THURSDAY CONCURRENT SESSION #1

S-1.

Breast Cancer, Endometrial Cancer, and Cardiovascular Events in Participants who used Vaginal Estrogen in the WHI Observational Study

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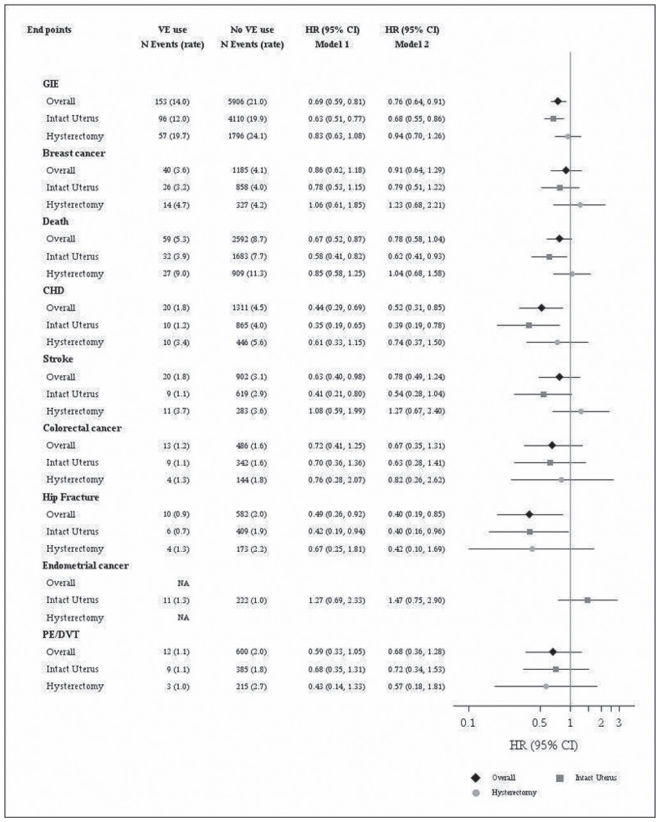
Objective: To determine the association between use of vaginal estrogen and risk of a global index event [GIE]: time to first occurrence of coronary heart disease (CHD), invasive breast cancer, stroke, pulmonary embolism, hip fracture, colorectal cancer, endometrial cancer, or death from any cause. **Design:** Prospective cohort study of data from Women's Health Initiative Observational Study of participants aged 50-79 years at baseline who did not use systemic estrogen therapy during follow-up (n = 45,663, median follow-up 7.2 years). We collected data regarding incident CHD, invasive breast cancer, stroke, pulmonary embolism, hip fracture, colorectal cancer, endometrial cancer, death, and self-reported use of vaginal estrogen (cream, suppository). **Results:** See Figure. GIE risk was not significantly increased in vaginal estrogen users. **Conclusion:** The risks of cardiovascular disease and cancer were not elevated among postmenopausal women using vaginal estrogens, providing reassurance about the safety of treatment.

Sources of Funding: National Institutes of Health

Figure 2. Hazard Ratio (HR) and 95% Confidence Interval (CI) for Global Index Events (GIE) and Components by Vaginal Estrogen (VE) Use Overall and by Hysterectomy Status



VE includes vaginal cream or suppository. VE and hysterectomy status were time-varying. Rate are crude rates per 1000 person-years. Model 1 adjusted for age, education, past estrogen use, and history of cancer, cardiovascular disease, deep vein thrombosis, or pulmonary embolism before baseline (N=45,251). Model 2 = Model 1 + race/ethnicity, BMI, DM, physical activity, hypertension, Gail breast cancer risk score, fracture after age 55, smoking, income, alcohol use (N=36,629).

S-2.

Differential Effect of Plasma Estradiol Levels Achieved with Hormone Therapy on the Progression of Subclinical Atherosclerosis in Early and Late Postmenopausal Women

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Objective: This study aimed to identify the association between plasma estradiol (E2) levels and atherosclerosis determined by rate of change in carotid artery intima-media thickness (CIMT) and test whether this association is equally evident in early (<6 years) compared with late (≥10 years) postmenopausal women using data from the Early versus Late Intervention Trial with Estradiol (ELITE). **Design:** ELITE was a randomized controlled trial of oral E2 with or without vaginal progesterone in healthy postmenopausal women stratified by time since menopause. We used mixed-effects linear models to test the association of E2 levels with the rate of change in CIMT assessed at baseline and every 6 months over the median range of follow up of 4.8 years. **Results:** A total of 596 postmenopausal women (248 early postmenopause and 348 late postmenopause) with follow-up data on E2 levels and CIMT were included in this analysis. Mean E2±SD levels on trial were 29.66±31.75 pg/ml for early postmenopause and 25.45±22.54 pg/ml for late postmenopause. The levels were similar, although somewhat higher in early than late postmenopause among active hormone therapy (HT) groups, despite similar compliance. Higher E2 levels were inversely associated with CIMT progression in early-postmenopausal women (p=0.04) and positively associated with CIMT progression in late-postmenopausal women (p=0.006) (p-for-interaction<0.001). The estimated rate of CIMT progression for women with E2 levels at the 25th and 75th percentiles was 6.88 μm/yr versus 5.62 μm/yr among the early-postmenopausal women, and 8.24 μm/yr versus 10.05 μm/yr among late-postmenopausal women, respectively. **Conclusion:** E2 levels achieved with oral estradiol therapy differentially affect carotid artery atherosclerosis progression according to timing of hormone therapy initiation. With higher E2 level, the CIMT rate is decreased among early-postmenopausal women, however, is increased among late-postmenopausal women despite the roughly similar E2 levels during the trial. The results further support a timing hypothesis of HT on cardiovascular benefit, suggesting that the timing of HT initiation is a determinant on the association of E2 level and atherosclerosis and hence suggesting specific recommendations for HT use by time since menopause.

Sources of Funding: None

Carotid artery intima-media thickness (CIMT) progression at different quartile of estradiol (E2) level according to time since menopause strata among total sample

Menopausal strata	Baseline CIMT (μm)	Estimates of CIMT rate (μm/year) at different quartile cut-point of E2 level		
		9 pg/ml (Q25%)	17 pg/ml (Q50%)	38 pg/ml (Q75%)
Early Postmenopause	747.1 ± 95.5	6.9 (5.4, 8.4)	6.5 (5.2, 7.9)	5.6 (4.3, 6.9)
Late Postmenopause	786.9 ± 109.2	8.2 (6.9, 9.6)	8.7 (7.6, 9.9)	10.1 (8.8, 11.2)

Baseline CIMT reported as mean ± standard deviation; Estimates of CIMT reported as estimates value (95% confidence interval), p-value from Wald's test<0.00; Number of subjects (%) in each quartile of E2: Q1 hormone therapy group N=10 (6.49%), placebo group N=144 (93.51%); Q2 hormone therapy group N=21 (14.89%), placebo group N=120 (85.11%); Q3 hormone therapy group N=122 (78.71%), placebo group N=33 (21.29%); Q4 hormone therapy group N=144 (98.63%), placebo group N=2 (1.37%)

S-3.

Cardio-protective Capacity of High-Density Lipoprotein Measures in Midlife and Older Women: Conventional vs. Ion Mobility Measures. The Multi-ethnic Study of Atherosclerosis (MESA)

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Objective: Recent findings have suggested that high levels of high-density lipoprotein cholesterol (HDL-C) may not always be cardio-protective in older women. Whether the cardio-protective capacity of HDL is compromised in postmenopausal women is not clear and cannot be evaluated by the crude measure of the total cholesterol carried by HDL (HDL-C). Ion mobility is a novel method that physically quantifies HDL particle (HDL-P) concentration, which might be a better predictor of CVD risk than HDL-C levels. We evaluated comparable associations of HDL-C and HDL-P with carotid atherosclerosis measures separately and adjusted for each other among a large sample of midlife and older women. Effect modifications by menopausal status, age at menopause, and time since menopause were evaluated. **Design:** Female participants from the Multi-Ethnic Study of Atherosclerosis (MESA) who had HDL-C, ion mobility HDL measures, and carotid artery ultrasound scans performed at baseline were included. Women with unknown menopausal status or early menopause (age at non-surgical menopause ≤45 years) were excluded. Linear and logistic regression models were used to assess associations between each HDL metric, and mean carotid intima-media thickness (cIMT) and carotid plaque presence (cPlaque), respectively. All models adjusted for age, race, study site,

menopausal status, body-mass index, systolic blood pressure, smoking, antihypertensive and lipid lowering medication use, hormone therapy use, physical activity, inflammatory markers, triglycerides, low-density lipoprotein cholesterol (LDL-C) and LDL particles (LDL-P). **Results:** We evaluated 1,380 women (mean age±SD 61.8±10.3 years; 61% natural menopause, 21% surgical menopause, and 18% perimenopause). Both natural (56.5±15.3mg/dL) and surgical menopausal (58.1±15.7mg/dL) women significantly had higher levels of HDL-C compared to perimenopausal women (53.7±14.8mg/dL; P<0.01 for both). Women with surgical menopause had greater HDL-P concentration than perimenopausal women (27.5±6.1 vs. 25.8±4.8 umol/L, respectively, P=0.0004). HDL-C correlated weakly with HDL-P and small HDL-P (ρ=0.33 and 0.17, respectively, P<0.0001 for both) but more strongly with large HDL-P (ρ=0.60, P<0.0001). Both natural and surgical menopausal women significantly had thicker cIMT and greater prevalence of cPlaque presence than perimenopausal women (P<0.0001). Adjusted for each other and for study covariates, higher HDL-P but not HDL-C was significantly associated with lower cIMT (P=0.001). This protective association was driven by small but not large HDL-P in models adjusted for study covariates in addition to HDL-C and large HDL-P. Significant interaction between large HDL-P and time since menopause was found in relation to cIMT independent of study covariates, HDL-C and small HDL-P; such that a greater concentration of large HDL-P was significantly associated with lower cIMT as time since menopause increased. For cPlaque, higher HDL-C was significantly associated with greater risk of cPlaque presence independent of study covariates and HDL-P (P=0.04). This positive association was more evident at older age at menopause; OR (95% CI) at mean (49.4 years: 1.21(1.00, 1.46)); at mean - 1SD (43.3 years: 1.07(0.85, 1.33)), and at mean +1SD of age at menopause (55.43 years: 1.38(1.09, 1.74)), P value for adjusted interaction = 0.05). **Conclusion:** Adjusting for each other and traditional risk factors, higher HDL-P was associated with lower cIMT, whereas higher HDL-C was associated with higher risk of cPlaque presence. The cardio-protective association reported for HDL-P could be driven by small HDL-P, although large HDL-P may play a role late after menopause. The pro-atherogenic association reported for HDL-C was most evident at a later age of menopause. Higher HDL-C in older women could be a marker of underlying HDL dysfunction that should be evaluated in future studies.
Sources of Funding: NIH, Quest Diagnostics

S-4.

Estrogen Synthesizing Gene Polymorphisms and Symptoms during the Menopausal Transition and Early Postmenopause: Toward Personalized Menopause Care

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Objective: During the menopausal transition and early postmenopause, women experience clusters of symptoms including hot flashes, sleep disruption, mood changes, pain, and cognitive symptoms. These clusteres vary in severity and have been associated with estrone and norepinephrine levels and menopausal transition stages. The objective of this study was to determine whether polymorphisms in estrogen synthesizing genes (CYP 19, 17 B HSD) account for clusters of symptoms women experience during the menopausal transition and early postmenopause. **Design:** SMWHS participants (N=137) recorded symptoms monthly in symptom diaries and provided buccal smears that were genotyped for polymorphisms in the estrogen synthesizing genes (CYP 19 and 17 B HSD). Three symptom clusters were identified: Cluster 1 included severe hot flashes and low to moderate severity sleep disruption, mood, pain, and cognitive symptoms; Cluster 2 included moderate severity symptoms of all types, and Cluster 3 included low severity symptoms. Multilevel latent class analysis with multinomial regression was used to determine associations between gene polymorphisms and symptom clusters. **Results:** Only the 17HSD polymorphisms (rs 615942 G/T and rs 592389 G/T) significantly differentiated the high severity hot flash cluster from the low severity symptom cluster. None of the other estrogen synthesizing gene polymorphisms were significantly associated with the symptom clusters. **Conclusion:** Polymorphisms in the 17HSD gene were associated with a symptom cluster including severe hot flashes, consistent with findings of 17HSD and hot flashes in the SWAN population and our findings of association of these polymorphisms with greater estrone levels. Replication of these analyses in a larger and more diverse population is necessary to guide personalized menopause care.
Sources of Funding: National Institute of Nursing Research (NINR 1R21NR012218-01 Menopause Symptom Clusters: Refocusing Therapeutics; NR 04141 - Menopausal Transition: Biobehavioral Dimensions; P30 NR 04001, P50-NR02323 – Center for Women's Health and Gender Research; Center for Ecogenetics and Environmental Health NIEHS P30ES07033)

S-5.

Chronic Pain and High-Risk Opioid Use in Women Veterans: Is there an Association with Menopause?

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Objective: Women are more likely than men to suffer chronic pain conditions, to be prescribed opioids, and to be prescribed opioids concurrent with sedative-hypnotics, despite the increased risk for overdose presented by this combination. Rates of chronic pain complaints, long-term opioid use, and sedative-hypnotic use are disproportionately higher among midlife women than other age groups, contributing to disability and mortality in this population. Although menopause is a primary feature of midlife affecting the health and well-being of women during this period, the relationship between menopause and chronic pain is poorly understood, and no studies have examined the role of menopause in chronic pain treatment. Understanding these issues should be paramount in the Veterans Affairs (VA) Health Care System, where chronic pain is a leading diagnosis, opioid use and misuse is a prevalent concern, and an estimated half of women Veteran VA users are peri- or postmenopausal. **Design:** We examined national VA administrative data from women Veterans aged 18-82 who had at least one VA outpatient visit during fiscal years 2014-2015. We used ICD-9 codes and national pharmacy data to categorize women with menopause-related diagnoses, treatments, and procedures (menopausal disorders and/or hormone therapy documented on two or more clinical encounters, or hysterectomy on at least one encounter), chronic pain (same pain diagnosis category on two or more encounters spanning at least 90 days), chronic pain multimorbidity (chronic pain criteria met for two or more unique pain diagnoses), long-term opioid use (prescribed oral opioid medication for ≥90 days), and concurrent opioid and sedative-hypnotic use (co-prescription of long-term opioids and benzodiazepines or sedative-hypnotics). Multivariable logistic and ordered logistic regression models were used to examine associations between menopause-related diagnoses with chronic pain and opioid-related outcomes, adjusting for age category (18-34, 35-44, 45-54, 55-64, 65+), race (white, black or African American, other), and body mass index, as documented in medical record; and mental health diagnoses (depression, posttraumatic stress disorder, and/or anxiety disorders) and substance use disorders (alcohol use and/or substance use disorders), as indicated by ICD-9 codes. **Results:** In this sample of 422,737 women Veterans (mean age 47 ±14 years), 6% had documented menopause-related diagnoses, which were present in women across the lifespan (ages 23-78). Chronic pain was documented in 194,989 (46%) women, and 77,491 (18%) had multiple unique chronic pain diagnoses. Among women with chronic pain, a full 40% were prescribed long-term opioids, and 24% were co-prescribed sedative-hypnotics. In independent multivariable analyses, women with menopause-related diagnoses were more likely to have diagnosed chronic pain (OR 1.85, 95% CI 1.80-1.91, p<.001), multiple chronic pain diagnoses (OR 1.78, 95% CI 1.73-1.82, p<.001), long-term opioid use (OR 1.15, 95% CI 1.12-1.20, p<.001), and concurrent opioid and sedative-hypnotic use (OR 1.18, 95% CI 1.14-1.22, p<.001). All outcomes were also more likely among African American women, women who were overweight or obese, and midlife and older women (ages ≥ 45 years). **Conclusion:** Among women Veteran VA users across the lifespan, menopause-related diagnoses were associated with a substantially increased risk of chronic pain, chronic pain multimorbidity, long-term opioid use, and concurrent opioid and sedative-hypnotic use, independent of age, mental health status, and other known risk factors. These findings shed light on this understudied area, raising the possibility that menopause is an under-recognized marker of risk for chronic pain as well as long-term and high-risk opioid use. Prospective studies are needed to better understand the role of menopause in chronic pain complaints and chronic pain treatment in both the VA and general health care settings.
Sources of Funding: *This research was supported, in part, by the VA Advanced Fellowship Program in Women's Health at the San Francisco VA Health Care System (CJG) and the VA HSR&D QUERI (Evaluation of the Implementation of the Integrated Pain Team Clinic; KHS, YL).*

THURSDAY CONCURRENT SESSION #2

S-6.

Genitourinary Symptoms of Menopause (GSM)—Impact on Sexually Active and Inactive Women

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Objective: Dyspareunia is often reported by sexually active postmenopausal women with vulvovaginal atrophy (VVA). Women who experience lower urinary tract symptoms may avoid sex for fear of wetting the bed or worry about the need to interrupt sex to urinate. Because GSM symptoms may prevent women from being sexually active, we explored the impact of GSM symptoms on concerns about sexuality among women who self-identified as either sexually active or inactive. **Design:** Between March and October 2015, we surveyed women aged ≥55 years within 2 weeks of a well-woman visit to their primary care or gynecology clinician in an integrated health system. We identified potentially eligible women using data from the electronic health record. Women received an email request to complete the survey. The online consent, eligibility, and survey data collection were conducted using REDCap™. Participants were asked about medical and prescription history and vulvovaginal, urinary, and sexual symptoms. We used condition-specific sexual symptom questions related to bladder symptoms from the International Urogynecology Association-Revised Pelvic Organ Prolapse/Incontinence Sexual Questionnaire, and we constructed similar questions for VVA symptoms. Women were asked if they had been sexually active in the last 6 months with or without a partner. Sexually inactive women were asked to indicate potential reasons (more than one response possible) why they were not sexually active. Both groups were asked about the impact of "bladder problems" and "vulvovaginal problems" on their sexual experience. **Results:** Of the 5,915 women we invited, 1,546 agreed to participate (26%) and 1531 provided responses to one or more of these items. The women were primarily White (94%) with mean age of 65.4 (SD=6.6) years (range 55-89). Systemic estrogen use was reported by 4% and vaginal estrogen reported by 16.2%. Overall, 41% of women reported the presence of ≥1 vaginal symptoms, 25% ≥1 vulvar symptom, and 71% ≥1 urinary symptom. "No sexual activity at all in the past 6 months" was reported by 48% of women,

most whom indicated that they were not sexually active due to lack of a partner (47%) or partner's lack of interest or physical inability (55%); however, 7% indicated they were not sexually active due to "bladder leaks, urgency or too frequent urination," 26% due to "vulvovaginal dryness, irritation, or pain" and 24% due to "pain with intercourse." Among sexually active women, 45% indicated they "Usually" or "Always" feel pain or discomfort with intercourse and 7% experienced leakage of urine. Among women who do not use lubricant with vaginal intercourse, 64% reported vaginal dryness. (Table). For both sexually active and inactive women, fear of experiencing VVA symptoms was reported as reason for avoiding or restricting sex more often (20%) than fear of bladder symptoms (9%) (Table). **Conclusion:** Postmenopausal women report that both VVA and bladder symptoms occur during sexual activity. Further, these symptoms limit the ability to be sexually active and negatively affect the emotional experience of their sexual life. Our findings underscore the need to further expand the sexual history after a woman reports that she is not currently sexually active.

