 92%). Nutrient intakes were higher with supplement usage for several key nutrients including calcium, magnesium, vitamin C, vitamin D and vitamin E as depicted in Figure 1. **Conclusion:** The analysis shows a significant percentage of women in menopausal transition are not meeting the recommendations for calcium, choline, dietary fiber, magnesium, vitamin A, vitamin C, vitamin D, and vitamin E. Supplement use helps fill some of these nutrient gaps. As one journeys from

early perimenopause (40 – 50y) to post menopause (51 – 65y), nutrient gaps increased for vitamin B_6 and calcium suggesting specific guidance is needed throughout menopause transition to meet nutrient needs to support general wellness and healthy aging.

Sources of Funding: This study was funded by Pharmavite LLC.

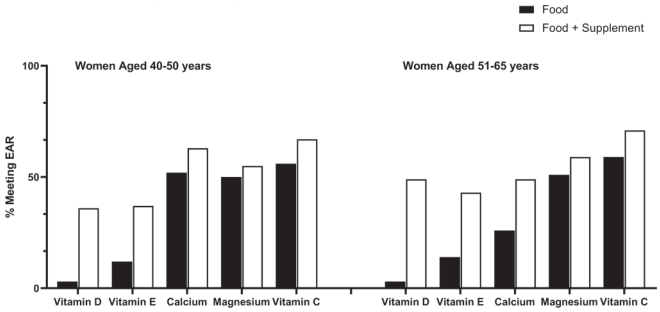


Figure 1. Percent Meeting EAR for Women in Menopausal Transition with Usual Intake from Food Only and Food + Supplements

P-21.

Differences in patient-reported rates of hormone therapy use by provider specialty

Megan McCarty, MD, Holly N. Thomas, MD. Medicine, UPMC, Pittsburgh, PA

Objective: Hormone therapy (HT) is a safe, effective treatment for menopause symptoms. There is a dearth of research on prescribing practices between different specialties. This is important because as women age, they may see a generalist more frequently than a gynecologist. This study aimed to determine if there are different rates of HT use among women who see a gynecologist versus a generalist more frequently. **Design:** This was a cross-sectional analysis using the third wave of a US-population-based sample of individuals aged 39 to 90 conducted in 2014. Data were collected via telephone interview and self-administered questionnaires. Frequency of hormone therapy use in the last 30 days and most frequently seen healthcare provider type were each assessed by a single question. Percentages, means, and standard deviations were calculated to describe the sample. Univariate logistic regression was used to assess factors that may be related to HT use, including demographic information and medical history. Variables with $p<0.10$ were entered into a multivariable logistic regression model to evaluate the relationship between provider specialty and HT use. **Results:** Of the 2,362 postmenopausal female respondents, 1,602 (78%) saw a family doctor or an internist most frequently and 57 (2%) women saw a gynecologist most frequently; 270 (14%) women used HT for menopausal symptoms in the past 30 days. Type of most seen healthcare provider was not associated with rate of HT use when controlling for other factors. More chronic health conditions, better self-rated health, past hysterectomy or oophorectomy, more frequent hot flashes, and seeing a gynecologist at all were associated with greater odds of HT use. Higher BMI, current smoking, and higher quality of life were associated with lower odds of HT use. **Conclusion:** Among women in MIDUS, the overall rate of HT use for menopausal symptoms was low (14%). The rate of HT use did not significantly vary by which provider was seen most frequently. However, women who saw a gynecologist for care at all had three times higher odds of HT use. Given that this data is cross-sectional, causality of this association cannot be determined. We cannot tell if women seeing a gynecologist are more likely to have HT offered, or if women with more severe menopausal symptoms seek out a gynecologist to obtain HT. Ensuring that generalists feel comfortable prescribing HT in appropriate scenarios may help eliminate disparities in care among menopausal women, as they are the most seen provider type by nearly ¾ of women.

Sources of Funding: None

Multivariable factors associated with women-reported rates of HT use for menopausal symptoms in MIDUS 3, controlled for age

	OR for taking HT (95% CI)	p Value	Overall p Value
Most seen HCP			0.089
> Family Practice/Internist	1 [ref]		
> Obstetrician/Gynecologist	0.28 (0.02, 3.40)	0.321	
> Other	2.13 (0.94, 4.85)	0.071	
Obstetrician/Gynecologist seen for healthcare	3.17 (1.33, 7.54)		0.009
Race			0.23
> Caucasian	1 [ref]		
> Black	Omitted*		
> Other	2.48 (0.56, 10.93)	0.23	
Number of chronic conditions	1.18 (1.05, 1.32)		0.004
Rating of overall health	1.45 (1.11, 1.89)		0.005
BMI	0.94 (0.88, 0.99)		0.03
Contraindications to HT use (versus no)	0.53 (0.22, 1.27)		0.16
Ovaries removed (versus no)	3.29 (1.37, 7.88)		0.008
Hysterectomy (versus no)	6.05 (2.33, 15.72)		< 0.001
Current smoker (versus no)	0.18 (0.06, 0.55)		0.002
Rating quality of life	0.60 (0.46, 0.76)		< 0.001
Frequency of hot flashes			0.045
> Never	1 [ref]		
> Few times/months to monthly	1.59 (0.65, 3.92)	0.31	
> Daily to Weekly	2.85 [1.25, 6.51]	0.013	

***Omitted because all black women were within one group (had hysterectomy)**

P-22.

Pelvic Floor Clinic model; collaborative and convenient delivery provides improvement in pelvic floor symptoms, mood, and quality of life.

Jean Marie F. McGowan, MD, NCMP[2,1], Siri Thaden, Bachelor of Science in Nursing[2], Bhargav Mistry, MD[2,1], Kristina Garrels, MD[3]. [1]University of North Dakota School of Medicine, Fargo, ND; [2]Sanford Health, Fargo, ND; [3]MetroHealth System, Cleveland, OH

Objective: To demonstrate an improvement in pelvic floor symptoms, quality of life (QOL), and mood by attending Sanford Health Pelvic Floor Clinic (PFC). PFC is a new service providing comprehensive evaluation, education, and multidisciplinary management with convienence. It is held at one location and in one day. Treatment includes primary, secondary, and nonsurgical options. **Design:** Retrospective observational study of women with pelvic floor issues, 18 years and older seen at Sanford PFC in Fargo, ND from July 2017 through April 2020. Pregnant women and men are excluded. PFC includes history intake and exam with provider, first session with Physical Therapist, and education delivered via handouts and group setting or video. Each patient completed the International Consultation on Incontinence Modular Questionnaire (ICIQ-UI) Short form and the ICIQ-Female Lower Urinary Tract Symptoms (FLUTS) form at an initial visit and for follow up 3 months later. ICIQ-UI and -FLUTS are standardized, validated methods measuring the impact of symptoms on QOL and outcome of treatment. Higher scores are associated with more symptoms and lower QOL. For mood, scores from the depression screening tool, Patient Health Questionnaire (PHQ9) and Generalized Anxiety Disorder 7 item (GAD7) for anxiety were reviewed. Scores within the 6 months before initial PFC visit are compared to scores 6-12 months after. Higher scores for PHQ9 and GAD7 reflect more mood symptoms. Change in scores is evaluated by paired t-tests. **Results:** 286 patients were seen in PFC from July 2017 through April 2020 with an average age of 60, ranging from 22 to 90 years old. Most common diagnoses were urinary incontinence, overactive bladder, and vaginal prolapse. 71 women came back to PFC with an average age of 63, ranging from 28 to 88. Table 1 summarizes all submitted initial and follow up ICIQ, PHQ9, and GAD7 scores. Table 2 shows the difference of each woman's initial scores to her follow up scores. For each ICIQ questionnaire, there was a statistically significant lower score on follow up, showing improvement. Statistically significant improvements also seen with PHQ9 and GAD7 responses. Though follow up numbers seem small in comparison, this study is well powered to demonstrate meaningful results. **Conclusion:** Sanford Health PFC is a comprehensive clinic that improves pelvic floor symptoms, mood, and QOL while offering convience for the modern day busy woman and could be a model for other healthcare systems.

Sources of Funding: Sanford Health Foundation

Table 1. Summary of all submitted scores

Questionnaire	Visit	n	Mean	Range
ICIQ-UI Short Form range 0-21	Initial	275	10.2	0-21
	Follow Up	67	7.8	0-18
ICIQ-FLUTS Filling (F) range 0-15	Initial	275	5.4	0-14
	Follow Up	71	3.9	0-12
ICIQ-FLUTS Voiding (V) range 0-12	Initial	279	2.4	0-11
	Follow Up	71	1.7	0-9
ICIQ-FLUTS Incontinence (I) range 0-20	Initial	279	8.2	0-20
	Follow Up	71	6.2	0-16
PHQ9 range 0-27	Inital	99	5.8	0-27
	Follow Up	61	5.3	0-25
GAD7 range 0-21	Inital	96	4.9	0-21
	Follow Up	59	5.0	0-21

Averages and ranges of submitted responses from initial PFC visit and all follow up scores. ICIQ ranges of scores given for each; higher scores correlate with more symptoms and lower quality of life. PHQ9 and GAD7 ranges of scores given for each; higher scores correlate with more symptoms.