Sources of Funding: Pfizer Independent Grant for Learning & Change, and the North American Menopause Society

IMPACTS	Sexually Inactive, 6 months n=716, 48%		Sexually Active, 6 months n=815, 52%	
Symptoms when sexually active:			Sometimes, Usually,Always	Never,Rarely
Leak urine			53 (7%)	762 (93%)
Feel pain/discomfort with vaginal intercourse			369 (45%)	446 (55%)
Feel vaginal dryness without lubricant use (n=608)			391 (64%)	217 (36%)
Feelings/Avoidance	Strongly/Somewhat Agree	Strongly/Somewhat Disagree	Strongly/Somewhat Agree	Strongly/Somewhat Disagree
I feel sexually inferior due to:				
Bladder problems	26 (4%)	690 (96%)	33 (4%)	782 (96%)
Vulvovaginal problems	77 (11%)	639 (89%)	148 (18%)	667 (82%)
I feel angry due to impact on my sex life from:				
Bladder problems	17 (2%)	699 (98%)	25 (3%)	790 (97%)
Vulvovaginal problems	60 (8%)	656 (92%)	124 (15%)	691 (85%)
	Some/a Lot	Not at All/a Little	Some/a Lot	Not at All/a Little
Avoid/restrict sexual activity due to fear of:				
Bladder problems	56 (8%)	660 (92%)	81 (10%)	734 (90%)
Vulvovaginal problems	100 (14%)	616 (86%)	197 (24%)	618 (76%)

S-7.

Depression and Anxiety Relative Risks in Women Newly Diagnosed with Vulvovaginal Atrophy and Dyspareunia

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Objective: Vulvovaginal atrophy (VVA) is a highly prevalent, underreported, and mostly untreated condition in women of postmenopausal age. The main symptoms include dyspareunia (DYSP) or pain at sexual activity, as well as vaginal dryness, and irritation. In addition to these symptoms, it is hypothesised that VVA is also associated with an increased risk of depression and anxiety. Living with these is well known to have a significant impact on relationship, including reduced sexual activity and even divorce. The study objective was to estimate the prevalence and relative risk of depression symptoms, major depressive disorder (MDD), and anxiety among women newly diagnosed with VVA compared to a control group of women. **Design:** A retrospective cohort analysis of individual-level healthcare claims data from Truven Health MarketScan® Commercial and Medicare Supplemental Databases was conducted with data from 01/2010 to 06/2015. Women with VVA were required to have ≥ 2 VVA/DYSP diagnoses (ICD9: 627.3, 625.0) on separate visits and ≥365 days of continuous insurance coverage (allowing enrollment gaps ≤45 days) before and after the first VVA/DYSP diagnosis (index date). Non-VVA controls were identified from individuals without a diagnosis of VVA/DYSP. Their index date was a randomly selected outpatient visit with ≥365 days of continuous insurance coverage before and after. VVA women were then matched 1:3 to Non-VVA women based on age, calendar year, health plan type, and US region (4) at index date. Women in both groups were required to be ≥45 years old as of the index date. MDD and anxiety outcomes were defined as having ≥2 separate visits with the indicated diagnoses. The overall depression outcome was defined as having ≥2 separate visits with a depression diagnosis or one visit with a depression diagnosis and ≥1 dispensing of an antidepressant. The observation period for the outcomes was the year before and that after the index date. The relative risk was defined as the ratio of the proportions of VVA/non-VVA women with outcomes during the observation period. **Results:** A total of 79,595 eligible women with VVA were identified (controls: 217, 296). Mean ± SD age was 60.92 ± 9.26 and the most common type of health plan was PPO (60.17%), followed by HMO (13.03%) and Comprehensive (12.25%). Women were predominantly from the South region (33.74%), followed by the Northeast (25.80%), West (23.21%), and North Central (17.07%) regions. Overall, the prevalence of MDD, overall depression, and anxiety was higher in women with VVA (5.79%, 22.06%, 12.85%, respectively) compared to non-VVA women (4.00%, 16.62%, 7.91%, respectively), translating in relative risks (RRs) of 1.45, 1.33, and 1.62, respectively. The largest difference in the risk of MDD, overall depression, and anxiety between women with versus without VVA was observed in the 45-54 age group (RR: 1.54, 1.48, 1.74, respectively). **Conclusion:** This study used claims data to identify the diagnoses of MDD and Anxiety which reflect real world clinical practice. For all outcomes examined, women diagnosed with VVA had a higher risk of depression and anxiety compared to controls. Since VVA is highly underdiagnosed, many women in the control group are also likely to suffer from the conditions and their associated symptoms. Accordingly, the reported relative risks are likely to be underestimates of the true burden of depression and anxiety among women with VVA.

Sources of Funding: This study was funded by Endoceutics Inc.

Table 1. Prevalence (%) of Depression and Anxiety in Women Newly Diagnosed with VVA

Age Groups	VVA Non-VVA (N)	MDD Only	Overall Depression	Anxiety
Overall	79,595 217,296	5.79 4.00	22.06 16.62	12.85 7.91
45-54	20,418 56,038	6.91 4.50	25.73 17.37	15.88 9.10
55-64	36,569 99,552	6.07 4.15	22.25 16.81	12.69 7.90
65-74	14,784 40,270	4.69 3.57	18.64 15.63	10.38 6.93
75+	7,824 21,436	3.63 2.85	18.02 15.57	10.34 6.72

Table 2. Relative Risks (95% CI) of Depression and Anxiety in Women Newly Diagnosed with VVA

Age Groups	VVA Non-VVA (N)	MDD Only	Overall Depression	Anxiety
Overall	79,595 217,296	1.45 (1.40,1.50)	1.33 (1.31,1.35)	1.62 (1.59,1.66)
45-54	20,418 56,038	1.54 (1.44,1.64)	1.48 (1.44,1.53)	1.74 (1.67,1.82)
55-64	36,569 99,552	1.46 (1.39,1.54)	1.32 (1.29,1.36)	1.61 (1.55,1.66)
65-74	14,784 40,270	1.31 (1.20,1.44)	1.19 (1.14,1.24)	1.50 (1.41,1.59)
75+	7,824 21,436	1.27 (1.11,1.46)	1.16 (1.09,1.23)	1.54 (1.42,1.67)

S-8.

Urinary Track Infection Relative Risk in Women Newly Diagnosed with Vulvovaginal Atrophy and Dyspareunia

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Objective: Vulvovaginal atrophy (VVA) is a highly prevalent, underreported, and mostly untreated condition in women of postmenopausal age. The main symptoms include dyspareunia (DYSP) or pain at sexual activity, as well as vaginal dryness, and irritation. In addition to these symptoms directly associated with VVA, other conditions accompanying VVA include urinary track infection (UTI), depression and anxiety. These symptoms are known to lead to workloss, absenteeism, and significant impacts on relationship, including reduced sexual activity and even divorce. The objective of this study was to estimate the prevalence, relative risk, and frequency of UTI episodes among women newly diagnosed with VVA compared to a corresponding control group. **Design:** A retrospective cohort analysis of individual-level healthcare claims data from Truven Health MarketScan® Commercial and Medicare Supplemental Databases was conducted with data from 01/2010 to 06/2015. Women with VVA were required to have ≥2 VVA/DYSP diagnoses (ICD9: 627.3, 625.0) on separate visits and ≥365 days of continuous insurance coverage (allowing enrollment gaps ≤45 days) before and after the first VVA/DYSP diagnosis (index date). Non-VVA controls were identified from individuals without a diagnosis of VVA/DYSP. Their index date was a randomly selected outpatient visit with ≥365 days of continuous insurance coverage before and after. VVA women were then matched 1:3 to Non-VVA women based on age, calendar year, health plan type, and US region at index date. Women in both groups were required to be ≥45 years old as of the index date. The UTI outcome was defined as having ≥1 visit with the indicated diagnosis. Because of the frequently episodic nature of UTI and based on the standard duration of a course of antibiotics, a diagnosis of UTI separated by at least 14 days from the previous diagnosis marked the beginning of a new UTI episode. The observation period for the outcomes was the year before and that after the index date. The relative risk of UTI was defined as the ratio of the proportions of VVA/non-VVA women diagnosed with UTI during the observation period. The number of UTI episodes during the observation period was also reported and the mean difference compared between VVA and non-VVA women using two-sided Student t-tests. **Results:** A total of 79,595 eligible women with VVA were identified (controls: 217, 296). Mean ± SD age was 60.92 ± 9.26 and the most common type of health plan was PPO (60.17%), followed by HMO (13.03%) and Comprehensive (12.25%). Women were more frequently from the South region (33.74%), followed by the Northeast (25.80%), West (23.21%), and North Central (17.07%) regions. Overall, the relative risk of UTI was about twice as high among women with VVA compared to controls, with the largest ratio observed among women aged 45-54 years. For both women with VVA and controls, the highest prevalence of UTI was observed among women ≥75 years old. Overall, women with VVA experienced 0.24 more UTI episodes per year/woman compared to controls, with the largest difference observed among women ≥75 years old. **Conclusion:** When compared to controls, women with VVA had approximately a twofold increased risk of UTI. Since VVA is highly underdiagnosed, many women in the control group are also likely to suffer from the conditions and their associated symptoms. Accordingly, the reported relative risks are likely to be underestimates of the true burden of UTI among women with VVA.

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Table 1. Prevalence (%) and Risk Ratio (95% CI) of UTI in Women Newly Diagnosed with VVA

Age Groups	VVA Non-VVA (N)	Risk (%)	Risk Ratio (95% CI)
Overall	79,595 217,296	31.69 15.58	2.03 (2.01,2.06)
45-54	20,418 56,038	30.58 13.82	2.21 (2.15,2.28)
55-64	36,569 99,552	30.48 14.69	2.07 (2.03,2.12)
65-74	14,784 40,270	29.76 16.09	1.85 (1.79,1.91)
75+	7,824 21,436	43.95 23.34	1.88 (1.82,1.95)

Table 2. Yearly Frequency of UTI Episodes per Woman Newly Diagnosed with VVA

Age Groups	VVA Mean ± SD	Non-VVA Mean ± SD	Mean Difference (95% CI)
Overall	0.37 ± 0.82	0.13 ± 0.41	0.24 (0.24-0.25)
45-54	0.32 ± 0.70	0.11 ± 0.33	0.22 (0.21-0.23)
55-64	0.34 ± 0.75	0.12 ± 0.37	0.22 (0.22-0.23)
65-74	0.37 ± 0.84	0.14 ± 0.45	0.22 (0.21-0.24)
75+	0.68 ± 1.20	0.23 ± 0.63	0.45 (0.42-0.47)

S-9.

The WISDOM Survey: Physicians' Behaviors and Attitudes towards Treating Vulvar and Vaginal Atrophy (VVA)

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Objective: To evaluate physicians' behaviors and attitudes regarding vulvar and vaginal atrophy (VVA) treatment in menopausal women using an internet-based survey. **Design:** The WISDOM survey was conducted by Rose Research via the internet from August to September 2016 and queried a nationally representative sample of US physicians. The panel was provided by GMI, an institutional review board-approved panel source. Eligible survey participants included obstetricians and gynecologists (OB/GYNs) who saw at least 50 menopausal women per month and primary care physicians (PCPs) who saw at least 25 menopausal women per month. Exclusion criteria were physicians who cited conflicts of interest, did not work in a community-based practice, and managed or treated less than 15 patients with VVA per month. The survey consisted of 23 multi-part questions that assessed physicians' behaviors and attitudes towards VVA treatment. Compensation was US $23 for a completed survey. **Results:** At least 2424 physicians were invited to participate in the survey, of whom 945 responded. Overall, 369 OB/GYNs and 275 PCPs completed the survey. The majority of respondents were male (64%), between 40 and 59 years of age (64%), and had been practicing for more than 15 years (66%). On average, OB/GYNs and PCPs saw 111 and 99 menopausal women per month, respectively, and of these women, 61 (55%) and 44 (44%) were reported to have had VVA symptoms, respectively. The most common VVA treatment recommended was prescription therapy (49%; with or without other therapies), followed by over the counter products alone (24%), no treatment (14%), behavioral/lifestyle management alone (10%), and vaginal laser therapy alone (3%). More OB/GYNs preferred to treat VVA with prescription therapy compared with PCPs (53% vs 43%) and OB/GYNs wrote more prescriptions per month (44 vs 35 per month). Compared with PCPs, OB/GYNs prescribed more Estrace® vaginal cream (31% vs 25%), Vagifem® (15% vs 12%), Osphena® (9% vs 7%) and Estring® (6% vs 5%), while PCPs prescribed more Premarin® vaginal cream (30% vs 38%), compounded vaginal estrogens (6% vs 8%) and DHEA (1% vs 2%; route not specified). Reasons why OB/GYNs and PCPs prescribed VVA treatments were effectiveness (77%, 76%, respectively), followed by patient out-of-pocket cost (33%, 34%), patient preference (28%, 30%), and ease of product use (29%, 28%). OB/GYNs and PCPs believed that out-of-pocket cost (64%, 51%, respectively) and fear of risks associated with estrogen therapy (59%, 51%) are the main barriers for why women choose not to get treated. They also believed that women discontinue treatment primarily because of cost (77%, 61%), symptom improvement (52%, 59%) and concerns about long-term estrogen exposure (47%, 54%). More OB/GYNs (72%) than PCPs (47%) disagreed or strongly disagreed that VVA was best treated with over-the-counter products than prescription products. Overall, 84% of the specialty physicians queried considered it important to use the lowest effective dose of hormone therapy when treating women experiencing VVA symptoms. **Conclusion:** More OB/GYNs than PCPs prescribed VVA treatment, especially vaginal estrogens, for menopausal women, but overall both types of physicians had similar attitudes and behaviors regarding VVA treatment. Effectiveness was the primary reason for prescribing VVA therapy, and patients' fear of estrogen therapy risks was believed to be both a primary barrier to treatment initiation and a main reason for discontinuing treatment. Most of both physician types preferred prescribing FDA-approved vaginal estrogen therapies at the lowest effective dose possible.

Sources of Funding: TherapeuticsMD

S-10.

The WISDOM survey: Physicians' Level of Comfort Prescribing Treatment for Vulvar and Vaginal Atrophy (VVA) Symptoms in Women with a Predisposition or History of Breast Cancer

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Objective: Use of local or systemic menopausal estrogen therapies for the treatment of VVA are currently contraindicated, as per their prescribing information, for women with known, suspected, or a history of breast cancer. Pharmacokinetic studies have found very low to non-existent systemic absorption of some low-dose local vaginal estrogen therapies.[1-4] Medical societies including the American College of Obstetricians and Gynecologists (ACOG) support the use of vaginal estrogens in women with a history of estrogen-dependent breast cancer who are unresponsive to non-hormonal therapies.[5-7] The objective of this internet-based survey was to evaluate physicians' behaviors and attitudes regarding VVA treatment in menopausal women. This report focuses on treating women with or without a history of breast cancer. **Design:** The WISDOM survey queried a nationally representative sample of US physicians and was conducted by Rose Research via the internet from August to September 2016. The panel was provided by GMI, an institutional review board-approved panel source. Obstetricians and gynecologists (OB/GYNs) who saw at least 50 menopausal women per month or primary care physicians (PCPs) who saw at least 25 menopausal women per month were eligible for the study. Physicians who cited conflicts of interest, did not work in a community-based practice, or managed or treated less than 15 patients with VVA per month were excluded. The survey consisted of 23 multi-part questions that assessed physicians' behaviors and attitudes towards VVA treatment. Physicians who completed the survey received a monetary compensation of US$23. **Results:** At least 2424 survey invitations were sent out, 945 physicians responded and a total of 369 OB/GYNs and 275 PCPs completed the survey. Physicians were male (64%), 40 to 59 years of age (64%), and had been practicing for more than 15 years (66%). On average, OB/GYNs saw 111 menopausal women per month, with 55% (n=61) reported to have had VVA symptoms, and PCPs saw 99 menopausal women per month, with 44% (n=44) reported to have had VVA symptoms. Menopausal women were most commonly treated with prescription therapy (49%; with or without other therapies), followed by over-the-counter products alone (24%), no treatment (14%), behavioral/lifestyle management alone (10%), and vaginal laser therapy alone (3%). Most OB/GYNs (87%) and PCPs (65%) agreed or strongly agreed that they were comfortable prescribing local estrogen therapy for menopausal women and that local estrogen therapies were preferred over other types of therapies (75% and 68%, respectively) for VVA. Almost all OB/GYNs (95%) and most PCPs (80%) felt comfortable or very comfortable prescribing existing VVA therapies to women with no personal history or predisposition to breast cancer. When asked about prescribing VVA therapies to women with a predisposition to breast cancer (family history, BRCA mutations, etc.), 49% of OB/GYNs and 23% of PCPs felt comfortable or very comfortable doing so. In women with a personal history of breast cancer, the percentages dropped to 34% for OB/GYNs and 17% for PCPs. **Conclusion:** Although ACOG and other medical societies support the use of vaginal estrogen therapy in women with a history of estrogen-dependent breast cancer who were unresponsive to non-hormonal therapies[5-7] and despite very low systemic absorption of estradiol,[1-4] a relatively low percentage of OB/GYNs and PCPs are comfortable prescribing VVA therapies to women who had a history of or a predisposition to breast cancer; however, twice as many OB/GYNs than PCPs felt comfortable doing so. 1. Bachmann G, et al. *Obstet Gynecol.* 2008;111:67-76. 2. Dorr MB, et al. *Fertil Steril.* 2010;94:2365-2368. 3. Pickar JH, et al. *Climacteric.* 2016;19:181-187. 4. Archer DF, et al. *Menopause.* 2016 [ePub]. 5. ACOG. *Obstet Gynecol.* 2016;127:e93-96. 6. NAMS. *Menopause.* 2013;20:888-902. 7. de Villiers TJ, et al. *Climacteric*. 2016;19:313-315.

Sources of Funding: TherapeuticsMD

TOP SCORING ABSTRACT SESSION

S-11.