Table 2. Paired t-test of initial and follow up scores

Questionnaire	n	Visit	Mean(SD)	MD(SD)	SE(CI)	t-score	p-value
ICIQ-UI range 0-21	67	Initial	10.0(5.8)	2.4(3.9)	0.5(1.5;3.3)	5.06	<0.0001
		Follow Up	7.6(0.6)				
ICIQ-F range 0-15	69	Initial	5.3(2.8)	1.4(2.0)	0.2(0.9;1.9)	5.71	<0.0001
		Follow Up	3.9(2.6)				
ICIQ-V range 0-12	70	Initial	2.2(2.1)	0.5(1.4)	0.2(0.1;0.8)	2.88	0.0053
		Follow Up	1.7(1.9)				
ICIQ-I range 0-20	69	Initial	7.8(4.4)	1.7(2.7)	0.3(1.1;2.4)	5.30	<0.0001
		Follow Up	6.1(4.4)				
PHQ9 range 0-27	59	Initial	7.0(5.6)	1.5(3.6)	0.5(0.6;2.4)	3.24	0.002
		Follow Up	5.5(5.5)				
GAD7 range 0-21	55	Initial	6.4(5.8)	1.3(4.2)	0.6(0.2;2.4)	2.28	0.0267
		Follow Up	5.1(5.4)				

Paired t-test comparing scores of women that returned for follow up to their initial scores. ICIQ ranges of scores given for each; higher scores correlate with more symptoms and lower quality of life. PHQ9 and GAD7: ranges of scores given for each; higher scores correlate with more symptoms. SD=standard deviation;MD=Mean Difference; SE=standard error; CI=confidence interval (95%); p<0.05.

P-23.

Withdrawn by author

P-24.

Adverse Childhood Experiences and Menopause Stage Impact Mood, Cognition, and Basal Inflammatory Markers

Christina Metcalf[1], Rachel Johnson, MS[1], Ellen W. Freeman, PhD[2], Mary D. Sammel, ScD[1], C N. Epperson, MD[1]. [1]University of Colorado Anschutz Medical Campus, Aurora, CO; [2]University of Pennsylvania, Philadelphia, PA

Objective: To determine the extent to which childhood adversity exposure and menopause stage impact mood, cognition, and basal inflammatory marker levels among women in a longitudinal community cohort. **Design:** A subset of the longitudinal Penn Ovarian Aging Study (POAS) community cohort was assessed for childhood adversity exposure at study end (n=243) using the Adverse Childhood Experiences (ACE) questionnaire. A smaller portion of these women had blood samples available for basal inflammatory marker assays (n=167). At study entry, the POAS cohort had regular menstrual cycles, were premenopausal and healthy, and had an intact uterus and at least one ovary. Participants completed cognitive and mood assessments and contributed blood samples approximately annually for 16 years. Cognitive assessments included measures of immediate verbal recall and delayed verbal recall (Buschke Selective Reminding Task), processing speed (Digit Symbol Substitution Task), and sensorimotor processing speed (Symbol Copy Test). Mood assessments included self-reported depressive symptom severity using the Center for Epidemiologic Studies Depression Scale. Menopause stage at each assessment was determined by questionnaire and menstrual diaries and categorized as pre-menopause, late pre-menopause, early transition, late transition, or post-menopause stage; cytokine analyses combined data from the first two stages, resulting in four stages. The ACE questionnaire was used to assess categories of adversity prior to age 18, with possible responses ranging from 0-10 that were categorized into "low" (ACE=0-1) and "high"-exposure (ACE>=2) groups. Blood samples were assayed for interleukin (IL) 6, IL-1B, tumor necrosis factor, and high-sensitivity C-reactive protein levels. Generalized estimating equation models with an exchangeable correlation structure were used to estimate associations of interest between our outcomes of interest (i.e., cognition, mood, and cytokine levels) and exposures (i.e., menopause stage, ACE status, their interaction) while controlling for relevant covariates. **Results:** Nearly forty percent of women endorsed high ACE exposure (38.2%, 93/243). Advancing menopause stage was significantly associated with worse cognitive performance on immediate verbal recall (p=.038) and sensorimotor processing speed (p=.036) controlling for exposure to childhood adversity, BMI, race, education, and age. Menopause stage progression was significantly associated with decreasing depressive symptom severity after controlling for exposure to childhood adversity, BMI, race, and smoking status (p=.001). Notably, exposure to two or more categories of childhood adversity was significantly associated with higher depressive symptoms after adjusting for stage, BMI, race, and smoking status (p=.001). Non-significant trends indicated a main effect of menopause stage on IL-6 controlling for BMI and smoking status (p=.11), such that log IL-6 was significantly higher in the late transition stage compared to premenopause (p=.04). Menopause stage interacted with ACE exposure on IL-6 and IL-1B outcomes at the trend level (p=.05 and p=.09, respectively); IL-6 and IL-1B were significantly higher in the late transition stage for individuals with greater ACE exposure relative to those with little or no exposure (p=.018 and p=.035, respectively), controlling for BMI and smoking status. **Conclusion:** Menopause stage and childhood adversity exposure contributed individually and synergistically to cognitive, mood, and inflammation outcomes for midlife women. Evidence indicated that the late transition stage represents a window of vulnerability for increased inflammation, particularly for women with greater childhood adversity exposures. Menopause stage and childhood adversity represent individual risk factors whose negative impact may be mitigated with targeted interventions to improve mood, cognitive, and inflammatory outcomes for midlife women.

Sources of Funding: Grants from the NIMH (T32 MH015442, CAM), ORWH (P50 MH099910, CNE, MDS), NIDA (K24 DA030301, CNE and R01 DA37289, CNE), and NIA (R01 AG048839, CNE, MDS and R01 AG012745-15, EWF, MDS) supported this research.

P-25.

A survey of healthcare provider knowledge, attitudes, and preferences in management of Genitourinary Syndrome of Menopause (GSM) in the Mid-South

Joshua Morris, M.D., M.A.[1], Cassidy Clark, BS[1], Laura Reed, DNP, APRN[2], Diane Pace, PhD, APRN[2], Xueyuan Cao, PhD[2], Pallavi Khanna, MD, NCMP[1]. [1]Department of Obstetrics and Gynecology, University of Tennessee Health Science Center, Memphis, TN; [2]College of Nursing, University of Tennessee Health Science Center, Memphis, TN

Objective: To survey healthcare providers in an urban Mid-South area who encounter genitourinary syndrome of menopause (GSM) complaints and investigate their knowledge, clinical, and prescribing practices for GSM. **Design:** An online 33-questionnaire survey was distributed to selected target respondents, including Attendings, Advanced Practice Registered Nurses (APRNs), and Trainees (Residents and Fellows). A subset of 17 questions directly addressed the objectives of this study. Free-response answers were analyzed and coded to match existing categories or added as independent responses. Descriptive statistics were summarized, and Chi-squared tests performed using R statistical software. Responses were tabulated in aggregate and analyzed for associations between demographics. **Results:** A total of 106 healthcare providers completed the survey. Demographically, survey respondents were 77(74%) female and 27(26%) male. Ethnicities included 14(13.2%) African American, 77(72.6%) Caucasian, and 15(14.2%) other. Professional credentials included 34(32.1%) Attendings, 28(26.4%) APRNs, and 44(41.5%) Trainees (Residents & Fellows). Among all respondents, 73(68.9%) stated they often had discussions with patients regarding menopausal symptoms, 22(20.8%) occasionally, & 11(10.4%) rarely or never discussed menopausal symptoms. Of the 85(80.2%) providers who reported performing pelvic exams on post-menopausal women, 64(75.3%) performed pelvic exams at least annually, and 18(21.2%) every three years or greater. There was no statistical significance between the level of training and the frequency of screening. Of note, 21(13.2%) respondents stated they never perform vaginal exams on post-menopausal women. As to when vaginal exams should cease, 60.9% reported never, 32.9% stated age 65, and 6.1% reported between ages 50-60. No statistical significance was found between training level. A total of 76.4% of respondents stated they had prescribed topical therapies for GSM. Most commonly prescribed products were lubricants/moisturizers (93.3%), estradiol cream (90.0%), conjugated equine estrogen (77.3%), estradiol tablets (55.1%), and estradiol vaginal inserts (50%). Only 55(55.3%) respondents reported being familiar with the boxed warning on low-dose vaginal estrogen. When asked if they were comfortable counseling about the warning, 48(51.1%) of respondents either agreed/strongly agreed compared to 46(48.9%) who answered neutral/disagreed/strongly disagreed. When accounting for educational background, 20(64.5%) Attendings were more aware of warning compared to 64% APRNs and 42.1% of Trainees (p = 0.028). Most notably, 16.1% Attendings, 28% APRNs, & 29.7% Trainees responded they ***never*** provided counseling on the boxed warning. Of these respective groups, 58.1%, 48%, and 18.9%, indicated they often provided counseling (p = 0.002). Notably, Trainees strongly disagreed 5(13.2%) that they were comfortable with counseling patients on the warning as compared to APRNs 1(4%) or Attendings 1(3.2%) (p = 0.003). **Conclusion:** This study identifies the knowledge of Mid-South healthcare providers and how they evaluate and manage patients with GSM. It further identifies gaps in provider awareness of the boxed warning and comfort level in counseling about low-dose vaginal estrogen. Results will be useful in providing continuing education to providers and more effective communication, evaluation, and treatment to patients.