TX-001HR is Associated with a Clinically Meaningful Effect on Vasomotor Symptoms

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Objective: TX-001HR (TherapeuticsMD, Boca Raton, FL) is an investigational combination of 17β-estradiol and progesterone (E2/P4; sometimes referred to as bio-identical hormones) in a single, oral softgel capsule, currently being developed for the treatment of vasomotor symptoms (VMS) in menopausal women with an intact uterus. A secondary objective of the REPLENISH trial was to determine the clinical meaningfulness of the effect of TX-001HR versus placebo for the treatment of moderate-to-severe VMS in menopausal women. **Design:** REPLENISH (NCT01942668) was a phase 3, randomized, double-blind, placebo-controlled, multicenter trial that evaluated TX-001HR in menopausal women (40-65 years) with an intact uterus. Women with hot flushes (≥7/day or ≥50/week) were included in the VMS substudy and were randomized 1:1:1:1:1 to daily E2/P4 of 1.0 mg/100 mg (n=141), 0.5 mg/100 mg (n=149),

0.5 mg/50 mg (n=147), 0.25 mg/50 mg (n=154), or placebo (n=135); others were randomized 1:1:1:1 to active E2/P4 doses as part of the primary safety endpoint analysis of endometrial hyperplasia. Participants assessed their VMS using the anchor-based Clinical Global Impression (CGI) score with a 7-level response scale ranging from "very much improved" to "very much worse," which were further categorized into a clinically meaningful response (CGI ratings of "much improved" or "very much improved"), minimally improved response (rating of "minimally improved"), and no change or worse (ratings of "no change" to "very much worse"). Response thresholds were determined by nonparametric discriminant analyses to define clinical responders. TX-001HR effects on quality of life using the menopause quality of life (MENQOL) questionnaire were also assessed (reported elsewhere). **Results:** Women enrolled in the VMS substudy (n=726) had a mean age of 55 years, a mean BMI of 27 kg/m^2; 67% were white and 31% were black. As assessed by the CGI, significantly more women experienced a clinically meaningful response to TX-001HR (50-63%) compared with placebo (33%; all, P<0.01) at week 4. Similarly, significant results in clinically meaningful responders were observed for TX-001HR versus placebo at week 12 (73-82% vs 53%; all, P<0.01). Based on the nonparametric discriminant analyses, clinical responders were determined by response thresholds of weekly reductions in frequency of ≥36 moderate-to-severe VMS at week 4 and ≥39 at week 12. Overall, significantly more clinical responders were found with all 4 doses of TX-001HR (46-59%) than with placebo (33%; all, P<0.05) at week 4, and at week 12 (68-73% vs 52%; all, P<0.05). **Conclusion:** These REPLENISH data demonstrate that TX-001HR provides clinically meaningful improvements in VMS frequency in menopausal women. A consistency of effect of TX-001HR was observed with statistically significant improvements in the frequency of VMS, as well as in the vasomotor domain of the MENQOL questionnaire. TX-001HR may provide a new oral option, as a single estradiol/progesterone capsule, for the treatment of VMS in menopausal women with an intact uterus, including those women taking unapproved and inadequately studied compounded bio-identical hormone therapy.

Sources of Funding: TherapeuticsMD

S-12.

Effects of Cognitive Behavioral Therapy for Menopausal Insomnia on Depressive Symptoms

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Objective: Given the high prevalence rates of insomnia (30-60%) and depressive symptoms (25-40%) in peri- and postmenopausal women, interventions which improve both conditions would be particularly beneficial. Cognitive behavioral therapy for insomnia (CBTI) is an efficacious, first-line treatment for insomnia. There is some preliminary evidence suggesting CBTI is also effective in ameliorating depressive symptoms in the general population. This pilot study is the first to examine the effects of cognitive behavioral therapy for menopausal insomnia (CBTMI) on depressive symptoms among midlife women and comparing high and low depression severity groups on improvement of insomnia severity pre-post treatment. **Design:** Forty women (mean age= 55±6.2) self-described as peri- or postmenopausal who met diagnostic criteria for insomnia disorder and reported ≥ 1 nocturnal hot flash/night were randomized CBTMI or menopause education control (MEC). Participants were not excluded if they had a comorbid diagnosis of major depression. Based on structured clinical interview, four participants met DSM-5 criteria for present major depressive episode. CBTMI included four individual 50-minute sessions over eight weeks focused on the treatment of insomnia and hot flashes, delivered by social workers or psychologists in gynecology clinics. MEC included a 1-hour meeting to discuss menopausal symptoms and sleep hygiene; and provide educational pamphlets and a non-directive suggestion to "make any behavioral changes as desired." Pre- and posttreatment measures included: Insomnia Severity Index (ISI), Center for Epidemiologic Studies Depression Scale (CES-D), and Hamilton Depression Rating Scale (HDRS). Comparisons of high and low depression severity were examined based cut-off scores of 8 on the CES-D and 16 on the HDRS. **Results:** Mixed models revealed a significant time x treatment arm interaction for subjective complaint of depression (p=0.019) and objective rating of depression (p=0.01), and significant main effects for time (p's < 0.001). Women receiving CBTMI had significantly greater reductions in depressive symptomology from pre to post treatment on the CES-D score (16 ± 9 to 8 ± 7) and HDRS score (11 ± 7 to 2 ± 3) compared to women receiving MEC [pre to post treatment changes for MEC group: CES-D score (15 ± 11 to 13 ± 9), HDRS score (9 ± 6 to 6 ± 4)]. Improvements in insomnia severity did not differ by high or low depression (p >.05). Pre and post-treatment ISI scores for treatment arms were: Low CES-D (14 ± 3 to 6 ± 5) vs. High CES-D (18 ± 4 to 10 ± 6) and Low HDRS (14 ± 3 to 6 ± 5) vs. High HDRS (17 ± 4 to 7 ± 6). **Conclusion:** For midlife women experiencing insomnia and nocturnal hot flashes, a 4-session CBT intervention targeting both insomnia and hot flashes led to clinically meaningful improvements in depressive symptoms. Results also suggest that pre- to post CBTMI improvements in insomnia symptoms were similar among patients with and without elevation in depressive symptom severity. Thus, the benefits of CBTMI extend beyond insomnia and include improvements in depressive symptom severity; and are equally beneficial to women, including those experiencing more severe depressive symptoms.

Sources of Funding: National Institutes of Health Grant #s K23NR014008 (PI: Nowakowski) and K24HL123565 (PI: Thurston). Registered trial on ClinicalTrials.gov (NCT02092844).

S-13.

The relationship between migraine, cardiovascular disease (CVD) and hormone therapy (HT) in postmenopausal women in the Women's Health Initiative Study (WHI)

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Objective: The evidence for the relationship between migraine and cardiovascular disease has been conflicting, depending on aura status, age of the population and CVD outcomes examined.The association between exogenous estrogen use and increased risk of stroke in women who have migraine with aura, has led to the recommendation that combined oral contraceptives (COCs) shall be avoided in migraine with aura and used with caution in migraine without aura. In comparison with COCs, the effect of hormone therapy (HT) on migraine and subsequent cardiovascular disease (CVD) risk, has not been extensively studied. The objective of the study was to further examine the relationship of migraine with incident composite CVD events and it's interaction with HT use, in both the Women's Health Initiative observational study (WHI-OS) and hormone therapy trial (WHI-HT) cohorts. **Design:** Incident CVD events were defined as the earliest of any following CVD outcomes: MI, stroke, Angioplasty of coronary arteries, Coronary bypass surgery, Coronary Heart Disease, Deep Vein Thrombosis, or Pulmonary Embolism. Migraine status was determined based on self-reported physician diagnosis at baseline. Hormone use status was defined by the randomization group within the HT trial (E, E&P and placebo). Cox proportional hazards regression models were used to determine whether migraine status predicts incident CVD, while adjusting for recognized potential confounders. Multivariate imputations were used in all models. The presence of effect modification was evaluated by testing the significance of the interaction between hormone use status and migraine using a Wald test. Where significant interactions were detected, we present the estimated hazard ratio and confidence interval stratified by hormone use. Tests were two-sided and conducted at the 0.05 significance level and all model estimates are shown with 95% confidence intervals. **Results:** WHI OS Analyses: Among 93,676 women in the WHI OS, 25,878 were excluded due to either pre-existing CVD or missing of end follow-up day. Of the remaining 67,903 participants, 7,322 (10.8%) had history of migraine, with the largest proportion (45.1%) in the youngest age group (50-59 years). The migraine group had more whites (87.5% vs 83.1%) and Latinos (4.1% vs 3.9%), while the control group had more African Americans (8.1% vs 5%) and Asians (3.4% vs 2%) Women with migraine tended to drink and exercise less than those without migraine, and had higher vitamin D and calcium intake. Migraineurs were more likely to have night sweats (SMD=0.137) and hot flashes (SMD=0.163). There was no increased risk of incident composite CVD events in women with history of migraine the WHI-OS cohort, with HR (95% CI) of 1.04 (0.82,1.31) in fully adjusted models (p=0.742, Table 1a). WHI HT Analyses: Of 17,357 participants in the HT, 1,482 reported migraine. A non-significant decrease in composite CVD events was observed in migraine group (HR= 0.71 (0.46,1.11) p=0.135) (Table1b). Comparison of women with migraine who received HT (E or E&P) vs placebo did not show HT as an effect modifier for the association between migraine and composite CVD (HR 1.04 (0.42, 2.58) p=0.929). **Conclusion:** We did not detect significant risk of incident composite CVD events associated with history of migraine in this longitudinal cohort of older postmenopausal women. Furthermore, hormone therapy was not an effect modifier of this relationship. As migraine is highly prevalent in the population and women with migraine are often advised to avoid HT, these findings may have significant public health implications. Further work should be done on exploring different categories of CVD events in different subpopulations of women with migraine.

Sources of Funding: None

Table 1.	a) WHI-OS				b) WHI-HT			
	Migraine n(%)	No Migraine n(%)	HR (95%CI)	p-value	Migraine n(%)	No Migraine n(%)	HR (95%CI)	p-value
Composite CVD event	84(10.0%)	751(89.1%)	1.04 (0.82,1.31)	0.742	25(8.5%)	265(89.8%)	0.71 (0.46,1.11)	0.135

S-14.

Neurokinin 3 receptor antagonism is a highly effective, novel treatment for menopausal hot flushes with rapid onset: a phase 2, randomised, double-blind, placebo-controlled trial

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Objective: Hot flushes affect 70% of menopausal women, can be long-lasting, and often severely impact on physical, psychosocial, sexual, and overall wellbeing. Hormone replacement therapy is effective but not without risk. Neurokinin B signalling is increased in menopausal women, and has been implicated as an important mediator of hot flushes. It is estimated that a novel treatment for menopausal flushes could benefit 20 million women in the US alone. **Design:** This phase 2, randomised, double-blind, placebo-controlled, crossover trial assessed the effectiveness of an oral neurokinin 3 receptor antagonist (MLE4901) on menopausal hot flushes in an ambulatory setting (Clinicaltrials.gov NCT02668185). Sixty-eight women were screened between February and October 2016 in a single-centre, of which 37 were randomised and included in an ITT analysis (aged 49-62yrs, experiencing ≥7 hot flushes/24h some of which were reported as bothersome or severe). They each received 4 weeks of MLE4901 and 4 weeks of placebo in random order separated by a 2 week washout period. Randomisation was completed by a central computer, and participants were allocated to treatment number in numerical order. Primary outcome was total number of hot flushes during the final week of both treatment periods. Posthoc time course analysis was conducted in a modified ITT population (minimum n=34) to ascertain the therapeutic profile of MLE4901. **Results:** Primary outcome: MLE4901 significantly reduced the total weekly number of hot flushes by 45 percentage points compared to placebo during the final week of the four week treatment period (adjusted means: placebo 49.01 (CI: 40.81-58.56), MLE4901 19.35 (CI: 15.99-23.42), p<0.0001), and by 73% compared to baseline. Time course analysis revealed that when taking MLE4901 the frequency of hot flushes was reduced by 72% compared to baseline as early as day 3 of therapy (CI: -81.3 to -63.3%, p<0.0001; 51 percentage point decrease compared to placebo (CI: -63.5 to -38.4)). This treatment effect size was then maintained throughout the four week treatment period (p<0.0001 at day 7, 14, 21, and 28 of treatment). After 3 days of treatment with MLE4901, the severity of hot flushes was also reduced by 38% compared to baseline (CI: -46.1 to -29.1%, p<0.001; 31 percentage point decrease compared to placebo), as was hot flush bother by 39% (CI: -47.5 to -30.1, p<0.0001; 34 percentage point decrease compared to placebo), and hot flush interference by 61% (CI: -79.1 to -43, p=0.0006; 37 percentage point decrease compared to placebo). Hot flush severity, bother, and interference continued to improve over the 4 week treatment period. Hot flush frequency, severity, and bother were all positively correlated (r=0.76-0.93, p<0.001). Sleep also improved as early as day 3 of treatment with MLE4901 compared to placebo (p=0.0061 using the MENQOL questionnaire and p=0.0026 using the HFRDIS questionnaire), and continued to improve over the 4 week treatment period. There was a linear concordance between the two questionnaire measures (r=0.70, p<0.0001). Treatment was well tolerated. **Conclusion:** Treatment with a neurokinin 3 receptor antagonist (MLE4901) could be practice changing as it is well tolerated and rapidly relieves hot flush symptoms without the need for oestrogen exposure. Larger scale studies of longer duration are now planned.

Sources of Funding: UK MRC, NIHR

FRIDAY CONCURRENT SESSION #1

S-15.

A Phase II clinical trial to assess the efficacy and safety of 0.005% estriol Vaginal gel in hormone receptor-positive postmenopausal women with early stage breast cancer in treatment with Aromatase Inhibitors (AIs).

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Objective: Breast cancer patients are frequently treated with AIs to provoke estrogen deprivation. Consequently, unpleasant side effects commonly emerge. Vaginal estrogens effectively relieve symptoms of vulvovaginal atrophy however their safe use in breast cancer women in which an increase of estrogens could counteract this treatment needs to be confirmed. 0.005% estriol vaginal gel is a new formulation delivering an ultra-low dose of estriol (50µg) with proven efficacy for the local treatment of GSM and negligible systemic absorption of estriol. A study is proposed to evaluate if this formulation is an efficacious and safe option to treat moderate to severe symptoms of vaginal atrophy in breast cancer women. **Design:** 71 patients were included and randomized 4:1 to receive 0.005% estriol vaginal gel or placebo, daily for 3 weeks and twice weekly for 9 additional weeks. A preliminary safety phase was run with 10 women over 3 weeks. A subsequent phase evaluated efficacy and safety by assessing changes in Maturation Value (MV), pH and other symptoms and signs of vaginal atrophy, and changes in hormonal levels. MV was calculated: MV=[1x(% superficial cells)]+[0.6x(% intermediate cells)]+[0.2x(% parabasal cells)]. Symptoms and signs were individually scored from 0 (absent) to 3 (severe) at baseline (B) and at w3 and w12. Total scores of symptoms (TSSy) and signs (TSSi) were calculated by summing the individual scores of all symptoms and signs at every visit. Estriol (E3), estradiol (E2) and estrone (E1) were analyzed by ultrasensitive LC-MS/MS assay at B and at w1, w3, w8 and w12. FSH and LH were determined by Chemiluminiscency at the same timepoints and also at screening. FSH was studied by evaluating the variations at w1, w3, w8 and w12 vs B, and comparing them with those shown before treatment. Adverse events were collected throughout the study. **Results:** ITT population comprised 61 women aged 59.2(7.1), 50 received estriol and 11 placebo. All women except one were treated with anastrozole or letrozole. 1/3 had moderate and 2/3 severe vaginal dryness. Women that received estriol improved MV, pH and vaginal dryness after 12 weeks of treatment, and differences between both groups were significant for these three variables (p<0.01, p=0.057; p<0.01 -Mann-Whitney-Wilcoxon-). Women under estriol improved vaginal dryness from 2.6(0.5) at B to 0.9(0.9) at w12, while women under placebo from 2.7(0.5) to 1.9(0.9). The improvement in TSSy at w12 was higher in the estriol group vs the placebo group (p<0.05 -Mann-Whitney-Wilcoxon-) as changed from 6.3(1.4) to 1.8(1.5) and 6.6(1.4) to 4.4(2.4) respectively. Similarly, the improvement in TSSi at w12 was higher in the estriol group than in the placebo group (p<0.001 -Mann-Whitney-Wilcoxon-) as changed from 6.6(1.6) to 2.1(2.1) and 6.8(1.0) to 5.2(1.6) respectively. In the estriol group hormone determinations showed a slight increase in E3 [median (Q25-75)] to 3.9(0.5-12.1), 1.9(0.5-6.8), 0.5(0.5-6.0) and 0.5(0.5-7.3) pg/ml at w1, w3, w8 and w12 respectively while E2 and E1 were below LOQ in all samples but 1 at w12. Small oscillations in FSH were shown between B-w1 and B-w3 (p<0.05 -Friedman Dunn's correction-) while no significant oscillations were detected between B-w12 (p=0.11, Wilcoxon). **Conclusion:** The study confirmed the efficacy of 0.005% estriol vaginal gel in the improvement of moderate to severe vaginal symptoms that appear as a consequence to AI in women with breast cancer. After 12 weeks the absorption of estriol was negligible (below LOQ in the majority of women) and no significant variations in FSH were observed.

Sources of Funding: None

S-16.

17β-Estradiol/Progesterone in a Single Oral Softgel Capsule (TX-001HR) Significantly Reduced Moderate-to-Severe Vasomotor Symptoms without Endometrial Hyperplasia

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Objective: TX-001HR (TherapeuticsMD, Boca Raton, FL), an investigational combination of 17β-estradiol and progesterone (E2/P4; sometimes referred to as bio-identical hormones) in a single, oral softgel capsule, is being developed to treat menopausal vasomotor symptoms (VMS) in women with an intact uterus. Objectives of the REPLENISH trial were to evaluate the efficacy, endometrial safety, and overall safety of 4 daily TX-001HR doses vs placebo. **Design:** REPLENISH (NCT01942668) was a phase 3, randomized, double-blind, placebo-controlled, multicenter trial that evaluated TX-001HR in menopausal women with VMS (40–65 years; intact uterus). Women with moderate-to-severe hot flushes (≥7/day or ≥50/week) were included in a VMS substudy and randomized 1:1:1:1:1 to daily E2/P4 of 1.0 mg/100 mg, 0.5 mg/100 mg, 0.5 mg/50 mg, 0.25 mg/50 mg, or placebo; other women were randomized 1:1:1:1 to E2/P4 doses only; all women were considered for the endometrial safety analysis. The 4 co-primary efficacy endpoints of the VMS substudy were change from baseline in frequency and severity of VMS at weeks 4 and 12 vs placebo. Responder rates (50% and 75% reduction in weekly VMS frequency) and daily frequency of VMS were also assessed. Incidence of endometrial hyperplasia (consensus 2 of 3 pathologists) at 12 months was the primary safety endpoint, analyzed in women who took ≥1 dose, had an acceptable biopsy at baseline, and biopsy at month 12 or endometrial hyperplasia/cancer before month 12 (endometrial safety population). Lipid, coagulation, and glucose parameters and overall safety were analyzed in women who took ≥1 treatment capsule (safety population). **Results:** Women (N=1835) were randomized to daily E2/P4 of 1.0 mg/100 mg (n=safety study [VMS substudy]; n=415 [141]), 0.5 mg/100 mg (n=424 [149]), 0.5 mg/50 mg (n=421 [147]), 0.25 mg/50 mg (n=424 [154]), or placebo (n=151 [135]). Participants had a mean age of 55 years, a mean BMI of 27 kg/m^2; 65% were white and 32% were black. Doses of E2/P4 1.0 mg/100 mg or 0.5 mg/100 mg vs placebo significantly improved the frequency and severity of moderate-to-severe VMS at weeks 4 (all, P<0.05) and 12 (all, P<0.001) from baseline (all 4 co-primary endpoints). E2/P4 0.5 mg/50 mg vs placebo significantly improved VMS frequency and severity at week 12 from baseline (both, P<0.05), while E2/P4 0.25 mg/50 mg vs placebo significantly improved VMS frequency, but not severity, at weeks 4 and 12 (both, P≤0.001). Significantly more women had 50% reduction in their moderate-to-severe VMS frequency with TX-001HR (73–81%) than with placebo (58%; P<0.05, all). Similar results were observed for 75% responder rates (50–68% vs 32%; P<0.01, all). The mean daily number of moderate-to-severe VMS

decreased from 10–11/day at baseline to 2–4/day with TX-001HR (5/day for placebo) at week 12. At 12 months, no cases of endometrial hyperplasia or cancer were noted in any participants (TX-001HR or placebo). Minimal clinically meaningful changes in lipid, coagulation and glucose parameters were found at 12 months. Incidence of treatment emergent adverse events was low. **Conclusion:** TX-001HR combinations of estradiol/progesterone 1.0 mg/100 mg, 0.5 mg/100 mg and 0.5 mg/50 mg improved menopause-related, moderate-to-severe VMS with no unexpected safety signals. All TX-001HR doses had 0% incidence of endometrial hyperplasia or malignancy. TX-001HR's effects on lipids, coagulation parameters, and glucose were small and generally favorable. If approved, TX-001HR (the first estradiol/progesterone combination formulation) may provide a new option for the treatment of VMS in menopausal women with an intact uterus, including the estimated 1 to 2.5 million US women currently using unapproved and inadequately studied compounded bio-identical hormone therapy.