Sources of Funding: None

P-26.

Patient Satisfaction With the Use of Revaree to Treat Vaginal Atrophy Symptoms

Lila Nachtigall[1], Sarah Sylla[2], Emir Veledar[3], James Komorowski[2]. [1]NYU Langone Health, New York City, NY; [2]Bonafide Health, LLC, Harrison, NY; [3]Emory University School of Medicine, Atlanta, GA

Objective: A national survey study was conducted to assess patient satisfaction with the use of Revaree® for vaginal atrophy symptom relief. Revaree is a hormone-free vaginal insert made from hyaluronic acid, which is a molecule found naturally throughout the body that hydrates and renews vaginal tissue. Clinical evidence supports that hyaluronic acid significantly reduces vaginal dryness, vaginal itching and burning, and dyspareunia. The following survey was conducted to confirm these beneficial effects in a real-world setting and gather further information on the effects of Revaree on vaginal dryness, intimacy, and quality of life. **Design:** An optional, rolling online survey was emailed to Revaree patients who had been taking Revaree for time periods ranging from less than one month to a year. Survey data was collected from 1,458 patients between March 2019 and June 2020. A 5-point Likert scale was used to assess patient satisfaction, with responses ranging from "strongly disagree" to "strongly agree." Response rate calculations combined "strongly agree" and "agree" responses to each question. Responses of "not applicable" were removed from the total number of responses for certain questions. During the initial 9 months of enrollment, patients received no compensation. To increase enrollment, after the initial 9 months, patients were compensated with a $5 gift card for completing the survey. The survey results were analyzed by an independent statistician. **Results:** Survey findings reflected the real-world opinions of patients taking Revaree (n=total applicable responses per question): 85% began experiencing relief within 8 weeks (n=1,458); 82% responded that Revaree reduced vaginal dryness (n=1,447); 72% responded that Revaree reduced vaginal burning (n=1,093); 75% responded that Revaree reduced vaginal irritation (n=1,237); 66% responded that Revaree reduced pain during sex (n=1,227); 69% responded that Revaree makes sex more comfortable (n=1,265); 65% responded that Revaree improved intimacy with partners (n=1,240); and 69% responded that Revaree improved quality of life (n=1,376). In addition, 77% responded that Revaree is easy to insert (n=1,434), 67% responded that Revaree is non-messy (n=1,442), 78% responded that the insert formulation makes Revaree convenient to use (n=1,435), and 59% responded that Revaree makes everyday activities more comfortable (n=1,245). Finally, 76% of women reported satisfaction with Revaree (n=1,434), 91% would recommend Revaree to any friends or family members (n=1,457), and 96% planned to continue using Revaree (n=1,457). **Conclusion:** This survey demonstrated a positive patient experience and high level of patient satisfaction with Revaree for the relief of vaginal atrophy symptoms. Patients also reported that the vaginal insert formulation was very convenient, non-messy, and easy to use. The objective findings of previously published randomized, controlled studies on Revaree's main ingredient, hyaluronic acid, were confirmed by the subjective opinions expressed by the patients in this survey. These data, combined with previously published studies, support the use of Revaree as a hormone-free, convenient treatment to relieve vaginal atrophy symptoms and enhance comfort during intimacy and everyday life.

Sources of Funding: This study was funded by Bonafide Health, LLC.

P-27.

Women and Cardiovascular Disease: Progress made since the Women's Health Initiative

Nancy A. Phillips, MD[1], John Kostis, MD[2], Kamana Misra, PhD[3], Gloria Bachmann[1]. [1]Women's Health Institute, Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ; [2]Rutgers Robert Wood Johnson Medical School, Cardiovascular Institute, New Brunswick, NJ; [3]NJ American Women in STEM - AWIS, New Brunswick, NJ

Objective: To review the literature on prevention of cardiovascular disease in midlife and older women, including the historic and evolving role of estrogen and current best practices. **Design:** A literature review was conducted on PubMed and Google Scholar using the terms cardiovascular disease, menopause, menopausal hormone therapy and estrogen. **Results:** Data suggest that annual deaths from heart disease in women are equivalent to men and that heart disease is the leading cause of death for US women. Further, 6.2% of women age 20 and older have coronary heart disease. After the menopause, this number increases to ~33%, with an overall increase in heart attacks in women 10 years post-menopause. Commencing in the 1960's, estrogen therapy for menopausal women was considered a preventative treatment for cardiovascular disease while also managing the distressing symptoms that may accompany this phase of the woman's life cycle. However, this prescribing practice came to a halt in the early 2000's when data from the Women's Health Initiative emerged that showed oral estrogen plus progestin carried increased risks of not only breast cancer, but also myocardial infarction, stroke and VTE. Further results showed that oral estrogen alone increased the risk of stroke but not myocardial infarction or VTE. Re-evaluation of the WHI recognized a cardiovascular benefit of HT if initiated within 5 years of menopause versus increased risk if >10 years (The Timing Hypothesis), although HT is not indicated for cardiovascular health. The overwhelming data suggest that estrogen use does not protect against coronary heart disease or stroke. **Conclusion:** Estrogen, although indicated for many symptomatic menopausal women cannot be considered an intervention to decrease the risk of CV disease. Rather, management of hypertension, serum lipids, and weight, a healthy diet and regular exercise appear to be management strategies that may reduce this risk. Midlife and older women should be asked about their cardiovascular health and have blood pressure and hyperlipidemia issues actively addressed. Healthy lifestyle interventions should be a regular part of the well woman visit for all midlife and older women. For those women where HT is appropriate for treatment of vasomotor symptoms, appropriate counseling regarding cardiovascular risk should be applied.

Sources of Funding: none

P-28.

Characterizing Breast Sensory Function in Pre- and Menopausal Women

El Pinkerton, MPH[1], Kate Doyle, MPH[1], Emily Abramsohn, MPH[1], Phil Schumm, MA[5], Sliman Bensmaia, PhD[3,4], Stacy T. Lindau, MD, MAPP[2]. [1]Department of Obstetrics and Gynecology, University of Chicago, Chicago, IL; [2]Departments of Obstetrics and Gynecology and Medicine-Geriatrics, University of Chicago, Chicago, IL; [3]Department of Organismal Biology and Anatomy, University of Chicago, Chicago, IL; [4]Grossman Institute for Neuroscience, Quantitative Biology, and Human Behavior, University of Chicago, Chicago, IL; [5]Department of Public Health Sciences, University of Chicago, Chicago, IL

Objective: In addition to lactation, the female breast plays an important role in psychosocial and sexual functioning across the life course. Yet little is known about women's perception of their breast sensory function (BSF) or how BSF relates to menopausal status. We report preliminary findings from the development and validation of a novel measure of BSF in a national panel of pre- and menopausal women. **Design:** Following the Patient-Reported Outcomes Measurement Information System Standards, we are developing a patient-reported measure to assess BSF. We created a candidate list of 108 survey items categorized into functional (touch, pressure, nipple erection, mobility, thermoreception) and global (satisfaction, pleasure, importance, discomfort and pain) domains. Refinement and pilot testing of the measure yielded 48 items which were administered via web-based survey to a national sample of 650 sexually active women with (n=350) and without (n=300) breast cancer for psychometric evaluation. Descriptive analysis of one representative item from each global domain was stratified by menopausal status among the subgroup of women without breast cancer. Menopause was defined as 12 months since last menses and endorsement of menopause. **Results:** Menopausal women were substantially less likely to get "quite a bit" or "a lot" of pleasure from contact with the breasts during sexual activity (39% versus 58%, p=0.01) (Table 1). Menopausal women were also less likely to feel that their breasts were "quite a bit" or "very" important to their sex life (29% versus 49% of premenopausal women, p=0.002). By contrast, reports of breast discomfort and pain were similar among menopausal and premenopausal women: discomfort ("quite a bit"/"a lot") was reported by 2.2% and 0.6%, and pain ("quite a bit"/"a lot") was reported by 1.1% and, 1.7%, respectively. **Conclusion:** Although menopausal women are less likely to endorse breast sensation as an important or pleasurable aspect of their sex life, they are no more likely to report breast discomfort or pain than premenopausal women, suggesting that differences in importance and pleasure may be due to other factors such as reduced sensation. These findings inform development of the validated patient-reported BSF measure and are informative to assessing and addressing sexual function concerns among women across the life course.

Sources of Funding: This work was supported by NCI Grant 1R21CA226726 and pilot funding from the Janet D. Rowley Discovery Fund. The content is solely the responsibility of the author and does not necessarily represent the official views of the NIH.