Sources of Funding: TherapeuticsMD

S-17.

TX-001HR Improved the Medical Outcomes Study-Sleep (MOS-Sleep) questionnaire in Menopausal Women with Vasomotor Symptoms

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Objective: TX-001HR (TherapeuticsMD, Boca Raton, FL), a single, oral softgel capsule consisting of 17β-estradiol and progesterone (E2/P4; sometimes referred to as bio-identical hormones) is being investigated for the treatment of vasomotor symptoms (VMS) in menopausal women with an intact uterus. The main objectives of the REPLENISH trial were to evaluate the efficacy and endometrial safety of TX-001HR (reported elsewhere). A secondary objective of the REPLENISH trial was to evaluate the effects of TX-001HR vs placebo on sleep parameters using the validated Medical Outcomes Study (MOS)-Sleep questionnaire. **Design:** TX-001HR was evaluated in the REPLENISH study (NCT01942668), a phase 3, randomized, double-blind, placebo-controlled, multicenter trial of menopausal women (40-65 years) with VMS and an intact uterus. Women with moderate-to-severe hot flushes (≥7/day or ≥50/week) were randomized 1:1:1:1:1 to daily E2/P4 of 1.0 mg/100 mg, 0.5 mg/100 mg, 0.5 mg/50 mg, 0.25 mg/50 mg or placebo (VMS substudy), and all other women were randomized 1:1:1:1 to active E2/P4 doses. Subjects were administered the MOS-Sleep questionnaire at baseline, week 12, and months 6 and 12. MOS-Sleep is a 12-item questionnaire measuring 6 sleep dimensions: initiation [time to fall asleep], quantity [hours of sleep each night], maintenance, respiratory problems, perceived adequacy and somnolence over the past 4 weeks. The last 4 items were scored using a 6-item Likert scale ranging from "All of the time" to "None of the time." Subscales are derived from the various questions and are reported as Sleep Problems Index I (short form), Sleep Problems Index II (long form), sleep disturbance, sleep somnolence, snoring and sleep shortness of breath or headache. Change from baseline in total and subscale scores were analyzed for each treatment versus placebo at each time point. Incidence of somnolence as a treatment-emergent adverse event (TEAE) was also reported. **Results:** Women were randomized to daily E2/P4 of 1.0 mg/100 mg (n=415), 0.5 mg/100 mg (n=424), 0.5 mg/50 mg (n=421), 0.25 mg/50 mg (n=424) or placebo (n=151). Mean age was 55 years and mean BMI 27 kg/m^2; 65% of subjects were white and 32% were black. At week 12 as well as at months 6 and 12, women treated with TX-001HR reported significantly better change in the MOS-Sleep total score compared with those treated with placebo (all, P<0.05), with the exception of those treated with 0.25 mg E2/50 mg P4 at week 12. Sleep disturbance subscale significantly decreased from baseline with TX-001HR versus placebo at all timepoints (all, P<0.05), with the exception of women randomized to the lowest TX-001HR dose at week 12. All doses of TX-001HR significantly improved the Sleep Problems Index I subscale from baseline to week 12 (all, P<0.05), with improvements maintained to months 6 (all, P<0.01) and 12 (all, P≤0.001). Similar significant improvements were observed with TX-001HR in the Sleep Problems Index II subscale (all, P<0.05), except for the lowest TX-001HR dose which was not significantly different from placebo at week 12. Compared with placebo, the sleep somnolence subscale significantly improved from baseline with TX-001HR doses 0.5 mg E2/100 mg P4 and 0.5 mg E2/50 mg P4 at month 12 (P=0.008 and P=0.014, respectively). TX-001HR had no effects on the snoring subscale, or the sleep shortness of breath or headache subscale. The TEAE incidence of somnolence was low, ranging from 0.2% to 1.2% in women treated with TX-001HR. **Conclusion:** In women with VMS treated with TX-001HR, significant improvements in sleep parameters typically associated with menopause from baseline to week 12 were consistently maintained up to 12 months compared with women treated with placebo. The reported incidence of somnolence was also very low. If approved, TX-001HR may provide the first oral combination of bio-identical estradiol/progesterone for VMS symptoms and could represent a new treatment option for menopausal women experiencing VMS who are currently using unapproved and inadequately studied compounded bio-identical hormone therapy products.

Sources of Funding: TherapeuticsMD

S-18.

Effects of TX-001HR on Uterine Bleeding Rates in Menopausal Women with Vasomotor Symptoms

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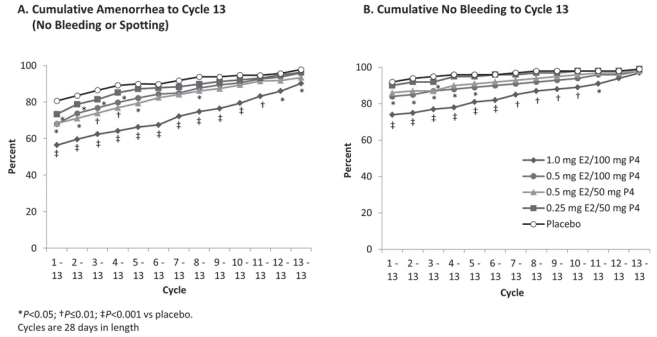
Objective: Uterine bleeding can be associated with endometrial pathology. Case reports[1-3] and a North American Menopause Society survey (n=1064)[4] suggest a potential increase in uterine bleeding and endometrial cancer with compounded bio-identical hormone therapy (CBHT). TX-001HR (TherapeuticsMD, Boca Raton, FL) is an investigational, single, oral softgel capsule of combined 17β-estradiol/progesterone (E2/P4; sometimes referred to as bio-identical hormones) currently being developed to treat vasomotor symptoms (VMS), while protecting the endometrium, in menopausal women. The objective of this analysis was to evaluate uterine bleeding in the REPLENISH trial with TX-001HR vs placebo. **Design:** Menopausal women (40-65 years) with VMS and an intact uterus were enrolled in REPLENISH (NCT01942668), a phase 3, randomized, double-blind, placebo-controlled, multicenter trial. Women with moderate-to-severe hot flushes (≥7/day or ≥50/week) were in the VMS substudy and randomized 1:1:1:1:1 to daily E2/P4 of 1.0 mg/100 mg, 0.5 mg/100 mg, 0.5 mg/50 mg, 0.25 mg/50 mg or placebo; all other women were randomized 1:1:1:1 to E2/P4 only for assessing endometrial safety. All women completed daily bleeding (requiring sanitary protection) and spotting (not requiring sanitary protection) diaries up to month 12. Bleeding profiles, including cumulative amenorrhea (no bleeding or spotting) were assessed over thirteen 28-day cycles in women who took ≥1 treatment capsule. **Results:** Women (n=1835) were randomized to daily E2/P4 of 1.0 mg/100 mg (n=415), 0.5 mg/100 mg (n=424), 0.5 mg/50 mg (n=421), 0.25 mg/50 mg (n=424) or placebo (n=151). Cumulative amenorrhea from cycle 1 to 13 was high with TX-001HR (56–73%), but lower than with placebo (81%; Fig 1A), and increased over time. Women with no bleeding was high (74–90%) with TX-001HR (Fig 1B). Few vaginal bleeding adverse events (1.0–4.6% TX-001HR vs 0.7% placebo) were reported and discontinuation due to bleeding was low (<1.5%). **Conclusion:** TX-001HR was associated with high amenorrhea rates and adequate endometrial protection in menopausal women with VMS and an intact uterus. Uterine bleeding and spotting improved over time; the potential for bleeding and abnormal pathology may be largely avoided with adequate doses of progesterone as studied with TX-001HR. TX-001HR, if approved, may provide the first oral combination of estradiol/progesterone for the treatment of VMS in menopausal women with an intact uterus, including the millions using unapproved and inadequately studied CBHT. 1. Eden JA et al. *Med J Aust* 2007;187:244-245 2. Davis R et al. *J Womens Health (Larchmt)* 2014;23:642-648 3. Dezman VL et al. *Int J Gynecol Cancer* 2015;25 Suppl 1:71 4. Gass M et al. *Menopause* 2015:22;1276-1284

Sources of Funding: TherapeuticsMD

Figure 1



*P<0.05; †P≤0.01; ‡P<0.001 vs placebo.
Cycles are 28 days in length

S-19.

TX-001HR Improved Quality of Life in Menopausal Women with Vasomotor Symptoms

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Objective: Use of unapproved compounded bio-identical hormone therapy (CBHT) has become the most prevalent form of hormone therapy (HT) used in the US by prescription volume. TX-001HR (TherapeuticsMD, Boca Raton, FL) is an investigational combination of 17β-estradiol and progesterone (E2/P4; sometimes referred to as bio-identical hormones) in a single, oral softgel capsule, currently being developed for the treatment of vasomotor symptoms (VMS) in menopausal women with an intact uterus. A secondary objective of the REPLENISH trial was to determine the effects of TX-001HR vs placebo on quality of life using the validated menopause-specific quality of life (MENQOL) questionnaire. **Design:** The REPLENISH study (NCT01942668) was a phase 3, randomized, double-blind, placebo-controlled, multicenter trial, which evaluated TX-001HR in menopausal women (40-65 years) with VMS and an intact uterus. Women with moderate-to-severe hot flushes (≥7/day or ≥50/week) were included in a VMS substudy and randomized 1:1:1:1:1 to daily E2/P4 of 1.0 mg/100 mg (n=141), 0.5 mg/100 mg (n=149), 0.5 mg/50 mg (n=147), 0.25 mg/50 mg (n=154), or placebo (n=135); all

other women were randomized 1:1:1:1 to active E2/P4 doses to assess the endometrial safety of TX-001HR (reported elsewhere). Subjects were administered the MENQOL questionnaire at baseline, and at week 12 and months 6 and 12. The questionnaire consisted of 29 items (symptoms), which if experienced were rated using a 7-item Likert scale ranging from "Not at all bothered" to "Extremely bothered." Items were grouped to form 4 domains: vasomotor (3 items), psychosocial (7 items), physical (16 items), and sexual (3 items). Baseline changes in the MENQOL overall and vasomotor domain scores as assessed in the VMS substudy population at those timepoints are reported here. Pearson correlations between changes in MENQOL and changes in moderate-to-severe VMS frequency at 12 weeks were also assessed. **Results:** Women in the VMS substudy had a mean age of 55 years and a mean BMI of 27 kg/m^2; 67% were white and 31% were black. Compared with placebo, women treated with TX-001HR had significantly better improvements from baseline in their MENQOL overall score at week 12, and months 6 and 12 (all, P<0.05, except for the 0.25 mg E2/50 mg P4 group at month 6). Overall scores ranged from 4.3–4.7 at baseline and were 2.3–2.8 with TX-001HR and 3.1 with placebo at month 12. Improvements from baseline for the MENQOL vasomotor domain score were significantly greater in all TX-001HR groups versus the placebo group at all timepoints (all, P<0.01). Vasomotor domain scores ranged from 6.9–7.2 at baseline and were 2.8–3.6 with TX-001HR and 4.4 with placebo at month 12. Correlations between changes in MENQOL scores and changes in VMS frequency were statistically significant. The largest correlation was observed between changes in the MENQOL vasomotor domain score and changes in moderate-to-severe VMS frequency (r=0.56). **Conclusion:** Compared with women randomized to placebo, women with moderate-to-severe VMS treated with the 4 estradiol/progesterone formulations of TX-001HR assessed in the REPLENISH trial reported clinically significant improvements in quality of life from baseline to 12 weeks, which were maintained up to 12 months. TX-001HR, if approved, may provide the first oral hormone therapy formulation combining estradiol and progesterone for the treatment of VMS in menopausal women with an intact uterus.
Sources of Funding: TherapeuticsMD

FRIDAY CONCURRENT SESSION #2

S-20.
Body image and sexual satisfaction among midlife women: A qualitative study

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Objective: Women may undergo changes in their appearance as they move through the menopausal transition. Most studies indicate that women's body image remains relatively stable over time despite these bodily changes. However, prior literature is mixed regarding how body image relates to sexual function in women. In this study, we used a qualitative approach to explore how body image and feelings of attractiveness relate to sexual function and satisfaction in midlife women. **Design:** We collected qualitative data among sexually active women aged 45-60 to explore: (1) women's perceptions of changes in their sexual function over time and (2) how midlife women respond to these changes. Twenty interviews and three focus groups were conducted by a trained facilitator using an interview guide; sessions were audio-recorded and transcribed. We used a template organizing approach for data analysis. The codebook was developed by two investigators using an iterative process; the primary investigator then coded all data. A second investigator coded a randomly selected 25% of data and kappa scores were calculated for inter-coder reliability. For this analysis, codes relating to body image were examined to identify key themes. **Results:** Thirty-nine women total participated, 19 in interviews and the rest in 3 focus groups. The mean age of the women was 58 (range 46-59); 53% were White, 46% were non-white. Most were perimenopausal 44% or postmenopausal (28%), with the remainder premenopausal (13%) or not sure (15%). Overall kappa score was 0.84 indicating excellent inter-coder reliability. All but 2 women identified as heterosexual. Many women discussed that **feeling attractive** was an important component of sexual satisfaction; many indicated that increased feelings of attractiveness was an important outcome of and reason for participating in sexual activity. However, some women felt as they got older, feeling sexually attractive was less important, and other aspects of the relationship such as having fun together and emotional intimacy became more important. Many women discussed feeling **insecure and self-conscious**. Most of these women expressed a strong desire to lose weight. However, women often emphasized that they were much more bothered by being overweight than were their partners. A smaller number of women expressed that they currently felt **confident and attractive**. These women attributed their confidence to increased self-acceptance with aging. White women were more likely to report feeling self-conscious, and Black women were more likely to report feeling confident. Several of the Black women discussed how their partners made them feel accepted and sexy regardless of their size. In contrast, several of the White women discussed feeling self-conscious naked and wanting to cover up or keep the lights dim during sex. **Conclusion:** Feeling attractive is an important component of overall sexual satisfaction in midlife women, although it may become less important over time. While bodily changes, such as weight gain, are common during midlife, and many women become more self-conscious about their bodies. A smaller proportion of women develop increased self-acceptance and self-confidence over time, and these women feel less self-conscious during sexual activity and discuss having higher overall sexual satisfaction. Supporting positive body image and self-confidence in midlife women may help women maintain sexual satisfaction with aging.

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S-21.
Interpersonal Violence, Posttraumatic Stress Disorder, and Menopause-Related Sexual Dysfunction in an Ethnically-Diverse, Community-Based Sample of Women

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Objective: Posttraumatic stress disorder (PTSD) and exposure to interpersonal violence are associated with sexual dysfunction among younger women, but little is known about the prevalence or impact of trauma experiences and sequelae among midlife and older women. We conducted the first study of the relationship of PTSD and interpersonal violence exposures to menopause-related sexual dysfunction in midlife and older women. **Design:** Data were drawn from a multiethnic, prospective cohort of women aged 40 to 80 years enrolled in Kaiser Permanente Northern California, a large integrated health care system. PTSD symptoms and lifetime history of interpersonal violence exposures (physical and emotional intimate partner violence, sexual assault) were assessed using standardized, structured-item questionnaire measures, including the Posttraumatic Stress Disorder Checklist-Civilian Version. Menopause symptoms associated with sexual dysfunction (vaginal pain with sexual intercourse, vaginal irritation, and vaginal soreness) were assessed using structured-item questionnaire measures that incorporated both prevalence and subjective bother. Multivariable logistic regression models were used to examine associations between PTSD or interpersonal violence exposures with menopause-related sexual dysfunction, adjusting for age, race/ethnicity, and body mass index. **Results:** In this sample of 2,016 community-dwelling women, (mean age 61 ±10 years, 36% non-Latina white, 22% Black, 23% Latina, 20% Asian), 450 (22%) had clinically significant PTSD symptoms (PCL ≥30), 316 (16%) reported a history of physical intimate partner violence, 423 (21%) reported a history of emotional intimate partner violence, and 382 (19%) reported having experienced sexual assault. Thirteen percent reported bothersome vaginal pain with intercourse, 32% reported bothersome vaginal irritation, and 7% reported bothersome vaginal soreness. In multivariable analyses, women with clinically significant PTSD symptoms were more likely to report bothersome vaginal pain with intercourse (adjusted odds ratio [AOR] 2.12, 95% CI 1.55-2.89, p<.001), vaginal irritation (AOR 2.22, 95% CI 1.68-2.95, p<.001), and vaginal soreness (AOR 3.70, 95% CI 2.56-5.35, p<.001). Emotional intimate partner violence was associated with bothersome vaginal pain with sexual intercourse (AOR 1.55, 95% CI 1.11-2.17, p=.01). Sexual assault was associated with bothersome vaginal pain with intercourse (AOR 1.46, 95% CI 1.03-2.09, p=.04) and vaginal irritation (AOR 1.44, 95% CI 1.05-1.98, p=.02). **Conclusion:** Over 20% of midlife and older women in this ethnically-diverse community-based cohort reported clinically significant PTSD symptoms and exposure to interpersonal violence, which contributed to their risk of menopause-related sexual dysfunction. These findings highlight the importance of systematic screening for PTSD and interpersonal violence among midlife and older women, and the need to determine best approaches for trauma-informed care of genital and sexual health in women across the aging spectrum.

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S-22.
Exposure to traumatic events and endothelial function among midlife women

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Objective: While biological and behavioral factors (e.g., lipids, blood pressure, smoking), have long been related to cardiovascular disease (CVD) risk, a growing literature links psychosocial factors to the development of CVD. However, little research has considered relations between traumatic experiences, a potent psychosocial factor, and endothelial function, a critical aspect of vascular health and an early marker of CVD risk. Moreover, little work has considered women during the menopause transition, often a time of accelerating CVD risk and deteriorating endothelial function. We tested whether a greater number of lifetime traumatic experiences was related to poorer endothelial function among midlife women, independent of demographic characteristics, psychosocial factors, CVD risk factors, estradiol, and childhood abuse history. **Design:** 272 peri- and postmenopausal nonsmoking women free of clinical CVD were recruited. Women completed questionnaires, including the Brief Trauma Questionnaire (measuring experiences such as sexual harassment, death of a child, being

in car accident, experiencing a natural disaster, being beaten or mugged), the Child Trauma Questionnaire, and measures of mood/anxiety. Women also underwent a fasting blood draw, 24 hours of ambulatory hot flash monitoring, and brachial artery ultrasound to assess flow mediated dilation (FMD), a marker of endothelial function. Relations between trauma and FMD were tested in linear regression models controlling for baseline lumen diameter, demographics, psychosocial factors, and CVD risk factors. A history of childhood abuse, hot flashes, and estradiol levels were also added to multivariable models. **Results:** Over 60% of the women had at least one traumatic life experience, and 18% had three or more traumatic experiences. Women reporting a greater number of traumatic experiences had lower FMD [beta, B(standard error, SE)=-.73(.37), p=.047] in multivariable models controlling for standard CVD risk factors. When further adjusting for a history of childhood abuse in multivariable models, associations persisted [e.g., sum exposures and FMD: B(SE)=-1.05 (.40), p=.01]. Findings were unchanged with further addition of hot flashes or estradiol levels. Relations between traumatic experiences and FMD were particularly pronounced for three or more traumatic experiences [B(SE)=-1.90(.71), p=.008, relative to none, multivariable models]. **Conclusion:** Women with a greater number of traumatic life experiences, particularly three or more, had poorer endothelial function. Relations were not explained by demographics, CVD risk factors, mood/anxiety, a history of childhood abuse, nor by hot flashes or estradiol. Findings underscore the importance of psychosocial factors such as trauma exposure in the development of CVD risk in midlife women.

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S-23.

Antidepressant Effects of Transdermal Estradiol in the Menopause Transition are Moderated by Stressful Life Events

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Objective: The menopause transition is associated with a 2-4 fold increased risk for major depression. Though the reasons for this increased risk have yet to be fully elucidated, the increased fluctuation in estradiol that characterizes the menopause transition has been implicated. Though a few small trials suggest that transdermal estradiol (E2) therapy effectively treats perimenopausal depression, this is the first study to examine the efficacy of transdermal E2 in preventing perimenopausal depression onset among initially euthymic women. The current study also sought to identify baseline characteristics predicting transdermal estradiol's beneficial mood effects. **Design:** 172 medically healthy women (ages 45-60) meeting STRAW+10 criteria for the menopause transition or early postmenopause (stages -2, -1 and +1a), not taking psychotropic medications, and free of current psychiatric disorders were recruited for a 12-month placebo-controlled double-blind RCT of transdermal E2 (0.1 mg). To examine the effect of treatment (placebo versus E2) on continuous Center for Epidemiologic Studies Depression Scale (CES-D) scores, a repeated-measures regression analysis using PROC MIXED in SAS 9.2 was used with 6 repeated measures (months 2, 4, 6, 8, 10 and 12). To test for potential moderating effects, each variable of interest and a treatment-by-variable of interest interaction term were added as predictors. Two covariates were included in all cases: 1) the pre-randomization value of the outcome variable, assessed at the initial study enrollment session, and 2) change in vasomotor symptom "bother" score on the Green Climacteric scale since study baseline, assessed at each visit. In addition, logistic regression was used to examine the effect of treatment and the potential moderation of treatment by the above-mentioned baseline characteristics on the risk of developing clinically significant depressive symptoms (CES-D score ≥16). **Results:** At baseline, women randomized to placebo did not differ from those randomized to E2 on mean CES-D scores (5.5 vs. 5.3, respectively). However, women randomized to placebo exhibited a significantly higher mean CES-D score across the 12-month intervention when compared to those assigned to estradiol (p=.02). Similarly, women assigned to placebo were more likely than those assigned to estradiol to score ≥16 on the CES-D at least once during the intervention phase (OR [95%CI] = 5.3 [1.8-15.8], p<.01). STRAW stage at study enrollment moderated the effect of treatment such that the mood benefits of E2 over placebo were evident among early and late perimenopausal (ps<.05), but not postmenopausal women (p=.36). Treatment also interacted with the number of stressful life events in the 6 months preceding enrollment such that a greater number of stressful events was associated with higher CES-D scores in the placebo group (p<.001) but not the E2 group (p=.99). In contrast, baseline E2 levels, baseline vasomotor symptoms, history of depression, and history of physical or sexual abuse did not moderate treatment effects (ps>.08). **Conclusion:** Twelve months of transdermal E2 (0.1 mg) considerably decreased the incidence of clinically significant depressive symptoms among initially euthymic women in the menopause transition. Stabilization of fluctuating E2 levels, which are characteristic of the menopause transition, may represent one mechanism underlying the prophylactic effect of E2 for the emergence of perimenopausal depression. This is supported, in part, by our observed mood benefit of E2 in perimenopausal but not postmenopausal women. A novel finding in this study is that the beneficial mood effects of E2 were particularly evident among women reporting more stressful life events at study entry. Assessment of recent life events in the clinical setting may be warranted in the individualized decision of whether to prescribe transdermal E2 for perimenopausal mood symptoms.

Sources of Funding: This research was supported by NIH grants RO1-MH087619 and T32 MH093315.

S-24.

Cognitive Behavioral Therapy for Menopausal Insomnia in Midlife Women with Insomnia and Nocturnal Hot Flashes

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Objective: Between 30-60% of peri- and postmenopausal women in the United States suffer from insomnia symptoms. Menopausal women with nocturnal hot flashes often report worse sleep quality and are more likely to meet criteria for insomnia disorder than those without nocturnal hot flashes. Thus, tailoring interventions to treat both insomnia and hot flashes may improve sleep and quality of life in millions of women. This pilot study examined the efficacy of cognitive behavioral therapy for insomnia and hot flashes among midlife women. **Design:** Forty women (mean age= 55±6.2) self-described as peri- or post-menopausal who reported ≥ 1 nocturnal hot flash/night and met diagnostic criteria for insomnia disorder were randomized to cognitive behavioral therapy for menopausal insomnia (CBTMI) or menopause education control (MEC). CBTMI included four individual 50-minute sessions over eight weeks focused on the treatment of insomnia and hot flashes, delivered by social workers or psychologists in gynecology clinics. MEC included a 1-hour meeting to discuss menopausal symptoms and sleep hygiene; and provide educational pamphlets and a non-directive suggestion to "make any behavioral changes as desired." Pre- and posttreatment measures included: Insomnia Severity Index (ISI), Self-Efficacy Scale for Sleep, and daily sleep diaries. Averages for sleep diaries were calculated for data collected between 5-30 nights before and after the intervention. **Results:** Mixed models revealed a significant time x treatment arm interaction for insomnia severity (p=.003), and sleep self-efficacy (p=.021), sleep diary wake after sleep onset (WASO; p=.005), and sleep diary sleep efficiency (p = .01). There was also a significant main effect for time for all domains (p's <.01) and for treatment arm for insomnia severity (p=.007). Women receiving CBTMI had significantly greater decreases from pre to post treatment in ISI score (15 ± 3.5 to 4 ± 3.7) and WASO (33 ± 20.6 to 9 ± 8.0 minutes) and significantly greater increases in self-efficacy score (26 ± 5.0 to 36 ± 7.4) and sleep efficiency (79% ± 13.5 to 91% ± 5.5) compared to women receiving MEC [pre to post treatment changes for MEC group: ISI score (16 ± 4.2 to 10 ± 5.0), WASO (33 ± 32.8 to 33 ± 38.5), self-efficacy score (26 ± 5.6 to 31 ± 7.7), sleep efficiency (82% ± 10.2 to 84% ± 9.2)]. **Conclusion:** For midlife women experiencing insomnia and nocturnal hot flashes, a 4-session CBT intervention targeting both insomnia and hot flashes led to clinically meaningful improvements in sleep.

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FEATURED POSTER PRESENTATIONS

P-1.

The Vulvovaginal Atrophy Questionnaire (VVAQ): A Novel Patient-Reported Outcome (PRO) for Assessing Symptoms of Vulvovaginal Atrophy in Menopausal Women

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Objective: Symptoms of vulvovaginal atrophy (VVA), a principal component of the genitourinary syndrome of menopause (GSM), are commonly reported in studies of menopausal women; however, the lack of a validated self-report measure of symptomatic VVA has greatly limited our ability to quantify its prevalence and associated outcomes in women. Given the prevalence of VVA symptoms and potential impact on women's health, quality of life and interpersonal relationships, there is an urgent clinical and research need for a patient-based, culturally-sensitive, validated instrument for assessing VVA symptoms and their impact on women's lives. We present results from the first four phases of development of a novel PRO measure for assessing VVA symptoms in menopausal women. **Design:** The overall goal of this project is to develop and validate a new PRO measure for assessing symptomatic VVA in both research and clinical settings. Following established standards and guidelines, this new PRO measure has been developed in four discrete stages. The first phase involved an extensive literature review with input from an expert advisory panel to develop a working conceptual model. In the second phase, concept elicitation interviews were conducted in 36 post-menopausal women with clinically confirmed, symptomatic VVA. Based on qualitative interview findings, a draft questionnaire was developed during the third phase. The draft questionnaire was then evaluated for comprehension and relevance (content validity) by means of cognitive debriefing interviews in focus groups of women with and without symptomatic VVA (N=26 with VVA, N=15 without VVA). Participants were recruited from three clinical sites. All interviews were performed by a trained qualitative interviewer and transcribed and coded for content analysis according to well-established coding procedures and analysis methods. **Results:** Based on findings from both phases

of qualitative interviewing, the draft questionnaire was modified and a revised conceptual model proposed. The revised VVAQ questionnaire consists of 14 individual items that assess vaginal and urinary health, impact on sexual function, and associated distress. The revised conceptual model and questionnaire includes the following domains: sensations, severity, perceived distress/bother, activities/function associated with symptomatic VVA and patient perception and experience of GSM/VVA. The sensation domain includes questions on dryness, burning, and pain during daily activities and urination. Pain during sexual activity is also addressed. Severity of GSM/VVA symptoms is also captured. In the perceived distress/bother domain, patients are asked if they have experienced any relief of their symptoms. Activities/Function domain includes items on sexuality (sexual function and spontaneity), other activities (clothing selection) and quality of life (relationships with partner(s)). Lastly, the patient perception and experience of GSM/VVA is addressed. Results from the cognitive debriefing phase confirmed that all of these items are comprehensible and relevant to women with and without symptomatic VVA. In the next phase of development, the draft questionnaire will be further evaluated in a quantitative validation study in women with and without diagnosed symptomatic VVA. **Conclusion:** In response to the urgent need for a patient-based, validated questionnaire of symptomatic VVA, a novel PRO measure has been developed based on qualitative responses of post-menopausal women with and without VVA. This new PRO measure was developed in close accordance with FDA's Guidance for PRO development and validation, and based also on expert advice from clinicians and researchers. Further clinical validation is planned, along with broader use of the measure in research and clinical settings.

Sources of Funding: Allergan, Shionogi, Pfizer

P-2.

Flibanserin in Postmenopausal Women With Hypoactive Sexual Desire Disorder: Responder Analysis of a Randomized, Placebo-Controlled Study

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Objective: Flibanserin, a 5-HT_{1A} agonist and 5-HT_{2A} antagonist, is approved by the US Food and Drug Administration (FDA) for the treatment of acquired, generalized hypoactive sexual desire disorder (HSDD). Although flibanserin is approved only for premenopausal women, it has also been studied in postmenopausal women with HSDD. In a randomized, placebo-controlled study of naturally postmenopausal women with HSDD (study name, SNOWDROP), treatment with flibanserin 100 mg once daily (qhs) was associated with significantly greater improvement in the number of satisfying sexual events (SSEs), sexual desire, and sexual distress compared with placebo (Simon JA, et al. *Menopause*. 2014;21(6):633-640). The aim of this post hoc analysis was to evaluate the probability of response and time to response in postmenopausal women with HSDD. **Design:** In this 24-week, double-blind placebo-controlled study (SNOWDROP), key measures of efficacy included the number of SSEs, Female Sexual Function Index desire domain (FSFI-d) score, and Female Sexual Distress Scale-Revised desire item (item 13; FSDS-R-13) score. Anchor analysis was used to identify threshold values for response for SSEs, FSFI-d, and FSDS-R-13. Responder data were compared for patients who received flibanserin 100 mg qhs or placebo. Kaplan-Meier survival analysis, with log-rank tests, was used to evaluate time to response. **Results:** This analysis included data for 450 women who received flibanserin 100 mg qhs and 476 women who received placebo. At week 24, the Kaplan-Meier estimate for probability of response in SSEs was 53.6% for the flibanserin group and 44.3% for the placebo group, in the FSFI-d was 54.0% and 44.1%, respectively, and in the FSDS-R-13 was 73.1% and 64.3%, respectively. There was significant separation of survival curves for flibanserin compared with placebo on all 3 efficacy measures (log-rank tests, all $P<0.01$). The Kaplan-Meier estimate of median time to response in flibanserin-treated patients was 61 days for SSEs, 57 days for the FSFI-d, and 56 days for the FSDS-R-13. **Conclusion:** In this post hoc analysis of data from a randomized, placebo-controlled study, the rate of treatment response was 53.6% to 73.1% in postmenopausal women with HSDD treated with flibanserin, depending on the efficacy measure assessed. Median time to response was approximately 2 months, suggesting that several weeks of treatment with flibanserin may be required before HSDD symptom improvement is observed. Flibanserin is approved by the FDA only for the treatment of premenopausal women with acquired, generalized HSDD and is to be discontinued if the patient reports no improvement in her symptoms after 8 weeks.

Sources of Funding: Boehringer Ingelheim; Valeant Pharmaceuticals North America LLC.

P-3.

Total vaginal thickness correlated with years since menopause and genitourinary syndrome of menopause

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Objective: The Genitourinary Syndrome of Menopause (GSM) affects up to fifty percent of postmenopausal women [1]. GSM symptoms include vulvo-vaginal dryness, burning and irritation and sexual symptoms including lack of lubrication and dyspareunia [1]. Data suggest that the transabdominal ultrasound measurement of total vaginal thickness (TVT) [2] can be used to verify a decline in vaginal thickness in postmenopausal women. To date, no study has correlated the number of years since menopause with the TVT and patient reported symptoms. This study measured TVT in pre and postmenopausal women by transabdominal ultrasound and compared TVT with the number of years since menopause in the postmenopausal population and TVT to the presence of GSM symptoms in the entire cohort. **Design:** In this pilot study, abdominal ultrasound measurements, including of total vaginal wall thickness and endometrial lining thickness at the level of the bladder trigone, were measured on fifty-three women (22 postmenopausal and 21 premenopausal). Exclusion criteria included previous oophorectomy or hysterectomy. The technique for taking these measurements has been outlined by Balica et. al (2017) [2] [3]. Additionally, a subset of women answered a standard set of questions regarding their GSM symptoms including but not limited to: vaginal dryness, irritation, burning, itching, and dyspareunia. Measurements were performed by the same team using GE Voluson E8, abdominal probe 2-8 MHz. Data were analyzed using linear regression with SPSS Version 22.0 (IBM corp., Armonk, New York). **Results:** The correlation between the number of symptoms and TVT in the entire cohort of pre and postmenopausal women trended in the negative direction, with the number of symptoms increasing with decreasing TVT. When only the data from the postmenopausal cohort was was analyzed, this relationship did not reach significance. In the postmenopausal cohort, the correlation between TVT and number of years since menopause also did not show a statistically significant relationship. **Conclusion:** The weak correlation in the negative direction between TVT and number of symptoms indicates that there may be a relationship between TVT and the symptoms of GSM. Number of years since menopause and TVT also did not show a statistically significant relationship in the post-menopausal cohort. More women, in a powered study, should be analyzed along with severity of symptoms, maturation index, and vaginal pH. References: [1] Portman, D. J., & Gass, M. L. (2014). Genitourinary syndrome of menopause: new terminology for vulvovaginal atrophy from the International Society for the Study of Women's Sexual Health and The North American Menopause Society. *The journal of sexual medicine*, *11*(12), 2865-2872. [2] Balica, A., Wald-Spielman, D. et. al, Assessing the Thickness of the Vaginal Wall and Vaginal Mucosa in Pre-menopausal versus Post-menopausal Women by Transabdominal Ultrasound: A Feasibility Study. *Maturitas* (2017) DOI: http://dx.doi.org/doi:10.1016/j.maturitas.2017.02.017 [3] Balica, A., et. al, Transabdominal sonography to measure the thickness of the total vaginal wall and vaginal mucosa: Clinical and research implications" *Journal of Clinical Ultrasound* Accepted for publication, DOI:22497

Sources of Funding: None

BONE/CANCER POSTER PRESENTATIONS

P-4.

Cervical Cancer in an Urban Academic institution: Analysis of an At-Risk Patient Population

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Objective: While the incidence of cervical cancer has declined in the United States, cervical cancer continues to be a significant source of morbidity and mortality among specific subsets of women. In a recent study published in *Cancer*, black women over the age of 85[1] were found to have the greatest mortality from cervical cancer. Importantly, cervical cancer screening guidelines do not extend to this age group, highlighting the importance of gaining a comprehensive understanding of these at risk populations. The objective of this study was to define the characteristics, risk factors and clinical course of patients treated for cervical cancer at a large urban public hospital. [1] Beavis,AL, Gravitt,P Rositch,A,Hysterectomy Corrected Cervical Cancer Mortality Rates;Cancer:2017:-1044-50 **Design:** A review of patients treated for cervical cancer by gynecologic oncologists at Bellevue Hospital between 2007-2015. **Results:** One-hundred and fifty-nine patients were treated for cervical cancer by gynecologic oncologists at an urban academic institution during the specified time period. The median age at diagnosis was 51 years (range 28-80), with 26 (16.4%) patients over 65 years. Sixty-nine (43.4%) patients identified as Hispanic or Latina, 36 (22.6%) as Black or African-American, 25 (15.7%) as Asian, 17 (10.7%) as Caucasian, and 12 (7.5%) were unknown. Seventy-six (47.8%) patients originated from the United States, while 57 (36%) patients reported their region of origin elsewhere – 24 (15.1%) from Asia, 16 (10.1%) South America, 5 (3.1%) Africa, 12 (7.5%) Europe, and 26 (16.4%) were unknown. The vast majority of patients had public insurance (71.1%), or were uninsured (20.8%). One hundred and seven (67%) patients presented with stage IB2 or higher disease, and the predominant stage at diagnosis was IIB (40, 24.2%). Only 34 (21.4%) patients had a known history of dysplasia, with HSIL being the most common cervical cytology prior to diagnosis. Forty-two (26.4%) patients were smokers, only 1 (0.6%) patient was HIV positive on antiretroviral therapy, and 5 (3.1%) had a history of radiation or chemotherapy from a prior cancer diagnosis. One hundred and eighteen (74.2%) underwent chemotherapy and radiation, while 55 (34.6%) were treated surgically, and 3 (1.9%) did not undergo treatment. At the most recent encounter, 85 (53.5%) patients had no evidence of disease, 67 (42.1%) were alive with disease, and 6 (3.8%) had died of their disease **Conclusion:** Despite advances in detection and treatment, cervical cancer remains a significant women's health care issue among at-risk patient populations in the United States. These findings draw attention to how the new screening guidelines may affect the care of women over 65 years of age.