Table 1. Breast sensory function

	Postmenopausal (N=109)	Premenopausal (N=191)	p value
	n (%)	n (%)	
In the past 30 days, during sexual activity, how satisfied have you been with the sensation (feeling) in your breasts?			0.117
Missing	17	17	
Not at all / a little	23 (25.0%)	40 (23.0%)	
Somewhat	30 (32.6%)	39 (22.4%)	
Quite a bit / very	39 (42.4%)	95 (54.6%)	
In the past 30 days, during sexual activity, how much pleasure did you get from contact with your breasts? (Contact can mean touching, mouth, kissing, blowing, pressure)			0.014
Missing	17	15	
None / a little bit	26 (28.3%)	35 (19.9%)	
Some	30 (32.6%)	39 (22.2%)	
Quite a bit / a lot	36 (39.1%)	102 (58.0%)	
In the past 30 days, how important have your breasts been to your sex life?			0.002
Missing	0	1	
Not at all / a little	50 (45.9%)	57 (30.0%)	
Somewhat	28 (25.7%)	40 (21.1%)	
Quite a bit / very	31 (28.5%)	93 (48.9%)	
In the past 30 days, during sexual activity, how much discomfort did you have in your breasts?			0.503
Missing	16	18	
None / a little bit	83 (89.2%)	158 (91.3%)	
Some	8 (8.6%)	14 (8.1%)	
Quite a bit / a lot	2 (2.2%)	1 (0.6%)	
In the past 30 days, during sexual activity, how much pain did you have in your breasts?			0.345
Missing	16	16	
None / a little bit	83 (89.2%)	163 (93.1%)	
Some	9 (9.7%)	9 (5.1%)	
Quite a bit / a lot	1 (1.1%)	3 (1.7%)	

P-29.

Novel metrics of high density lipoprotein and cognitive function among perimenopausal women in the Study of Women's Health Across the Nation (SWAN) HDL ancillary study

Meiyuzhen Qi, MPH[1], Trevor Orchard, PhD[1], Dan McConnell, PhD[2], Maria Brooks[1], Samar R. El Khoudary, PhD[1]. [1]University of Pittsburgh, Pittsburgh, PA; [2]University of Michigan, Ann Arbor, MI

Objective: The brain contains 23% of all cholesterol in the body. High Density Lipoprotein (HDL), the only lipoprotein that promotes reverse transportation of cholesterol from cells, may contribute to main pathological pathways of cognitive decline by modifying the metabolism of amyloid β-peptide (Aβ) deposition. Women are disproportionally affected by dementia and they experience adverse changes in HDL subclasses and function as they traverse menopause. However, limited studies assessed the relationship between novel metrics of HDL and cognitive function among perimenopausal women. Our objective was to assess associations of novel metrics of HDL with measures of cognitive function among midlife women. **Design:** Participants from the SWAN HDL ancillary study who had available measures of cognitive function (processing speed and verbal episodic memory (immediate and delayed)) along with HDL-cholesterol (HDL-C) and novel metrics of HDL (nuclear magnetic resonance (NMR) HDL subclasses (total HDL-Particle (HDL-P), large HDL-P, medium HDL-P, small HDL-P), size, and HDL cholesterol efflux capacity (HDL-CEC)) measured at the same time were included in this study. Processing speed was measured using the symbol digit modalities test and episodic memory was measured using the East Boston memory test. Linear regression models were created to assess the relationship between each HDL metric and each cognitive function measure separately. Final models were adjusted for age, education level, race, menopausal status, and total HDL particles (for models with HDL-C) or HDL-C (for models of NMR HDL subclasses and size). **Results:** Five hundred and fifty-seven women with mean age of 53.0 (SD=3.75) years old were included, with 42.7% of them being post-menopausal. In final models, higher HDL-C, HDL-CEC/total HDL-P and larger HDL size were significantly associated with lower processing speed, while higher total HDL-P was significantly associated with better processing speed. HDL subclasses, but not function, were related to verbal episodic memory. As such, higher concentration of large HDL-P and larger HDL size were significantly associated with worse immediate and delayed episodic memories while higher concentration of small HDL-P was associated with better verbal immediate and delayed episodic memories (Table). **Conclusion:** In perimenopausal women, small HDL particles and size may have a neuroprotective effect. The associations of HDL-C, HDL-CEC with cognitive function among midlife women remain unclear and need to be assessed in future longitudinal study. A better understanding of pathways through with HDL metrics might relate to cognitive function may help the prevention of dementia at an early reversible stage of cognitive decline.

Sources of Funding: 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 SWAN repository (U01AG017719). The SWAN HDL ancillary study has grant support from national institute on aging (NIA) AG058690. 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.

The relation between HDL metrics and cognitive function measures^

HDL metrics	Processing speed		Verbal episodic memory (immediate recall)		Verbal episodic memory (delayed recall)	
	β (SE)	p-value	β (SE*)	p-value	β (SE*)	p-value
HDL-C	-0.09 (0.04)	0.01	-0.01 (0.01)	0.33	-0.01 (0.01)	0.24
HDL-CEC	0.77 (0.90)	0.39	0.16 (0.14)	0.26	0.02 (0.16)	0.90
HDL-CEC/total HDL-P	-47.60 (22.63)	0.04	-1.08 (3.42)	0.75	-2.61 (3.68)	0.48
Total HDL-P	0.24 (0.09)	<0.01	0.02 (0.01)	0.12	0.02 (0.01)	0.20
Large HDL-P	-0.38 (0.25)	0.13	-0.13 (0.04)	<0.01	-0.13 (0.04)	<0.01
Medium HDL-P	0.07 (0.08)	0.37	-0.02 (0.01)	0.08	-0.02 (0.01)	0.22
Small HDL-P	0.11 (0.07)	0.10	0.04 (0.01)	<0.01	0.03 (0.01)	<0.01
HDL size	-3.02 (1.18)	0.01	-0.64 (0.17)	<0.01	-0.64 (0.19)	<0.01

^We adjusted for age, education level, race, menopausal status, and total HDL-P (for HDL-C) or HDL-C (for NMR HDL metrics).
*** The distributions of immediate and delayed episodic memory scores were skewed, so we applied linear regression with robust standard error.**

P-30.

A double-blind, randomized, placebo-controlled trial of suvorexant for the treatment of hot flash-associated insomnia in midlife women

Shadab A. Rahman[1,2], Margo D. Nathan[3], Aleta Wiley[3,4], Sybil Crawford[5], Aviva Y. Cohn[6], Jessica A. Harder[3], John W. Winkelman[1,7], Suzanne M. Bertisch[1,2], Leilah K. Grant[1,2], Athena Erickson[3], Akanksha Srivastava[3], Kathleen McCormick[3], Hadine Joffe[3,4]. [1]Division of Sleep Medicine, Harvard Medical School (HMS), Boston, MA; [2]Division of Sleep and Circadian Disorders, Brigham and Women's Hospital (BWH), Boston, MA; [3]Dept of Psychiatry, BWH, HMS, Boston, MA; [4]Connors Center for Women's Health and Gender Biology, BWH, HMS, Boston, MA; [5]University of Massachusetts Medical School, Worcester, MA; [6]Division of Endocrinology, Diabetes, and Hypertension, BWH, HMS, Boston, MA; [7]Dept of Psychiatry, Massachusetts General Hospital, HMS, Boston, MA

Objective: One-quarter of women meet criteria for chronic insomnia, primarily with disrupted sleep maintenance, during the menopausal transition. Nocturnal vasomotor symptoms (VMS) are the primary cause of both sleep disturbance and chronic insomnia disorder. The hypothalamic neuropeptide orexin-A promotes wakefulness and modulates thermoregulation, potentially underlying hyperarousal and sleep disruption. Orexin-A levels increase after menopause and are suppressed by estrogen therapy, suggesting a role for orexin antagonism as a novel approach to treat VMS-associated insomnia. We therefore tested the efficacy of the dual orexin receptor antagonist suvorexant for chronic insomnia disorder related to nighttime VMS in peri- and postmenopausal women. **Design:** In a parallel-arm, double-blind, placebo-controlled trial, 60 women were randomized in a 1-to-1 ratio to receive suvorexant 10-20 mg orally per day or matching placebo for 4 weeks. All participants had clinically diagnosed insomnia lasting 3+ months associated with nighttime VMS, an Insomnia Severity Index (ISI) score ≥15, and 30+ minutes diary-reported wake after sleep onset (WASO), no other diagnosed sleep disorder nor psychiatric illness. The primary endpoint was the percentage change in the ISI between baseline and study end. Secondary outcomes included the percentage change in diary-reported sleep parameters (time in bed [TIB], total sleep time [TST], WASO) and VMS (nighttime and daytime frequency). Data from study completers were analyzed using generalized linear models. **Results:** Of 60 randomized (30/arm), there were 25 completers in the suvorexant arm and 28 in the placebo arm. For the group overall, mean (±SD) age was 54.1 (±4.3) years, ISI was 18.4 (±3.1) (consistent with moderately severe insomnia), TIB was 8.3h (±0.9), TST was 5.6h (±1.3), WASO was 1.5h (±0.9), nighttime VMS was 3.7 (±1.6), and daytime VMS was 4.3 (±3.2). Due to group differences at baseline in TIB, TST and WASO ($p<0.1$), statistical models were adjusted for baseline values. On average, ISI scores decreased significantly more on suvorexant than on placebo (-42.1% ± 26.9 vs. -28.6% ± 20.4, p=0.043), such that final ISI scores were 10.6 (±5.6) and 13.0 (± 4.0), respectively. TIB increased (2.0% ± 8.2) on suvorexant but decreased (-7.0% ± 21.1) on placebo (p=0.02), and TST increased more on suvorexant than on placebo (12.0% ± 22.1 vs. 6.4% ± 22.7, p=0.042). There were no group differences in WASO (-53.7% ± 36.2 vs. -37.5% ± 30.3, p=0.16). The number of nighttime VMS reported per night decreased significantly more on suvorexant than on placebo (-45.2% ± 31.6 vs. -17.5% ± 30.6, p=0.005), whereas reductions in the number of VMS reported during the daytime did not differ by group (-28.5% ± 43.7 vs. -3.7% ± 67.8, p=0.17). Suvorexant (final dose 20mg in 96%) was well tolerated. Of 7 non-completers, only one (on suvorexant) was adverse event-related (due to headache). Adverse events reported by >1 participant were sleepiness, dry mouth, gastro-intestinal symptoms, and worsening mood in the suvorexant arm, and dry mouth and headache in the placebo arm. **Conclusion:** Results of this randomized placebo-controlled trial show that suvorexant therapy is a well-tolerated and effective treatment for VMS-associated insomnia in midlife women, with additional benefits for self-reported nighttime, but not daytime, VMS. Antagonism of orexin provides a robust novel therapeutic option for midlife women with VMS-associated chronic insomnia, possibly due to specific menopause and thermoregulatory effects of orexin.