Sources of Funding: None

P-5.

Incidence of Osteoporosis in Postmenopausal Patients from the Biology of Human Reproduction Service at Hospital Juarez in Mexico **Ivan Gómez del Angel MD ObGyn, Jhonatan Hidalgo Ledesma MD ObGyn, Francisco Valdez Morales PhD, Leobardo Valle Molina PhD, Imelda Hernández Marín PhD.**

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Objective: Osteoporosis is a skeletal disorder characterized by a compromise of bone strength that predisposes to an increase in the risk of fractures. The global epidemiological transition with the decline in mortality and an increase in life expectancy, in addition to the growing number of elderly people, has increased the number of chronic degenerative diseases, such as osteoporosis. This is important, since Mexico has 7 years without new data reporting on the incidence of this disease. The Objective of the study is to determine the incidence of osteoporosis in menopausal patients attending the Biology of Human Reproduction Service at Hospital Juarez in Mexico, from April 2016 to March 2017, as well as to characterize the osteoporosis patient by age, body mass index (BMI) measurement and STAW+10 staging, to identify the most frequently affected anatomical region, and finally, to identify patients with decreased and normal bone mineral density. **Design:** A prospective, cross-sectional, observational and descriptive study was carried out, with a sample of 207 patients (n=207), in whom bone mineral density was measured by means of central bone densitometry with a General Electric Healthcare Lunar Prodigy 14614 densitometer, certified by the International Osteoporosis Foundation (IOF), getting a T-Score cut-off between -1 and -2.4 for diagnosis of low bone mineral density and a T-score greater than -2.5 for osteoporosis. **Results:** Population was distributed among 3 age groups, and such distribution was homogeneous. The patients were divided into age groups of 50 to 59 years, 60 to 69 years and over 70 years, each accounting for about 30% of the sample. This age relationship was also described according to reproductive stages, stressing that the patients included in the study would stay in the reproductive stages related to menopause. Within this classification, the group with the highest representation was classified as a +2 or late menopause. The sample was also divided by BMI, in order to classify patients by weight; such division had a representation of Low weight at 2%, normal weight 29%, overweight 49% and obesity 20%. Fulfilling the main objective of the study, the incidence of osteoporosis was 30% of the total (62 patients), of which 25% (52 patients) was affecting the lumbar segment and 5% (10 patients) had hip osteoporosis. A lesser degree of bone mineral deficit was manifested in 45% (92 patients) in both regions. As mentioned earlier, there was an incidence of osteoporosis of 30%, a figure that becomes relevant in our setting because the latest reported prevalence rate in our country is 16% in women, and in this study the incidence rises to almost twice. **Conclusion:** Osteoporosis remains a public health problem in our country. Since 2009, a prevalence of 16% of osteoporosis has been reported, and a 43% of low bone mineral density in postmenopausal patients in our country. This study has yielded results that reveal an increase in the incidence of this disease of almost twice, a situation that had not been seen in recent years. Thus, it was found that the most affected age group is that between 60 and 69 years, then the group of older than 70 years, and finally the group of 50 to 59 years; however, in this last group there are 15 patients affected, so perhaps a good screening strategy for this disease would be to lower the age limit to perform central bone densitometry to 50 years old, at least in our population. Regarding the menopause stages, as expected by the pathophysiology of osteoporosis secondary to hypoestrogenism, STRAW +2 stage was the most frequent. A relationship between the patients with osteoporosis and those who are overweight was also noted in this study. The lumbar segment was the most affected by osteoporosis, and regarding decreased bone mineral density, there was no difference, as the hip and the lumbar segment were equally affected.

Sources of Funding: none

P-6.

Change of BMD in gynecologic cancer

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Objective: To evaluate the bone mineral density (BMD)in the lumbar spine and femur in postmenopausal women with cervical cancer and endometrial cancer without bone metastasis in comparison with that in healthy control postmenopausal women, and to assess the loss of BMD according to the cancer stage **Design:** We analyzed the BMD of the lumbar spine and femur using dual-energy X-ray absorptiometry (DEXA) in 218 patients with cervical cancer, 85 patients with endometrial cancer, and 259 healthy controls. The serum levels of calcium (Ca), phosphorus (P), osteocalcin (OSC), and total alkaline phosphatase (ALP), and urine deoxypyridinoline(DPL) were measured in all participants. **Results:** Age, body mass index, parity, and time since menopause were not significantly different between the three groups. Serum Ca level was higher in the cervical cancer group ($p = 0.000$), however, urine DPL was lower in endometrial cancer group ($p = 0.000$). The T-scores of basal BMD at the second and fourth lumbar vertebra (L2, L4) were significantly lower in patients with cervical cancer ($p = 0.038$, 0.000, respectively) compared to those in the healthy control groups. Additionally, the incidence of osteoporosis and osteopenia basal status of bone mass was significantly higher in patients with cervical cancer compared to that in controls ($p = 0.016$). No differences in basal BMD of the lumbar spine and femur were observed between patients with cervical cancer according to their stages. **Conclusion:** Our results suggest that postmenopausal women with cervical cancer have a lower BMD and are at increased risk of osteoporosis in the lumbar spine before receiving anticancer treatment compared with postmenopausal women with endometrial cancer.

Sources of Funding: None

P-7.

Neglect of Bone Loss in Menopausal Mothers with Primary Ovarian Insufficiency

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Objective: Women with premature ovarian insufficiency (POI) have increased risk for osteoporosis given earlier onset of estrogen deficiency. Pregnancy and lactation can occur spontaneously, and advances in reproductive techniques have augmented their ability to conceive. We report on two women with POI who had pregnancies with prolonged lactation periods and were diagnosed with severe osteoporosis. **Design:** Cases **Results:** A 45 year-old woman with a history of POI and Hashimoto's thyroiditis presented to Endocrine Clinic. She underwent menarche at age 13 with regular 28 day cycles and was on oral contraceptives (OCP) from age 20 to 36 years. When she discontinued the OCP to attempt conception, she developed hot flashes, palpitations, and amenorrhea; work-up revealed FSH 147 ng/ml, and she was diagnosed with menopause. She received no treatment until age 39, when oral contraceptives were resumed. At age 42, she underwent in vitro fertilization with a donor egg, delivered a full-term infant, and breastfed for 2 years without subsequent hormone treatment. She also endorsed intermittent vegetarianism since age 38 and running 3 miles per day though more recently, she began eating meat and dairy once a week and decreased her exercise to 4 times a week. On exam, her BMI was 20.1, with no thyromegaly and normal physical and pelvic evaluations. Additional labs: TSH 0.999 IU/ml, 25 OH D 35.9 ng/ml, negative celiac screen, normal chemistry, blood count, urinalysis. Her DXA showed T-scores in spine: -3.4, femoral neck: -1.6, total hip -1.3. She was started on 17βB estradiol 1mg and micronized progesterone 200mg daily for 10 days out of the month as well as calcium 500mg, a prenatal vitamin, cholecalciferol 1000 IU daily, and provided with dietary counselling. After several months, she became pregnant with an in vitro donor egg. Her pregnancy was complicated by bleeding and a wrist fracture. At 7 months postpartum, she continued to nurse, and repeat DXA showed additional bone loss with T-scores spine: -3.8, femoral neck: -2.5, total hip: -1.9. The patient was reluctant to stop nursing, declined nutritional evaluation, but was amenable to hormone therapy with an estradiol patch and micronized progesterone. After one year of treatment, she had a 15.8% increase in spine BMD and 7% increase in hip BMD with T-scores: -2.9 and -2.3, respectively. The second case is a 36 year-old woman with POI. She underwent menarche at age 11 with regular periods from age 11 to 24 years. Subsequently, she developed irregular menses and hair loss and took an OCP for the next six years. At age 29, she lost 15 pounds, attributed to the stress of her wedding and demanding career. She also endorsed an hour of daily exercise. Her history was further notable for sternum and rib fractures at age 28 in a motor vehicle accident and inferior pubic ramus fracture in a go-cart accident at age 31. When she stopped the OCP in anticipation of conception at age 31, she developed amenorrhea lasting over a year. Exam was unremarkable. Work-up revealed: FSH 41 ng/ml, estradiol 15.9 pg/ml, undetectable anti-mullerian hormone. She was diagnosed with POI and started on micronized estradiol 2mg daily with cyclic progesterone. She had brief return of spontaneous menses, became pregnant, and delivered a healthy infant. Her DXA showed T-scores in spine: -3.7, hip -2.0, femoral neck -1.8, distal radius -2.7. After several months of lactation, the patient considered a second pregnancy but decided against it after a bout of sacral pain concerned her for a fracture, and resumed transdermal estrogen and cyclic progesterone. On treatment, repeat DXA one-year post-weaning showed an 11.8% increase in spine BMD, 3.6% increase in hip BMD, and 2.3% increase in femoral neck BMD with T-scores -3.0, -1.8, and -1.6, respectively. **Conclusion:** The physiologic post-weaning rise in estradiol does not occur in women with POI and requires exogenous replacement. Failure to meet dietary calcium and vitamin D intake recommendations and replace hormones will exacerbate bone loss in a population already at high risk for low bone mass, yet these simple interventions are not routine practice. These cases highlight the importance of comprehensively addressing the ante-, peri-, and postpartum needs of mothers with POI to prevent early osteoporosis and optimize the health of mothers who will be raising children to an advanced age.

Sources of Funding: None

CARDIOVASCULAR/OBESITY/METABOLIC HEALTH POSTER PRESENTATIONS

P-8.

Greater Volumes of Peri-aortic Fat at Midlife is Associated with Lower Gait Speed Later in Life in Women: The Study of Women's Health Across the Nation Cardiovascular Fat Ancillary study

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Objective: Higher peri-aortic adipose tissue (PVAT), the fat surrounding the descending aorta, has been associated with vascular function impairments and lower extremity peripheral artery disease. Several lines of evidence support a physiologic link between vascular and physical functions. PVAT may contribute to adverse dynamic physiologic alterations in the vascular wall, which may limit normal physical activity later in life. However, association between volumes of PVAT in women at midlife and physical functioning later in life has not been addressed before. We hypothesize that higher volumes of PVAT at midlife is associated with lower gait speed later in life, independent of overall adiposity and other traditional risk factors. **Design:** Participants from the Study of Women's Health Across the Nation (SWAN) cardiovascular fat ancillary study at the Pittsburgh and Chicago sites who had available data on PVAT volume measured early at midlife (during SWAN visits 4-7) and gait speed measured after a mean ± SD of 10.4 ± 0.7 years of follow-up (at SWAN visit 13) were included in this analysis. PVAT was quantified using existing CT scans and gait speed was calculated from the average time of the 4-meter walking assessment by dividing distance in meters (4 meter) by time in seconds. PVAT was log transformed and linear regression modeling was used for statistical analyses. **Results:** The study included 276 women (at PVAT assessment: mean ± SD age 51.3±2.8 years; 63% White and 37% Black; 58.3% pre-/early peri- and 41.7% late peri-/postmenopausal). The average gait speed at visit 13 was 0.95 ± 0.21 m/s. Adjusting for study site, race, socioeconomic factors, length of the descending aorta, age at visit 13 and menopausal status at PVAT assessment, women with greater volumes of PVAT had significantly lower gait speed, P value <0.0001. This negative association remained significant after further adjustment for the following covariates from visit 13: body mass index, overall self-rated health, current smoking, and presence of any of the following comorbid conditions by visit 13: diabetes mellitus, hypertension, CVD, any cancer, osteoporosis, and osteoarthritis; in this model, every 1 SD increase in log PVAT was associated with 3.2% lower gait speed (95% CI: 0.3%-6.2%), P value=0.03). Additional models adjusted for ever use of hormone therapy or time elapsed between PVAT and gait speed assessments showed similar results. **Conclusion:** Independent of overall adiposity and comorbid conditions, greater volumes of peri-aortic fat at midlife is associated with lower gait speed later in life among women. A fast decline in gait speed has been recently defined as 2.4% decrease per year, and those with fast decline in gait speed had a 90% greater risk of mortality than those with slow decline. Identifying PVAT as a potential risk factor for physical function limitation later in life, in addition of being linked to vascular health, supports the importance of monitoring this fat depot during midlife. Future studies should assess the interrelationship between PVAT, vascular health indices and physical functioning to better understand the underlying mechanism of the reported association.

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 U01NR004061; U01AG012505, U01AG012535, U01AG012531, U01AG012539, U01AG012546, U01AG012553, U01AG012554, U01AG012495). **The content of this abstract** is solely the responsibility of the authors and does not necessarily represent the official views of the NIA, NINR, ORWH or the NIH.SWAN Heart was supported by the National Heart, Lung, and Blood Institute (Grants HL065581, HL065591). The SWAN Cardiovascular Fat Ancillary Study was supported by an award from the American Heart Association Great River Affiliation Clinical Research Program: 12CRP11900031.

P-9.

Frequency of metabolic syndrome in the different STRAW +10 substages of post-menopausal patients treated at the Hospital Juarez of Mexico. Jhonatan Hidalgo Ledesma MD ObGyn, Ivan Gómez del Angel MD ObGyn, Francisco Valdez Morales PhD, Leobardo Valle Molina PhD, Imelda Hernández Marín PhD.

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Objective: Menopause is the permanent cessation of menstruation, determined retrospectively, after 12 consecutive months of amenorrhea without pathological causes; in the post-menopausal patients, there is an increased risk of cardiovascular disease and diabetes mellitus. The metabolic syndrome (MetS) is defined as a set of risk factors for identifying persons with an increased risk of cardiovascular diseases, especially important in post-menopausal women. The empirical evidence suggests a predisposition for metabolic syndrome in women; however, there is scarcity of research addressing the MEtS in post-menopausal women at the various STRAW +10 stages. The objective of this study was to identify the stage at which the metabolic syndrome is more frequent in the different STRAW +10 substages in post-menopausal patients, and to evaluate the influence of each ATP III variable on the occurrence of the MetS. **Design:** The analysis of 1 year of data, was completed using the ATP III criteria for MetS diagnosis, and the STRAW +10 classification was used to categorize post-menopause. Each criterion for MetS and type of menopause was assessed, a risk assessment by OR was performed, and the statistical significance was determined by Chi^2 or student-t according to the type of variable used. **Results:** The participants (n=159) were in the middle age (47.2+2.69 years). The frequency of metabolic syndrome was 38%, patients with stage +2 MetS had a frequency of 51.6%, followed by stage +1A, with 25.8%, finally stages 1b and 1c with 14.5% and 8%, respectively. The three most common criteria for the diagnosis of MetS according to ATP III were waist circumference (WC) >88 cm, with a 96%, followed by hypertriglyceridemia >150 mg/dl with 85.4%, and finally, hypoalphalipoproteinemia <50 mg/dl with 82.2%. Obesity was the most frequent BMI degree with 57%, followed by overweight with 41%, and finally normal weight with 2%. The average age of onset of spontaneous menopause was 47.2 years, and the induced menopause was 45.9 years. WC maintains an OR of 1.50 for development of MetS in post-menopausal patients with a 95% CI (1.279-1.766) p<0.05; in contrast, a WC <88 cm, showed a protective effect with an OR of 0.134 95% CI (0.43-0.416) p< 0.05; systolic blood pressure (SBP) >130 mm Hg, with an OR of 5.02 95% CI (2.421-10.409) p<0.05, in the presence of SBP <130mmHg the protective effect is maintained with an OR of 0.646 95% CI (0.517-0.799) p<0.05. Diastolic blood pressure (DBP) > 85 mmHg maintained an OR of 3.902 95% CI (1.718-8.860) p< 0.05; DPB <85mmHg is maintained with protective effect with an OR of 0.777 95% CI (0.658-0.915) p<0.05. Fasting Glucose (FG) > 100mg/dl presented an OR of 4.131 95% CI (2.436-7.005) p<0.05, FG <100 with OR 0.478 95% CI (0.358-0.653) p< 0.05, Triglycerides >150 mg/dl showed an OR of 3.902 95% CI (2.628-5.792) p< 0.05, while a TGL level of <150 mg/dl had an OR of 0.209 95% CI (0.117-0.317) p<0.05, the decrease of HDL cholesterol (HDL-C) <50mg/dl had an OR of 2.434 95% CI (1.800-3.932) p< 0.05, the increase in HDL-C >50mg/dl was presented with an OR of 0.272 95% CI (0.156-0.473) p<0.05, spontaneous menopause was presented with an OR of 1.134 95% CI (0.855-1.504) p>0.05. In contrast, surgical menopause was presented with an OR of 0.855 95% CI (0.593-1.231) p>0.05; the type of menopause does not have statistical significance for MetS. **Conclusion:** The most frequent stage for MetS was identified as STRAW +2, the subsequent stages were found with STRAW +1A and STRAW +1b. Post-menopause predisposes women to develop MetS at a late stage. The frequency found in this study of MetS in post-menopause was 38%, which reflects a notable rise in this life stage for women. According to the diagnostic criteria for MetS, abdominal obesity predominated in the first place, followed by hypertriglyceridemia and hypoalphalipoproteinemia in second and third place, respectively. The OR values with greater association on the MetS were SBP, fasting glucose and hypertriglyceridemia, no association was found for the type of menopause.

Sources of Funding: None

P-10.