Sources of Funding: Sponsored by Merck Investigators Studies Program grant.

P-31.

Women's Experience of The Late Reproductive Stage: Findings from the Women Living Better Survey

Nina Coslov, MBA[2], Marcie Richardson, MD[3], Ellen S. Mitchell, PhD[1], Nancy F. Woods, PhD, BSN, MN[1]. [1]School of Nursing, University of Washington, Seattle, WA; [2]Women Living Better, Boston, MA; [3]Menopause Service, Harvard Vanguard Medical Associates, Boston, MA

Objective: The Late Reproductive Stage *(LRS)* precedes the Menopause Transition *(MT)* as defined by 2010 Staging Reproductive Aging Workshop (STRAW+10) conferees. A scoping review (Woods, Coslov, Richardson, Mitchell, 2020) highlighted limited research characterizing the LRS. The aim of this research is to examine the prevalence of symptoms in the LRS as defined by STRAW+10. **Design:** Women ages 35-55 were eligible to complete an 82-question online survey hosted on Survey Monkey and offered in English and Spanish. Participants responded to links posted on WomenLivingBetter.org, shared in the Women Living Better newsletter, on social media channels, with women's groups and through personal networks. The survey was opened March 3, 2020. The five-part survey first invited women to describe their current menstrual patterns and recent changes and whether and how they tracked their cycles. The second part queried about symptoms phrased in women's own words, their frequency, and degree of bother. In the third part, respondents indicated degree to which symptoms interfered with their lives, identifying their most bothersome symptom and whether they had sought health care for that symptom. Participants were invited to comment on their health care experience. The fourth part asked about their overall health, life satisfaction, and stress. Women shared self-care and stress-management activities. The final section covered demographic characteristics. Women were classified as either in the LRS or MT based on their reports of menstrual cycle characteristics using STRAW+10 criteria and those reported by Mitchell (2000). Women were excluded if they were using hormonal birth control or hormones, had had an endometrial ablation, a hysterectomy, had had a recent major life event, had been pregnant or lactated in the past three months or had gained or lost 20% of their body weight in the past 6 months. Cycles were classified as LRS if women reported regular cycles, had 3 or 4 cycles in the past three months, and had noticed changes in either cycle length, days of flow or amount of flow. Women with MT cycles had 2 or fewer periods in the past 3 months and not having regular cycles. Results presented here include data collected through June 2020 from the English language survey. **Results:** To date 2133 women responded to the English language survey with 867 meeting the criteria for the LRS. Participants included 37% from outside the US, 13% were racially diverse, and 17% reported having a very hard or somewhat hard time paying for basics. Participants identified which of sixty-five symptoms they had experienced in the past three months. The most prevalent symptoms for women in the LRS were forgetfulness (60%), irritability (57%), less interest in sex (53%), difficulty concentrating (52%), fatigue (49%), dry skin (48%), anxiety (48%), breast soreness (47%), weight gain (47%), stress incontinence (41%), awakening during the night with >1 hour wakefulness (42%), night sweats (40%), and feeling overwhelmed (40%). In addition, over 30% of women experienced hot flashes, heart palpitations, worrying, low mood, tearfulness, tension headaches, difficulty making decisions, skin itchiness, dry eyes, dry hair, thinning hair, facial hair growth, bloating, joint/muscle pain, and difficulty with sexual arousal. When asked to reflect on when they expected the changes associated with the menopausal transition would begin, 60% said age 50 or older and another 27% said 45-49. **Conclusion:** Women in the LRS experience potentially hormone related symptoms before their cycles become irregular. In addition, they report not anticipating these changes until they reach their late 40s or early 50s. This mismatch between expectations and lived experience causes women distress. Lack of acknowledgement by the healthcare community that symptoms could be related to ovarian aging before their cycles differed by 7 days, leads to women feeling at best unvalidated and at worst fearful that something is wrong. Education for women and healthcare providers about the prevalence of symptoms during the LRS and strategies to alleviate them is needed along with research to understand their physiology.

Sources of Funding: None

P-32.

Genitourinary Symptoms in Breast Cancer Survivors: Prevalence, Correlates, and Relationship with Sexual Functioning

Ying Sheng, Doctoral[1], Janet S. Carpenter, PhD[1], Andrea Cohee, PhD[1], Susan Storey, PhD[1], Victoria L. Champion, PhD[1,2]. [1]School of Nursing, Indiana University Purdue University Indianapolis, Indianapolis, IN; [2]Indiana University Melvin and Bren Simon Comprehensive Cancer Center, Indiana University, Indianapolis, IN

Objective: The purpose of this study was to better understand persisting genitourinary symptoms in breast cancer survivors. Study aims were to: 1) evaluate the prevalence of genitourinary symptoms (vaginal/vulvar irritation, pelvic discomfort, problem with urinary control, vaginal infection, and vaginal bleeding); 2) evaluate demographic and clinical correlates of genitourinary symptoms; and 3) evaluate the association between genitourinary symptoms and sexual functioning (Total score and enjoyment and difficulty subscales). **Design:** A secondary analysis of cross-sectional survey data included 1,085 women who were 45 or younger or 55 to 70 years old when diagnosed with breast cancer and 3-8 years from initial diagnosis. Self-reported questionnaires and scales were used to collect demographics, clinical factors, genitourinary symptoms, and sexual functioning (Total score and enjoyment and difficulty subscales). Prevalence of the genitourinary symptoms and correlations between symptoms and demographic variables, clinical factors, and sexual functioning were computed using descriptive analysis, chi-square tests, t-tests, multiple logistic regression analysis, and Pearson correlation coefficients. **Results:** Among these breast cancer survivors, reported genitourinary symptoms included: vaginal/vulvar irritation (15.0%), pelvic discomfort (14.9%), problem

with urinary control (9.1%), vaginal infection (4.2%), and vaginal bleeding (4.1%). About one-third (33.6%) of breast cancer survivors reported at least one symptom and 10.1% reported two or more. A multiple logistic regression analysis showed that younger age (odds ratio [OR] = 0.98, 95% CI [0.96, 0.99], p=.010), more comorbidities (OR = 1.19, 95% CI [1.09, 1.29], p<.001), and taking treatment for menopausal symptoms (OR = 1.73, 95% CI [1.31, 2.30], p<.001) were significantly related to reporting at least one genitourinary symptom. In addition, compared to premenopausal women, those who were artificially postmenopausal (due to breast cancer treatment and other or unsure) were less likely to report genitourinary symptoms (OR = 0.50, 95% CI [0.28, 0.89], p=.018). Except for vaginal bleeding, individual symptoms and having one or two more symptoms were associated with lower sexual functioning total score, less sexual enjoyment, and more sexual difficulty (all p<.04). The number of genitourinary symptoms was weakly related to sexual functioning total score, sexual enjoyment, and sexual difficulty: -.16, -.15, and .15 (all p<.001), respectively. **Conclusion:** This study identified the prevalence, correlates, and relationship of five genitourinary symptoms to sexual functioning in breast cancer survivors. Results support the need for additional studies of genitourinary symptoms in this population. Moreover, the relationship between these symptoms with demographic and clinical factors can facilitate the identification of those at higher risk of experiencing these symptoms and inform appropriate treatment and care.

Sources of Funding: Dr. Sheng is supported as a postdoctoral fellow (5T32CA117865). The data in this manuscript came from a study that was coordinated by the ECOG-ACRIN Cancer Research Group (Robert L. Comis, MD and Mitchell D. Schnall, MD, PhD, Group Co-Chairs) and supported in part by Public Health Service Grants CA189828, CA180795, CA37403, CA35199, CA17145 and CA49883, and from the National Cancer Institute, National Institutes of Health and the Department of Health and Human Services. Dr. Cohee is supported by Indiana Clinical and Translational Sciences Institute (KL2 Program), UL1TR002529 (A Shekhar, PI). Dr. Storey is supported by an RE01 from the Oncology Nursing Foundation. The manuscript content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

P-33.

Segesterone Acetate/Ethinyl Estradiol Contraceptive Vaginal System (SA/EE; CVS): An Option That May Be Suitable For Perimenopausal Women

James Simon, MD[1], David F. Archer, MD[2], Shelli Graham, PhD[3], Brian Bernick, MD[3], Sebastian Mirkin, MD[3]. [1]1George Washington University and IntimMedicine Specialists, Washington, DC; [2]Eastern Virginia Medical School, Norfolk, VA; [3]TherapeuticsMD, Boca Raton, FL

Objective: To review the characteristics of SA, describe the anovulation and bleeding profile with CVS use, and explore the potential for use of the CVS in perimenopausal women. Perimenopausal women may still be fertile and menstruate. Low-dose birth control products are known to ease the perimenopausal transition by preventing ovulation, regulating cycles and possibly reduce hot flashes. A 1-year (13 cycles), long-lasting, procedure free, woman controlled, reversible contraceptive [Annovera® (segesterone acetate and ethinyl estradiol vaginal system); TherapeuticsMD, Boca Raton, FL], approved for use by females of reproductive potential to prevent pregnancy, releases an average of 150 mcg SA and 13 mcg EE daily. The ring-shaped CVS is made of a squishy silicone elastomer. Previous PK modelling data predicted mean serum SA levels above the anovulatory threshold if the ring was used continuously (no removal of the CVS) for 1 year.[1] **Design:** Characteristics of SA, anovulation and bleeding profiles were reviewed from published studies. **Results:** SA is a progestin derived from progesterone with high progestogenic activity and no androgenic effects at contraceptive doses.[2] SA exerts contraceptive efficacy at low doses when given vaginally.[3] In studies, consistent ovulation inhibition was observed with mean serum SA >73 pmol/L.4-7 In two phase 3 trials of women (≤40 years), CVS was associated with bleeding control, where 98% of CVS users had a mean of 4.9 scheduled bleeding/spotting days/cycle and 13%–22% of women/cycle had a mean of 3.9 unscheduled bleeding/spotting days/cycle (in those who had unscheduled bleeding).[8] Few (1.7%) women discontinued early due to unacceptable bleeding.[9] **Conclusion:** The SA/EE CVS effectively inhibits ovulation in a 21/7-day in/out cyclic regimen for up to a year and users have a regular bleeding profile. The SA/EE CVS is a reversible, procedure-free contraceptive that may be an appropriate option for perimenopausal women. **1.** Liu J, et al. *Journal of the Endocrine Society*, Volume 4, Issue Supplement_1, April-May 202, SAT-013. **2.** Kumar N, et al. *Endocrinology*. 2017;158:170-182. **3.** Brache V, et al. *Steroids*. 2000;65:687-691. **4.** Haukkamaa M, et al. *Contraception*. 1992;45:49-55. **5.** Brache V, et al. *Contraception*. 2001;63:257-261. **6.** Sivin I, et al. *Contraception*. 2005;71:122-129. **7.** Sivin I, et al. *Contraception*. 2004;69:137-144. **8.** Vieira CS, et al. *Contraception*. 2019;100:438-444. **9.** Annovera® (segesterone acetate and ethinyl estradiol vaginal system) Prescribing Information. TherapeuticsMD. Boca Raton, FL. 2018.

Sources of Funding: TherapeuticsMD

P-34.

Burden of Illness in Women with a Diagnosis of Hypoactive Sexual Desire Disorder

James Simon, MD[1,2], Amod Athavale, PhD[3], Rahul Ravindranath, MEng[3], Nandini Hadker, MA[3], Amama Sadiq, MD, MPH[4]. [1]George Washington University, Washington, DC; [2]IntimMedicine, Washington, DC; [3]Trinity Life Sciences, Waltham, MA; [4]AMAG Pharmaceuticals, Inc., Waltham, MA

Objective: Hypoactive sexual desire disorder (HSDD), the most prevalent form of female sexual dysfunction, is marked by persistent deficiency or absence of desire for sexual activity that is associated with distress and is not secondary to other disorders. While HSDD is associated with psychological and interpersonal consequences, the impact of HSDD on quality of life among patients is poorly understood. The aim of this study was to assess burden of illness and impact on quality of life among postmenopausal and premenopausal women reporting a diagnosis or symptoms of HSDD. **Design:** A 30-minute, IRB-approved internet-based survey was designed to explore patient experience and the physical, social, mental, emotional, and economic burden related to HSDD. Key inclusion criteria were the following: ≥18 years of age; a diagnosis or symptoms of HSDD in accordance with the Decreased Sexual Desire Screener; and currently being in a stable, monogamous relationship with a partner for ≥6 months. The physical component score (PCS) and the mental component score (MCS) derived from the SF-12 Health Survey were computed and compared with general population norms. A score of 50 on both the MCS and PCS of the SF-12 represents the general population norm; a score lower than 50 indicates poorer mental or physical health than the norm. **Results:** Five hundred thirty (530) women completed the survey and were included in this analysis. The mean age was 36.7 years, and the majority were white (68%) and married (62%). The mean Female Sexual Function Index (FSFI) questionnaire total score of all participants was 17.5±7.1, signifying that sexual functioning was significantly below normal. Furthermore, the mean FSFI total score in postmenopausal women (15.0) was significantly lower (P<0.001) than in premenopausal women (18.3). When assessed for each aspect of sexual function, participants reported a score of 2.6 in the arousal, desire, and orgasm domains out of a maximum score of 6 for each domain of the FSFI. Postmenopausal women exhibited significantly lower scores on the arousal (P<0.001), desire (P<0.001), orgasm (P<0.001), and lubrication (P<0.001) domains compared with premenopausal women. Sexual activity was measured by mean number of events of caressing, foreplay, and vaginal intercourse/penetration; both post- and premenopausal women reported a 50% decrease in frequency of all 3 events after the onset of HSDD symptoms. Regardless of menopausal status, women with HSDD reported that relationships with their partners/spouses were impacted most. On the SF-12, 40.7% of postmenopausal women had an MCS lower than that of the general population norm; however, more premenopausal women had lower MCS scores (65.0%) than the general population norm. **Conclusion:** This is the first study that illustrates the burden of HSDD in a quantifiable manner in both premenopausal and postmenopausal women. Sexual functioning in postmenopausal women was significantly lower than that in premenopausal women, and both groups experience interference in social relationships due to HSDD. The results of this study demonstrate the pervasive effects of HSDD on the psychosocial aspects of patients' lives.

Sources of Funding: AMAG Pharmaceuticals, Inc.

P-35.

Safety of transdermal hormone therapy in menopausal women at increased risk for venous thromboembolism

Talia Sobel, MD, Wen Shen, MD. Johns Hopkins University School of Medicine, Baltimore, MD

Objective: It is estimated that over 45% of women in the United States are menopausal. Many of these women suffer from vasomotor symptoms such as hot flashes and night sweats, as well as sleep disturbance, fatigue, and mood changes. Menopause hormone therapy (MHT) is the gold standard treatment, but its use is controversial since the Women's Health Initiative (WHI) study found an increased risk of breast cancer, coronary heart disease, stroke, and venous thromboembolic events (VTE) with use of oral conjugated equine estrogen and medroxyprogesterone acetate. However, several studies have shown no increased risk of VTE with transdermal MHT use in healthy postmenopausal women. The proposed mechanism is avoidance of hepatic first-pass metabolism by transdermal estrogens, and therefore, no activation of coagulation factors. Several societies have endorsed use of transdermal MHT over oral MHT in healthy postmenopausal women. The Endocrine Society provides a level C of evidence that "transdermal estrogen does not increase venothrombotic episode risk" and ACOG's committee opinion from 2013 recommends prescribers consider "the possible thrombosis-sparing properties of transdermal forms of estrogen therapy," while the International Menopause Society (IMS) reports "The risk of venous thromboembolism is less with transdermal than with oral estradiol." However, there is a paucity of data surrounding use of transdermal MHT in women at increased risk for VTE. These include women with personal or family history of VTE, overweight/obesity, hereditary or acquired thrombophilia, tobacco use, autoimmune disease, chronic inflammatory disorders, recent surgery, trauma, immobilization, etc. Given the limited data, clinicians are hesitant to prescribe MHT in these at-risk women who are left to suffer with vasomotor symptoms without relief. It is our objective in this literature review to provide clinicians with evidence on the risk profile of transdermal MHT use in postmenopausal women at increased risk of VTE. **Design:** We performed a search of PubMed, Embase and