The weight control in obese, perimenopausal and menopausal women with Ipragliflozin and Phentermine: Preliminary results

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Objective: Most women gain weight as they age, but excess weight is not inevitable. The purpose of this study was to determine whether it is effective in the treatment of obesity women with diabetic drug ipragliflozin(Suglat) alone or in combination with ipragliflozin and anti obesity agent, phentermin(Adipex). **Design:** The subjects were 102 women aged 40-72 years who visited the Inha University Obstetrics and Gynecology Department in Incheon from October 1, 2016 to May 30, 2017. They were overweight or obese with a BMI greater than 23, had not used other obesity drugs, and did not take steroids or antidepressants. We randomly divided into two groups, ipragliflozin 50mg alone in one group(n=52) and ipragliflozin 50mg and phentermin 18.75mg in another(n=50). After 90 days, the weight of each subjects was measured to confirm the degree of weight loss. **Results:** The combination of ipragliflozin and phentermin significantly reduced body weight compared to subjects treated with ipragliflozin alone. Subjects treated with combined therapy lost on average 5.84% of body weight compared with 2.25% loss in the ipragliflozin alone group(p<0.001). 58% of combination group were high responders who lost ≥5% body weight, compared with 11% in the ipragliflozin alone group. **Conclusion:** Although both the ipragliflozin monotherapy and combination with phentermine reduced body weight, the combined therapy was significantly more effective.

Sources of Funding: None

P-11.

The Association of Dietary Intake and Metabolic Syndrome in Korean Postmenopausal Women

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Objective: We aimed to evaluate the dietary factors affecting metabolic syndrome (MetS) in Korean postmenopausal women from the population-based study. **Design:** This cross-sectional study was based on nationwide representative survey data from the Korean National Health and Nutrition Examination Survey (KNHANES) 2008. A total of 751 postmenopausal women (mean age 64.8 years) were included from the KNHANES 2008. The KNHANES has been conducted periodically since 1998 and is

composed of data from the civilian, non-institutionalized population of the Republic of Korea using a stratified, multi-stage sampling with a probability proportional to size. The sampling frame was based on the 2005 population and housing census in Korea. MetS was identified according to the new criteria from a joint scientific statement endorsed by major organizations including National Heart, Lung, and Blood Institute. The food frequency questionnaire (FFQ) was used to evaluate dietary intakes. **Results:** Overall, a total of 342 participants (45.5%) were diagnosed as having MetS. The intake of energy, carbohydrate, protein, fat, soda, coffee, calcium, vitamin A, carotene, retinol, thiamine, riboflavin, niacin and vitamin C was assessed according to the status of MetS. The β-carotene intake was significantly lower in participants with MetS compared with those who not having MetS (2776.4 ug vs 3537.7 ug, P=0.03). Additionally, the group with lower β-carotene (less than 2000 ug/day) intake has 1.14 times higher odds for MetS, but the statistical significance was modest (P=0.07). The number of MetS components was not associated with the intake of β-carotene after adjustment for potential confounders including age, years since menopause, body mass index. **Conclusion:** Considering the β-carotene contribution in antioxidant protection, it is suggested that great attention be given to the dietary pattern in patients with MetS. In conclusion, the intake of β-carotene was associated with MetS in Korean postmenopausal women, and further investigation is needed for the pathophysiologic mechanism.

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P-12.

Assessment of Body Adiposity Index and fasting glucose according with the ACE I/D genotype in postmenopausal women

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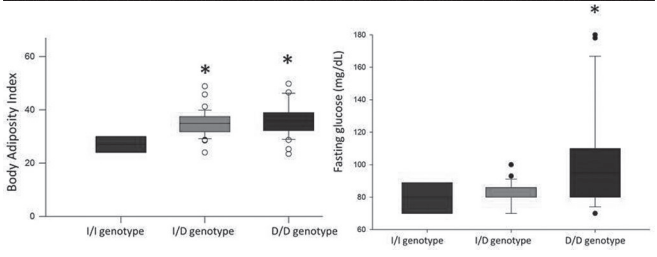
Objective: The aim of this study was to assess the Body Adiposity Index and fasting glucose according with the ACE I/D genotype in postmenopausal women. After menopause it has been demonstrated the increase of the adipose tissue and central obesity incidence in postmenopausal women. The visceral fat tissue promotes the enlargement in the synthesis of the atherosclerotic lipids and the insulin resistance. Both factors are linked with a higher risk of metabolic and cardiovascular diseases, such as hypertension. The "D" allele of the I/D ACE polymorphism has been related with a higher income of carbohydrates and therefore, coupled with the hormonal suppression can be considered as a part of the insulin resistance and is involved in central obesity pathological mechanism. The Body Adiposity Index evaluates the quantity of fat mass, and considers the height and the hip circumference. **Design:** An transversal, cohort study was carried out in 75 women, anthropometric data were collected, Body Adiposity Index (BAI) was calculated; DNA was isolated from blood. ACE I/D genotype was determinate by real time PCR, the "D" allele was corroborated trough a second real time-PCR. **Results:** The antropometric parameters are described in table 1.The mean of the fasting glucose according genotype of ACE I/D polymorphism, was 102±31.87 mg/dL (D/D); 86±28.50 mg/dL (I/D) and 79±9.67mg/dL (I/I) (graph 1). There was statistically significant difference in the fasting glucemy (Kruskall-wallis, Dunn's Method, p=0.05).With respect BAI, the mean was 37.81±13.39 (D/D); 34.84±4.7 (I/D) and 26.73±2.8 (I/I) (Graph 1) (Kruskal-wallis, Dunn's Method, p=0.05). **Conclusion:** The patients with D allele of ACE I/D polymorphism had a higher fasting glucose and BAI compared with the other genotypes.

Sources of Funding: none

Table1. antropometry

Variable	D/D	I/D	I/I
Waist (cm)	91±11.1	87.41±10.06	94±10.9
Hip (cm)	105.39±24.10	102.7±7.22	96±8.1
Body mass index (kg/m2)	28.7±3.9	27.1±3.8	26.5±5.7



P-13.

Assesment of waist to heigth ratio as a novel marker of cardiovascular risk in posmenopausal women

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Objective: The aim of this study was to assess the waist to height ratio as a novel marker of cardiovascular risk in menopausal women. **INTRODUCTION** Menopause is defined as the permanent end of menstruation and fertility. It is a normal, natural event associated with reduced functioning of the ovaries, resulting in lower levels of ovarian hormones primarily estrogen[1], the mean age for the menopause is 51 years old in north American women[2]. After this stage the distribution of the body fat is concentrated in the abdominal area[3]. The visceral fat has been related with the enlargement in the synthesis of the atherosclerotic lipids and promotes proinflamatory factors such as C reactive protein, plasminogen activator factor type 1 (PAF-1), and proinflamatory interleukins[4] (IL.1, IL-6 and TNFα), those phenomena are linked with a higher risk of cardiovascular and metabolic diseases [5]. The body mass index (BMI), has been used for many years to classify the grade of overweight or obesity in patients, indistinctly of sex. But this index is affected by hydration status and muscle mass, and do not consider the modification in fat distribution. The waist to height ratio is a novel marker related with the quantity of visceral fat, and this utility has been demonstrated in childhood and adolescent population, however, its use has not been studied in postmenopausal women. The aim of this study was to assess the waist to height ratio as a novel marker of cardiovascular risk in menopausal women. **Design: MATERIALS AND METHODS** A descriptive, observational, prospective, transversal, cohort study was carried out in 200 women. The data was obtained from a primary data base, from patients to the climacteric clinic of the "Hospital de la Mujer", optometric, and odontology clinic of the Centro Interdisciplinario de Ciencias de la Salud-Instituto Politécnico Nacional. The expedients were classified according with the hypertensive status. Data of anthropometric parameters as weight, height, waist and hip circumference; bicipital, tricipital, subscapular and iliac crest skin fold thickness were collected and the BMI, WHR, Waist to height ratio, body fat percentage and conicity index were calculated. **Results:** The mean age was between 50 and 60 years, the mean pressure was higher in hypertensive group (p=0.03, Man-whitney). The correlations of the anthropometric parameters in both groups are resumed in table 1. Figure 1. Pearson correlations of anthropometric parameters in normotensive and hypertensive patients. **Conclusion:** There was a strong positive correlation between the anthropometric parameters classically related with the cardiovascular risk in both groups normotensive and hypertensive patients, so then, this index can be used as a novel marker for cardiovascular risk in menopausal women.

Sources of Funding: None

Figure 1. Pearson correlations of anthropometric parameters in normotensive and hypertensive patients.

Pair of variables	Normotensive		Hipertensive	
	r	p	r	p
BMI vs waist to height ratio	0.595	<0.001*	0.70	<0.001
BF% vs waist to height ratio	0.65	<0.001*	0.65	<0.001
Hip circumference glucose vs waist to height ratio	0.498	<0.001*	0.385	0.272

P-14.

Associations between obesity and health problems in climacteric women assisted in Primary Health Care

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Objective: To identify the associations between obesity and health problems in climacteric women assisted in Primary Health Care (PHC). **Design:** Cross-sectional and analytical study, carried out in 2014 and 2015, with a population of 30,018 women registered in 73 Family Health Strategies in Montes Claros, Minas Gerais, Brazil. The sample was probabilistic type. Data collection was performed through questionnaires (sociodemographic, behavioral, reproductive, gynecological and clinical), anthropometric evaluation and blood collection. The dependent variable was overweightness and obesity, following recommendations and classification of the World Health Organization (WHO), being dichotomized in non-obese classified (BMI < 25kg/m2), or overweight and obese (BMI ≥ 25kg/m2). For statistical analysis, absolute and relative frequency were estimated. To analyze the associations between the dependent variable and the independent variables (sociodemographic, reproductive, quality of life, clinical factors, eating and behavioural habits), the bivariate analysis was performed using the Poisson regression test to select variables for the multiple model, being adopted p≤0.25. In the multiple analyzes phase, the Poisson regression model was used to obtain adjusted prevalence rates (PR). At the end of the analysis, the final model was constructed, adopting a level of significance of p ≤0.05. **Results:** The sample consisted of 874 women between the ages of 40 and 65, of

whom more than half were in the postmenopausal period and approximately 74% were overweight. By means of hierarchical multiple regression, it was observed that in the distal block, low schooling (PR = 1.11, 95% CI: 1.01-1.23) and attended private school (RP = 1.30, CI 95%: 1.14 -1.50) were associated with overweightness and obesity. In the intermediate block, having a child above 18 years old (PR = 0.90, CI 95%: 0.82 -0.97) had a protective effect for the non-occurrence of overweightness and obesity. And, in the proximal block, overweightness and obesity were associated to the presence of gout (RP = 1.18, CI 95%: 1.05 -1.32), kidney disease (PR = 1.18, CI 95%: 1.08 -1.29), metabolic syndrome (PR = 1.29, CI 95%: 1.16 -1.44), high risk for cardiovascular diseases (PR = 1.19, CI 95%: 1.05 - 1.34) and to make the fat intake (RP = 1.12, CI 95%: 1.02 -1.23). **Conclusion:** The data provided useful information to understand the associations between sociodemographic and reproductive variable, clinical factors and eating habits, and the occurrence of overweight and obesity in the climacteric, making possible the development of educational actions directed to these women.

Sources of Funding: none

Crude and adjusted prevalence for overweightness/obesity according to demographic, reproductive, of life quality, clinical, eating and behavioral factors for obesity in climacteric women.

	Variables	PR (CI95%) Crude	Value p	PR (IC95%) Adjusted	Value p
Socio-demographic factors (distal level)					
School attended	Public	1.00	0.000	1.00	0.000
	Private	1.26 (1.11 – 1.43)		1.30 (1.14 -1.50)	
School level	High/Superior	1.00		1.00	
	Elementary II	1.03 (0.92 – 1.15)	0.560	1.05 (0.94 – 1.17)	0.420
	Elementary I	1.11 (1.01 – 1.21)	0.039	1.11 (1.01 -1.23)	0.033
Reproductive/ quality of life (intermediate level)					
Age at first	≤18 years old	1.00	0.004	1.00	0.010
childbirth	> 18 years old	0.89 (0.82 – 0.96)		0.90 (0.82 -0.97)	
Clinical Factors/Eating Habits/Behavioral (Proximal Level)					
Gout disease	Absent	1.00		1.00	
	Present	1.27 (1.15 – 1.40)	0.000	1.18 (1.05 -1.32)	0.004
Metabolic Syndrome	Absent	1.00		1.00	
	Present	1.39 (1.25 – 1.53)	0.000	1.29 (1.16 -1.44)	0.000
Kidney disease	Absent	1.00		1.00	
	Present	1.20 (1.10 – 1.31)	0.000	1.18 (1.08 -1.29)	0.000
Cardiovascular diseases	Low risk	1.00		1.00	
	Intermediate risk	1.15 (1.06 – 1.26)	0.001	1.05 (0.95 – 1.15)	0.332
	High risk	1.31 (1.16 – 1.46)	0.000	1.19 (1.05 – 1.34)	0.006
Fat intake	No	1.00		1.00	
	yes	1.09 (1.00 – 1.19)	0.065	1.12 (1.02 -1.23)	0.014

ENDOGENOUS HORMONES POSTER PRESENTATIONS

P-15.

Identification and prioritization of dermatological disorders influnced by female hormonal fluctuations during and beyond menopause.

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Objective: The purpose of this study was to generate expert consensus regarding the most significant skin disorders in the context of fluctuating hormonal levels during and beyond natural or induced menopause, that should be included in the curriculum for dermatology residents. The review of the current dermatology and menopausal medicine curriculum indicated that there was a lack of significant educational content on gender specific skin conditions as well as certain pre-existing skin disorders that are influenced by menopausal hormonal fluctuations. **Design:** In order to diversify the dermatology curriculum, this research effort was focused on identifying and prioritizing the most significant dermatological disorders in the context of female hormonal fluctuations during and beyond natural and induced menopause using the Delphi Method. A convenience sample of thirty-three physicians from five different departments of a large medical institute in southwest of United States (dermatology, gynecology, rheumatology, internal medicine, and family medicine) participated in the study to identify and prioritize these conditions. **Results:** The median for the ranking of each skin disorder was three or above in both the rounds with significant convergence and minimum variability. The most highly ranked category of skin disorders affected by hormone changes, was identified to be gynecological disorders. The most highly ranked skin disorder due to hormonal fluctuations was identified to be hirsutism followed by vulvovaginal disorder. **Conclusion:** It was concluded, that the women's health experts from different disciplines had the consensus of opinion to include the list of skin disorders prepared by literature review and feedback from expert Panel A, towards preparation of a curriculum.

Sources of Funding: None

Topics	Sub Topics	Median	
		Round 2	Round 3
Autoimmune Disorders	a. Discoid Lupus	4	4
	b. Vitiligo	4	4
Endocrine Disorders	a. Hirsutism	5	5
	b. Hyperthecosis	4	4
Gynaecological Disorders	a. Vulvovaginal atrophy	5	5
	b. Vaginal lichen planus	4	4
Breast Disorders	a. Paget's Disease	3	3
	b. Intertriginous candidiasis	3	3
Hair loss Disorders	a. Male pattern baldness	5	5
	b. Alopecia Areata	4	4
Nail Disorders	a. Distal Nail splitting	4	4
	b. Dystrophic nails	4	4
Aging Skin Disorders	a. Wrinkles	5	5
	b. Thinning of skin	4	4
Oncologic Disorders	a. Basal cell carcinoma	3	3
	b. Squamous cell carcinoma	3	3
	c. Melanoma	3	3
	d. Bowen's disease	3	3
Vascular Disorders	a. Chronic venous insufficiency changes	3	3
	b. Telangectasia	3	3
Infectious Disorders	a. Hidradenitis suppurativa	3	3
	b. Folliculitis	3	3
Others	a. Rosacea	4	4
	b. Acne Vulgaris	4	4

Top Two highly Ranked Skin Disorders in each Organ System Category

P-16.

Relationship Between Serum Anti-Mullerian Hormone with Vitamin D and Metabolic Syndrome Risk Factors in Late Reproductive-Age Women

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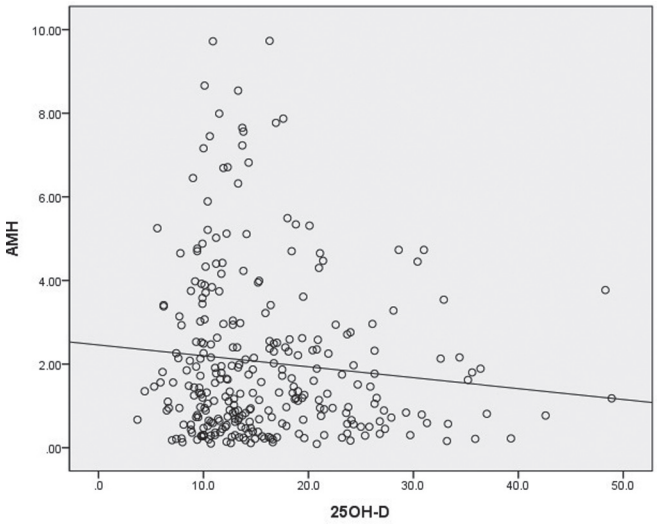
Objective: To evaluate the relationship between serum Anti-Mullerian hormone (AMH) with vitamin D (25OH-D) and metabolic syndrome (MetS) risk in generally healthy late reproductive-age women (range of 35-49 years) with regular menstrual cycles. **Design:** Cross sectional study in retrospective and prospective cohort **Results:** Among the 291 participants (mean age of 42.5), most (76.6 %, n=223) were serum vitamin D insufficient (<20ng/ml). Mean serum levels of AMH and vitamin D were 2.04 ng/mL and 15.9 ng/mL respectively. The prevalence of MetS was 2.1% (n=6); abdominal obesity (waist circumference ≥85 cm), 6.5% (n=19); high blood pressure (systolic blood pressure/diastolic blood pressure ≥130/85 mmHg), 7.9% (n=23); high TG (≥150 mg/dL), 5.5% (n=16); low HDL-C (<50 mg/dL), 21.3% (n=62); and high blood sugar (fasting glucose ≥100 mg/dL), 8.2% (n=24). There was no correlation between AMH and 25OH-D after adjustment for age (r=-0.093, p = 0.113). Subjects with higher MetS score, higher waist circumference (WC) and higher diastolic blood pressure had significantly higher serum AMH level when adjusted for age but the association all attenuated when BMI was considered together. There was no significant correlation between MetS risk components with serum level of AMH or vitamin D. **Conclusion:** There was no association between AMH with serum 25OH-D or MetS risk factors in this population.

Sources of Funding: Seoul National University Hospital & SK-Telecom Health Connect Research fund [grant no. 34-2013-0340]

Regression coefficients between all covariates and serum AMH

Log10AMH			
	B	t	p-value
Age	-0.072	-10.104	<0.001
Age at Mn	0.012	0.659	0.510
Parity	-0.027	-0.918	0.359
Log 10 25OH-D	-0.046	-0.370	0.711
BMI	0.025	1.508	0.133
WC	0.003	0.535	0.593
SBP	-0.004	-1.307	0.193
DBP	0.007	1.562	0.119
TG	-8.214E-5	-0.156	0.876
HDL-C	0.000	0.222	0.824
Glucose	0.002	1.119	0.264

Overall R2=0.331 (corrected R2=0.285)



Relationship between AMH and 25OH-D

P-17.