Scopus using these MeSH terms: “transdermal menopause hormone therapy”, “hormone replacement therapy”, “estrogen replacement therapy”, “hypercoagulability”, “venous thromboembolism”, “thrombophilia”, “transdermal patch”, “immobilization”, “surgery”, “autoimmune”, and “high risk menopause hormone therapy”. We searched all relevant papers from 2000 to 2020, resulting in 136 papers, the majority of which were after the WHI study from 2001. We included 13 primary articles on transdermal MHT use in postmenopausal women at increased risk of VTE. These include four randomized controlled trials, eight observational trials, and one non-randomized clinical trial. **Results:** Two studies included women with prior history of VTE and found transdermal MHT use was associated with decreased fibrinogen levels, and not associated with increased VTE risk or increased coagulation factor levels. 11 studies included women with risk factors for VTE. Of these, three found no increased VTE risk in overweight or obese women using transdermal MHT. Three found a lower risk of VTE in transdermal MHT users compared to oral MHT users with hereditary thrombophilias or prothrombotic genetic polymorphisms. One found decreased levels of prothrombotic factors in women with insulin resistance who used transdermal MHT, while one found no activation of coagulation in women with angiographically proven coronary artery disease who used transdermal MHT. One found no increase in VTE risk amongst transdermal MHT users with a variety of VTE risk factors including: obesity, varicose veins, active smokers, recent immobilization, recent surgery, malignancy, cardiovascular or cerebrovascular disorders, myeloproliferative disorders, and inherited thrombophilia. Two found no significant difference in coagulation factor levels in oral or transdermal MHT users who were postoperative or had well-controlled non-insulin dependent diabetes mellitus or impaired glucose tolerance. **Conclusion:** This literature review provides evidence supporting the safety of transdermal MHT use in postmenopausal women with risk factors for VTE. These studies found no increased risk of VTE with transdermal MHT use in obese/overweight women, women with hereditary thrombophilias, women who recently underwent surgery, or women with prothrombotic genetic polymorphisms.
Sources of Funding: None

P-36.

Body Mass Index and Percentage Body Fat Are Negatively Associated with Severe Dyspareunia in Japanese Post-menopausal Women

Masakazu Terauchi, MD, PhD[1], Tamami Odai[1], Kiyoko Kato[1], Naoyuki Miyasaka[2]. [1]Department of Women’s Health, Tokyo Medical and Dental University, Tokyo, Japan; [2]Department of Obstetrics and Gynecology, Tokyoe Medical and Dental University, Tokyo, Japan

Objective: Dyspareunia, or pain with sexual intercourse, is one of the most bothersome symptoms constituting genitourinary syndrome of menopause. This study aims to investigate the factors associated with dyspareunia in Japanese post-menopausal women. **Design:** The first-visit records of 1,702 Japanese pre-, peri-, and post-menopausal women aged 40 to 79 years who enrolled in the Systematic Health and Nutrition Education Program at the Menopause Clinic of Tokyo Medical and Dental University Hospital were analyzed cross-sectionally. Two-group comparison was performed using the unpaired t-test and the Mann-Whitney test. The relationship between severe dyspareunia and the background characteristics was examined by multivariate logistic regression analysis. The research protocol was approved by the institutional review board. **Results:** The average age of the participants was 53.0 ± 6.3 years (mean ± SD). The women were categorized as pre-menopausal (N=379, 22.3%), peri-menopausal (N=153, 9.0%), post-menopausal (N=816, 47.9%), surgically menopausal (N=238, 14.0%), or receiving hormone therapy (N=116, 6.8%). The percentage of women who were bothered by severe dyspareunia in the pre-, peri-, and post-menopausal group, and in those who were receiving hormone therapy, was 7.1%, 10.5%, 14.6%, and 7.8%, respectively. In the post-menopausal group, the percentage of women bothered by severe dyspareunia was greatest at two to five years after menopause (18.8%), partly because the number of women who were sexually active decreased with the years since menopause. In sexually active post-menopausal women (N=453), those who were bothered by severe dyspareunia (N=119) were compared with those without (N=334), regarding background characteristics, including age, years since menopause, body composition, cardiovascular parameters, resting energy expenditure, physical fitness, symptom scores of somatic, vasomotor, insomnia, depression, and anxiety. Among them, only body mass index (BMI) and percentage body fat (%BF) were found to be significantly different between the two groups. Even after adjustment for age and years since menopause, these two factors were negatively associated with severe dyspareunia (adjusted odds ratio [95% confidence interval]: BMI, 0.894 [0.825-0.964], p=0.003; %BF, 0.947 [0.909-0.985], p=0.006). **Conclusion:** Dyspareunia is prevalent in Japanese post-menopausal women, and is negatively associated with BMI and %BF. This could partly be explained by the production of estrogen by adipose tissue. Post-menopausal loss of body weight and body fat might have negative impact on sexual intercourse.
Sources of Funding: Ibaraki Prefecture, Japan.

P-37.

Women’s Health Network: An Evaluation of a Community Program

Inneke L. Vargas, n/a[1], Nikki Keene Woods, PhD[2], Tracy Williams, MD[4], Melody McCray-Miller, BA[3], Amy Chesser, PhD[2]. [1]Psychology, Wichita State University, Wichita, KS; [2]Public Health, Wichita State University, Wichita, KS; [3]Wichita State University, Wichita, KS; [4]Univeristy of Kansas School of Medicine, Wichita, Wichita, KS

Objective: 3 Learning Objectives: 1Describe the Women’s Health Network 2Discuss the health issues identified by the Women’s Health Network Board of Directors 3Discuss the results of the surveys and interviews and discuss possible educational solutions for future women in the state of Kansas. **Design:** Health equity continues to be an important health issue in the US. High risk, vulnerable populations are of specific concern. Equal access to quality healthcare, along with equity in outcomes, should be the gold standard, yet disparities remain. To address these issues, a Women’s Health Network with a focus on health equity was created. This project is being conducted to identify and deconstruct the barriers faced by women in Kansas, with a purpose to connect women with community stakeholders to engage in health equity discussions around health outcomes and educational interventions. The Network began by identifying local partners to serve on the Board of Directors. The Board of Directors meet quarterly and identified organizations throughout the state to address key health topics to include: 1Reproductive health, 2Health literacy and health education, and 3Mental health. This process evaluation research project was conducted as part of the community-based initiative. The evaluation includes quantitative and qualitative data from the Board of Directors, Network members, and community participants. Surveys were administered through the online Qualtrics system. Qualitative data was collected through ethnographic survey interviews. This presentation will provide results from the evaluation. Findings highlight the opportunities and barriers to health equity for women in Kansas. **Results:** After the major health concerns were identified, the Board was tasked with recommending trusted community advocates whose missions were in line with the Network goals: facilitating and maintaining equitable health access to all women. Network members are recruited through board recommended partnerships, word of mouth, and via Network event invitations. The Network events include a series of keynote presentations given by subject matter experts. The presentations facilitate knowledge sharing on all three of the major health concern categories: mental health, reproductive health, and health literacy and access to education. Patient round tables and community member discussion panels gather more qualitative data on the patient experience in the Kansas healthcare system. Over 60 Network alliances have been formed through Network recommendations. Demographic composition of the Board Membership participation included: 9 Survey participants out of 13 members, majority female 77.78%, Age: 45 to 54, all participants have Post-secondary degrees and all are full-time employees. There are a number of limitations to the study including age. Persons age 65 and older are not reprsented, employment status to include part time, retired, and unemployed. Educational groups with lower than post-secondary degrees is necessary as health literacy is affected by education. Racial and cultural diversity needs to be present particularly considering the health outcome disparities for minority women. Finally, representatives of underrepresented groups including LGBTQ+ must be present. **Conclusion:** Based on the data analysis of board member survey results it can be concluded that women are being underserved across multiple areas of health and wellness, particularly in the areas of mental health, reproductive health, and health literacy. Considering the board members are aggregated from multidisciplinary areas of study and practice, as well as community representatives, it is clear the Women’s Health Network is on target and a necessary resource to improve women’s care.
Sources of Funding: Patient Centered Outcomes Research Institute (PCORI) Eugene Washington PCORI Engagement Award 10663-WichSU

P-38.

A Novel Curriculum to Improve Resident Knowledge and Comfort with Menopause Care

Kimberly Vesco, MD, MPH[1,2], Tovi Anderson[2], Neon Brooks[1], Melanie Francisco[1], Amanda Clark[1,2]. [1]Kaiser Permanente Center for Health Research, Portland, OR; [2]Kaiser Permanente Northwest, Portland, OR

Objective: Surveys of residents in internal medicine (IM), family medicine (FM) and obstetrics and gynecology (OBGYN) have demonstrated low levels of knowledge and comfort in treating patients with menopausal symptoms, suggesting a need for improved training during residency. To address this problem, we implemented a novel menopause curriculum for medical residents to deliver information efficiently and engagingly through podcasts and case discussions. We hypothesized that this curriculum would improve residents’ knowledge and comfort with treating women experiencing menopause. **Design:** Using a flipped classroom design, menopause content was delivered in 6 podcast episodes, 13-21 minutes in length, prior to an interactive, 2-hour case-based classroom session. The content, based on published practice guidelines, aimed to prepare residents to counsel women and prescribe appropriate therapy. The classroom discussion allowed residents to apply the content using case examples to diagnose and treat menopause symptoms. Target learners were 48 FM residents, 49 IM residents and 28 OBGYN residents at Oregon Health & Science University during the 2019-2020 academic year. The residency program directors approved the curriculum and integrated it into regularly-scheduled didactic sessions. Residents were assigned podcast listening 4-6 weeks before the classroom sessions, which ranged in size from 2 to 24 residents. After March 2020, classroom sessions were conducted virtually due to the coronavirus

pandemic. Residents were asked to complete evaluations electronically (via REDCap) before and after the curriculum. Knowledge was measured by a 15-item test covering the management of vasomotor and genitourinary symptoms. Residents were also asked to rate their knowledge and comfort with addressing menopause topics (Table). Per IRB review, informed consent was not required. No incentives were provided for survey completion. Statistical analysis was conducted using paired *t*-tests, ANOVA and generalized estimating equation models. **Results:** The curriculum was assigned to 125 residents; 66 (52.8%) completed both a pre- and post-survey for analysis (Table). The proportion of correctly-answered knowledge questions rose from 62.0% to 82.3% following the curriculum (p=.0001). There were no differences in improvement by specialty. Residents' self-ratings of their knowledge (Table) and comfort (data not shown) improved (p<.01*)*. After this curriculum, 87.5% of residents indicated that they intended to prescribe hormone therapy. **Conclusion:** This novel curriculum improved resident knowledge and comfort in the treatment of women with menopause symptoms. The use of podcasts leverages modern technology to provide an on-demand opportunity for learners to engage in curriculum while away from the classroom, office, or computer. Once developed, the podcast format allows for inexpensive and wide dissemination via existing platforms. Next steps should include comparison to traditional education methods in randomized trials.

Sources of Funding: Pfizer Independent Grant for Learning and Change #42360015

Resident Knowledge Survey Results

	Overall n=66		IM n=33		FM n=18		ObGyn n=15	
	Pre %	Post %	Pre %	Post %	Pre %	Post %	Pre %	Post %
15-Item Knowledge Test								
Proportion correct	62.0	82.3	58.0	81.2	61.9	81.5	71.1	85.8
Resident Self-Rating of Knowledge								
---- *Etiology/Physiology of Menopause* ----								
Very knowledgeable, can teach others	0	0	0	0	0	0	0	0
Competently knowledgeable	18.2	57.6	9.1	54.5	16.7	44.4	40.0	80.0
Some knowledge, need to learn	63.6	40.9	66.7	45.5	72.2	50.0	46.7	20.0
No knowledge, need to learn	18.2	1.5	24.2	0	11.1	5.6	13.3	0
---- *Patients Needing Hormone Therapy* ----								
Very knowledgeable, can teach others	0	3.0	0	0	0	11.1	0	0
Competently knowledgeable	6.1	53.0	3.0	57.6	5.6	44.4	13.3	53.3
Some knowledge, need to learn	80.3	43.9	78.8	42.4	88.9	44.4	73.3	46.7
No knowledge, need to learn	13.6	0	18.2	0	5.6	0	13.3	0
---- *Patients Asking for Nonhormone Therapy* ----								
Very knowledgeable, can teach others	0	6.1	0	12.1	0	0	0	0
Competently knowledgeable	6.1	47.0	3.0	48.5	5.6	44.4	13.3	46.7
Some knowledge, need to learn	78.8	47.0	75.8	39.4	88.9	55.6	73.3	53.3
No knowledge, need to learn	15.2	0	21.2	0	5.6	0	13.3	0
---- *Management of Bone Health* ----								
Very knowledgeable, can teach others	0	1.5	0	3.0	0	0	0	0
Competently knowledgeable	12.1	34.8	15.2	42.4	5.6	22.2	13.3	33.3
Some knowledge, need to learn	71.2	62.1	66.7	54.5	83.3	77.8	66.7	60.0
No knowledge, need to learn	16.7	1.5	18.2	0	11.1	0	20.0	6.7

P-39.

Real-world Outcomes of Patients New to Osteoporosis Therapies

Setareh Williams[1], Rich Weiss[1], Yamei Wang[1], Lianzhou Cui[2], Hily Nichols[2], Andrew Gernert[2]. [1]Radius Health, Inc., Wayne, PA; [2]Cobbs Creek Healthcare, Newtown Square, PA

Objective: Abaloparatide (ABL) has been shown to reduce the risk of vertebral and nonvertebral fractures (fxs) compared to placebo in clinical trials; however, clinical trial populations are generally restricted and represent only a small fraction of patients (pts) with osteoporosis (OP) in the real-world. Here we evaluate fx outcomes in pts new to osteoanabolic therapy using real-world claims data. **Design:** This retrospective cohort study used pharmacy claims linked to medical and hospital claims including commercial and Medicare Advantage from Symphony Health. Data are payer agnostic and provide access to de-identified, individual-level healthcare claims for more than 280 million US-based pts. Pts ≥18 years at index date with ≥1 prescription fill of ABL or teriparatide (TPTD) and a matched cohort without history of OP treatment (tx) (no tx cohort) were included. Index was defined as the date of the initial prescription fill for ABL or TPTD May 1, 2017 – June 30, 2019 (identification period) or date of any healthcare encounter claim for the no tx cohort between May 1, 2017 and May 1, 2018. Pts with a prior fx in the year preceding treatment initiation were considered high risk. Kaplan-Meir plots were used to evaluate time to fx. Propensity score matching was carried out including 64 variables (pt characteristics, comorbidities, tx history/duration, and fx history). **Results:** 11,021 ABL and 22,084 TPTD were identified with ≥1 pharmacy claim, and ≥1 medical claim within the 12 months prior to their index date. 40.4% (n=4,449) of ABL pts had a history of fx, 15.1% (n=1,669) of ABL pts had a prior fx within one year, and 49.1% (n=5,414) had prior OP tx. In propensity score matched comparative evaluation, ABL-treated pts had greater reduction in hip fx vs TPTD over 18 months period after tx initiation. According to KM estimates, in the 0-18 months of tx initiation, ABL-treated pts (N=5,268) had a lower rate of hip fx (0.6%) vs 1:1 matched TPTD treated pts (1.1%), Log-rank p-value was 0.17. The hip fx rate in high risk subset (N=744), defined as prior fx in the year preceding tx initiation, were 6.6% for TPTD and 1.9% for ABL, p-value was 0.02. **Conclusion:** ABL is an effective tx for fx reduction in real-world particularly hip fxs compared to TPTD. This is the first real-world comparative effectiveness evaluation between the two tx cohorts and further benefit/risk comparison of the products is needed.

Sources of Funding: Radius Health, Inc.

P-40.

The Late Reproductive Stage: A Scoping Review

Nancy F. Woods, PhD, RN[1], Nina Coslov, MBA[2], Marcie Richardson, MD[3], Ellen S. Mitchell, PhD[1]. [1]School of Nursing, University of Washington, Seattle, WA; [2]Women Living Better, Boston, MA; [3]Obstetrics/Gynecology, Atrius Health Medical Group/ Harvard University, Boston, MA

Objective: Objective: In 2001 Staging Reproductive Aging Workshop conferees described the late reproductive stage (LRS) of reproductive aging preceding the onset of the menopausal transition, yet there has been little attention to either the physiology or symptoms of this portion of reproductive aging. The aim of this scoping review was to examine publications referencing the LRS to map what is known about this stage with particular focus on reproductive endocrine patterns, menstrual cycle changes, and symptoms. **Design:** Methods: The initial search strategy included PubMed and CINAHL searches for the phrase "late reproductive stage" and "human". Given a low yield of research articles, a second stage used "late reproductive age" (LRA) as a search term. These strategies yielded 9 and 28 research articles, respectively. Publications meeting inclusion criteria (data-based research studies, focus on LRS or LRA and hormonal patterns, menstrual characteristics, and symptoms) were reviewed by co-investigators. Excluded studies were related to pathologic conditions, such as cardiovascular disease and treatment studies. Data were summarized using qualitative methods. **Results:** Results: Studies of Late Reproductive Stage addressed changing patterns of cytokines and chemokines, lipids, hormone patterns/levels and gene polymorphisms; reproductive endocrine changes and gene polymorphisms in relation to symptom clusters; symptom experiences (bladder symptoms, urinary incontinence, urinary frequency and nocturia, anxiety and mood symptoms); cognitive function testing results; and association of lifestyle factors such as smoking to hormone levels and symptoms. Most studies of Late Reproductive Age focused on reproductive hormones (such as AMH) and menstrual cycle patterns. Remaining studies addressed symptoms, gene variants, health-related behaviors, and approaches to classifying menstrual cycles. **Conclusion:** Conclusions: LRS has not been well characterized either physiologically or with respect to symptoms. Instead, in many research reports LRS serves as a comparison stage against which menopausal transition hormonal, cycle patterns, and symptoms are compared. Our search has identified a starting point to look at this stage of women's reproductive life cycle. Furthermore, harmonizing the results of studies of the LRS and LRA is essential to further understanding women's LRS experiences.

Sources of Funding: None