Estrogen Metabolism and Epigenetics

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Objective: Estrogen metabolism is a commonly under recognized aspect affecting hormonal health with vast implications on health, risk of disease and cancer. Explore our innate detoxification system to understand the key steps and determinants of estrogen metabolism that enable the detoxification, inactivation and elimination of endogenous and exogenous estrogens as well as xenoestrogens. **Design: OUTLINE FOR PRESENTATION** Understanding the three phases of innate detoxification Innate Detoxification: Phase 1 Innate Detoxification: Phase 2 Innate Detoxification: Phase 3 Steroidogenic hormonal pathway Estrogen Metabolism Genetic Determinants of Estrogen Metabolism Epigenetic Factors: Nutritional Epigenetic Factors: Environmental Exposures Impaired Estrogen Metabolism: Phenotypic Presentations Clinical Cases: Functional approach to optimize Estrogen Metabolism **Results:** The important processes of estrogen metabolism and detoxification are affected by genetic variability and epigenetic influences such as nutritional deficiencies and environmental toxic exposures. Alterations that impair the ability to inactivate and eliminate estrogen metabolites can increase risk of endometriosis, infertility, early menopause and breast cancer. **Conclusion:** Harnessing the new science of genomics and epigenetics to identifiy risks based on alterations in estrogen metabolism, it is now possible to develop personalized targets for therapeutic intervention.

Sources of Funding: none

P-18.

Variation in levels of AMH by Maya ethnicity in Campeche, Mexico

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Objective: Previous studies indicate that level of anti-Müllerian hormone (AMH) may serve as a predictor for age at menopause, but less is known about AMH levels among women in low and middle income countries. In addition, there has been limited research on AMH levels just prior to and during the menopausal transition. The purpose of this study was to examine AMH levels among women of Maya and non-Maya ancestry in the city of Campeche, Mexico. Previous studies have found an early mean age at menopause (about 44 years) among the Maya. **Design:** Women aged 40-60 (n=97) participated in semi-structured interviews, anthropometric measures, and gave blood samples for the assay of AMH. Maya/non-Maya ethnicity was determined by the last names, languages spoken, and birthplace of the woman, her parents, and her grandparents. Menopausal status was categorized into stages by the criteria of STRAW+10. An index of socioeconomic status (SES) was constructed from 10 dimensions, e.g., housing construction and access to public services. Body mass index (BMI) was computed as kg/m^2. AMH values were categorized as detectable (>0.05 ng/mL, n=36) and undetectable (<0.05 ng/mL, n=61). Logistic regression analyses were used to calculate odds ratios (OR) for the event of undetectable AMH. Of particular interest were associations between level of AMH and ethnicity, menopausal status, BMI, and history of tubal ligation. **Results:** Women were categorized as Maya (n=44), not Maya (n=39), or not able to be clearly defined (n=14). Mean BMI was high (30.1 kg/m^2, s.d. 4.7), and 55% of the women reported a history of tubal ligation. In bivariate comparisons, women with detectable levels of AMH were younger, more likely to be pre-menopausal, and not Maya. In logistic regression models, age, menopausal status, and ethnicity remained significant after controlling for BMI, smoking habits, socioeconomic status, parity, use of oral contraception, and history of tubal ligation. Maya women were almost five times as likely to have non-detectable AMH levels as non-Maya women. BMI and history of tubal ligation were not significant determinants of AMH levels. **Conclusion:** As expected, increasing age and progression through the menopausal transition were associated with declining levels of AMH. The association between Maya ethnicity and a lower likelihood of detecting AMH is consistent with previous reports of earlier ages at menopause among the Maya. Ethnic differences in levels of AMH may be genetic or related to variation in developmental environments. Currently, in this sample, Maya and non-Maya women have the same level of SES; however, this may not be true for SES during infancy or childhood. It is possible that, 40 or 50 years ago, Maya families had more nutritional and health-related stress compared to non-Maya families in Campeche which may have had an impact on ovarian reserves.

Sources of Funding: NSF Grant #BCS-1156368

GENITOURINARY/VAGINAL HEALTH POSTER PRESENTATIONS

P-19.

Is Genitourinary Syndrome of Menopause Truly a Syndrome?

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Objective: In 2014, the term genitourinary syndrome of menopause (GSM) replaced the term vulvovaginal atrophy (VVA) to describe symptoms and signs in the vulva, vagina, and lower urinary tract associated with the decrease in sex steroids in postmenopausal women. Most studies to date have studied VVA or lower urinary tract symptoms separately rather than concurrently. Our goal was to determine whether VVA and urinary symptom bother occur concurrently as a global syndrome in postmenopausal women. **Design:** In 2015, we surveyed women aged ≥55 years within 2 weeks of a well-woman visit to their primary or gynecology care provider in an integrated health system. We identified potentially eligible women using data from the electronic health record. Women received an email request to complete the survey using REDCapTM. Participants were asked about vulvar, vaginal, urinary, and sexual symptoms. Participants indicated whether the symptom was present and reported associated bother using a 4-point scale ranging from 0="Not at all" to 3="Quite a bit." Women who responded that they did not have the symptom were coded as "Not at all" on bother. We conducted a confirmatory factor analysis to determine whether a one-factor model of GSM provided adequate fit to the data, and whether a two-factor model (vulvovaginal vs urinary) improved the fit. Symptoms included in the factor analysis were 6 vaginal symptoms, 4 vulvar symptoms and 7 urinary symptoms. Because 3 of the vulvar and vaginal symptoms shared the same descriptor (dryness, itching, and soreness), we created parcels by taking the mean of the vulvar and vaginal items of each descriptor. We assessed model fit using the root mean square error of approximation (RMSEA) and the comparative fit index (CFI). Our criteria for good fit was a RMSEA of ≤.08 and a CFI of ≥.95. **Results:** Of the 5915 women we invited, 1546 agreed to participate and 1533 provided valid data. The women were 94% White with mean age of 65.4 (SD=6.6) years (ranged from 55 to 89). Overall, 41% of women reported the presence of ≥1 vaginal symptom, 25% ≥1 vulvar symptom, and 71% ≥1 urinary symptom. The one factor model had poor fit, CFI=.49, RMSEA=.18, with most loadings below .30. The two factor model improved fit, CFI=.73, RMSEA=.13, $\chi 2$ (1)=1694, p<.01, but still fit poorly. Allowing odor and discharge to become a factor, moving (vulvar) pain with urination to load as a VVA factor, and the addition of two error covariances resulted in a model with better fit; CFI=.94, RMSEA=.06, $\chi 2$ (4)= 1533, p<.01 (Table). **Conclusion:** While the term GSM encourages women and clinicians to broadly consider the consequences of estrogen deficiency to the genitourinary tissues, our results suggest that these effects do not occur simultaneously as a syndrome. The concept of GSM is valuable, but a more specific definition may be required. Further research is needed to confirm whether a 3-factor model of GSM replicates in other samples.

Sources of Funding: Pfizer Independent Grant for Learning & Change, and the North American Menopause Society

Confirmatory Factor Analysis Results of 3-Factor Model of GSM Symptom Bother

		Factors	
	Vulvovaginal Discomfort	Urinary Urgency, Frequency, Leakage	Vaginal Odor & Discharge
Loadings			
Irritation in and around the vagina	.82		
Vulvovaginal soreness or pain	.76		
Vulvar burning or stinging	.75		
Vulvovaginal itch	.66		
Vulvovaginal dryness	.64		
Pain with urination	.40		
Urine leakage associated with a feeling of urgency (a strong sensation of needing to go to the bathroom)		.85	
A sudden urge to urinate, with little or no warning		.85	
Frequent urination when you are awake		.62	
Any other urine leakage		.56	
Frequent urination at night that wakes you up		.52	
Urine leakage related to coughing, sneezing or laughing		.46	
Vaginal odor			.81
Increase in vaginal discharge			.57
Correlations of factors			
Urinary Urgency, Frequency, Leakage	.16		
Vaginal Odor & Discharge	.39	.12	

r=.35 for unique variances of frequent urination-awake and -night, r=.19 for urine leakage related to coughing, sneezing, or laughing and other urine leakage.

P-20.

Paget's Disease of the Sacrum—An Unusual Cause for Urogynecologic Pelvic Pain

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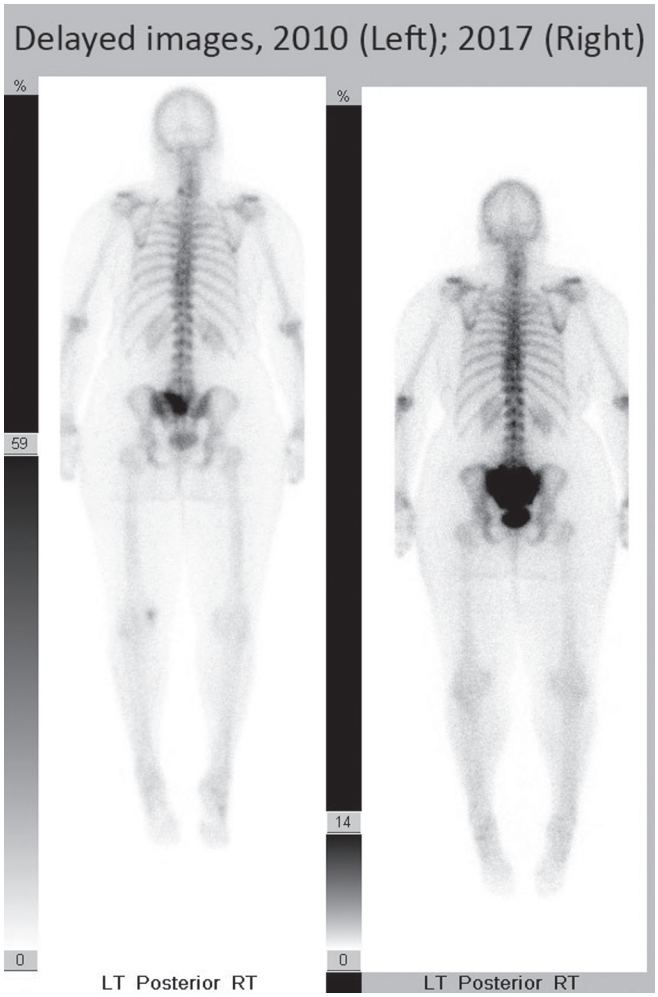
Objective: Female pelvic pain is a common, vexing condition; its etiology is often elusive. We aim to describe an unusual diagnosis that may be suggested by pelvic examination findings. **Design:** This is a case report. **Results:** This 69-year-old woman, para 2, presents with a 7-year history of chronic pelvic pain and >20-year history of fibromyalgia. She has anxiety and depression. She describes her pain as originating in the left pelvis and extending into her back, hips and legs. CT scan in 2010 showed a lytic lesion in the sacrum; bone scan confirmed this as a solitary lesion. A directed bone biopsy showed no abnormality. She was diagnosed with levator myalgia in 2011 and in 2016. Pelvic floor physical therapy worsened her pelvic pain. A spinal stimulator provided some relief. Injections of local anesthetic and steroids and two pelvic floor muscle injections of onabotulinumtoxinA provided no relief. She has been on an opiate management plan for 9 years. Over 7 years, she had over 610 visits to health care providers. In 2017, she attended a multidisciplinary clinic which focuses on musculoskeletal and urogynecologic causes for pelvic pain. CT scan showed progression of the lytic sacral lesion with deranged internal architecture. Alkaline phosphatase levels had risen from 71 (normal 33-130) in 2007 to 141 in 2013; then to 228 in 2016, with the bone isoenzyme being 72% (normal 28-66%). Collagen crosslinked N-telopeptide, a marker of bone resorption, was 220 (normal 4-64). Repeat bone scan in 2017 showed increased size of the sacral lesion (Figure). The diagnosis of Paget's disease was made, and the patient received intravenous zolendronic acid 5 mg. **Conclusion:** We posit that sacral bone pain triggered her levator muscle spasm and myalgia and we hope that alleviating this pain generator will allow physical therapy to address her myalgia. Paget's disease occurs more frequently in the postmenopausal years and often affects the pelvic bones. Skeletal disorders such as Paget's disease should be considered by menopause practitioners in the evaluation of female pelvic pain.

Sources of Funding: None



P-21.

Improvement in the genitourinary syndrome of menopause following fractional CO_2 laser treatment in post-menopausal women

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Objective: The genitourinary syndrome of menopause (GSM) is a general term encompassing the host of changes in the vaginal and vulvar surfaces that occur during menopause. Clinical presentations of GSM include vaginal burning, discharge, itching, dryness, irritation, dysuria, and dyspareunia. Fractional CO_2 laser treatment is considered the gold standard in skin resurfacing, improving appearance as the result of neoformation of collagen and elastin fibers. The vaginal epithelium can also benefit from structural changes and results in improved clinical outcomes post laser treatment. This prospective study investigated the safety and efficacy of a new fractional CO_2 laser system in treating postmenopausal women with clinical symptoms of GSM. **Design:** Twenty-eight healthy post-menopausal women (mean age 60±5.65) with one or more of the GSM-related symptoms (e.g. dryness, itching, burning, dysuria or dyspareunia) were recruited. Three treatment visits were scheduled 4 weeks apart (FemTouch by Lumenis LTD). Follow up visits were done at one, three and six months following the third laser treatment. All patients were evaluated for Vaginal Health Index Score (VHIS), Subject Assessment of VVA Symptoms and Female Sexual Function (FSFI). Procedure discomfort was assessed at the end of each treatment by the visual analogous scale (VAS). **Results:** Fractional CO2 laser treatment was effective in improving the VHIS (11.93 ± 3.82 at baseline vs. 16.43 ± 4.20 ; $p<0.05$) at the three months follow up. In addition, significant improvement in GSM symptoms (such as vaginal burning, vaginal dryness and dyspareunia) was noted at the three month follow up. For both, the VHIS and the GSM symptoms, significant improvement was already noted after the first laser treatment and this continued up to the six months follow up. The FSFI total score was improved (baseline 13.78 ± 7.70 vs 20.48 ± 11.44; $p<0.05$) at the three months follow up, as well as all the FSFI domains. Satisfaction with the laser procedure was reported by 23 women (89%) at the six months follow up and a minimal discomfort was associated with laser procedure mainly due to the insertion of the probe. **Conclusion:** Fractional CO_2 laser treatment for GSM symptoms is safe and effective procedure with clinical benefits of improving symptoms and sexual function noted already after the first laser treatment and lasted up to the six months follow up.

Sources of Funding: Lumenis LTD., Israel

P-22.

Laparoscopic sacrocolpopexy using prolene mesh in the treatment of uterine prolapse

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Objective: STUDY OBJECTIVE: The aim of this study was to evaluate the long-term results of a laparoscopic sacrocolpopexy using prolene mesh for the treatment of uterine prolapse **Design:** DESIGN: Retrospective analysis **Results:** 102 patients, from June 2005 through May 2016, underwent a laparoscopic sacral colpopexy after laparoscopic assisted vaginal hysterectomy. 48 patients had uterovaginal prolapse stage III, and 54 patients had uterovaginal prolapse stage IV. Intraoperative and postoperative complications included 8 middle sacral bleed managed by electrocauterization or suturing in the middle sacral region and 2 postoperative vaginal stump abscess requiring reoperation and removal of the mesh.. 7 patients complained pelvic pain. We treated them by analgesics. All patients were evaluated at 1 weeks and 5 weeks after surgery, and pelvic examination and vaginal sonogram was performed. They were then followed up every 6 months. Median age was 67 years (range 52–83 years). Laparoscopic sacral colpopexy was performed successfully in 94 patients. 8 patients has been converted abdominal sacral colpopexy. Median blood loss was less than 100 mL (range 50–350 mL), and the median hospital stay was 4 day (range 3-6 days). 95 patients satisfied with the surgery. There have been no cases of colpopexy graft exposure or recurrence with a follow-up of 12 months. The patient with vaginal stump abscess and graft removal has also healed with no recurrance of her prolapse. **Conclusion:** Laparoscopic sacral colpopexy using prolene mesh in the treatment of uterine prolapse is a safe and effective procedure with excellent results. Gynemesh (Ethicon, Inc.), a wide-pore polypropelene mesh seems to be an excellent graft material with low risk for graft infection or erosion.

Sources of Funding: None

P-23.

The Burden of Illness Associated with Symptomatic Vulvovaginal Atrophy (VVA): A Systematic Review

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Objective: Vulvovaginal atrophy (VVA), a feature of genitourinary syndrome of menopause (GSM), is a chronic condition associated with reduced estrogen in postmenopausal women. The purpose of this systematic literature review (SLR) was to summarize the epidemiological, clinical, humanistic, and economic burden of symptomatic VVA. **Design:** Following established PRISMA guidelines, literature searches were conducted in MEDLINE and Embase databases using indexing and free-text keywords related to VVA paired with terms for topic areas of interest; articles were limited to English publications from 1/1/2000–12/21/2016. Relevant conference abstracts from the past 2 years were also searched. Inclusion criteria were epidemiological and observational studies with ≥20 adult menopausal/postmenopausal women with symptomatic VVA (self-reported or clinically diagnosed). Outcomes of interest included epidemiological, clinical, humanistic, and economic burdens of VVA. **Results:** Searches yielded 1267 abstracts across literature databases; after removing duplicates, 1000 unique citations remained. Of these, 167 abstracts met criteria for full-text review; 44 of these publications were included, as were 5 conference abstracts. Thus, 49 publications were included in the SLR, corresponding to 37 studies (some studies were in ≥1 publication). Most studies were conducted in Europe (13) or the US (9); the remaining 15 were multinational or in other individual countries. A total of 21 studies occurred in a clinical setting and 16 were population-based. Study sample sizes ranged from 30–18,020 participants. Mean age was 53–63 y and mean time since menopause was 5.5–16.5 y, when reported. In the US, VVA prevalence estimates ranged from 37.7–45%, with higher values reported in clinical vs population-based settings; prevalence in Europe was estimated at 34–43%. Though a wide range of symptoms were reported, vaginal dryness was most common (up to 85% in the US, up to 100% in Europe), followed by dyspareunia and irritation in the US, and itching and burning in Europe. Across US studies, approximately 1/3–2/3 of women discussed their symptoms with a gynecologist. Overall, 66%–91% of European women discussed symptoms with their general practitioner, where 33%–96% did not initiate discussion of symptoms with their gynecologist. The humanistic burden of VVA was assessed primarily via study-specific questionnaires; validated questionnaires were used in fewer studies. In the US, women with symptomatic VVA reported lower health-related quality of life (HRQoL); reduced self-esteem; and a negative impact on lifestyles, intimate relationships, and sexual function. Among studies assessing HRQoL, sexual intimacy and enjoyment of sex were negatively impacted in 41%–75% of women. Mean baseline Female Sexual Function Index (FSFI) scores in one study ranged from 2–25 (scores ≤26.55 indicate dysfunction). In several European studies, low mean scores were also reported on the FSFI (range 13.7–19.6). Further, pain during sex was the most bothersome symptom among sexually active women. Healthcare resource utilization (HCRU) was the only outcome identified in this SLR related to the economic burden of VVA. In one study, US women were more likely to use lubricating gels and creams vs hormone therapy (77% vs 31%); additional US-based studies reported that 4.4%–16.9% of women used topical (vaginal) estrogen, and 6.3%–22.2% used oral or systemic estrogen to manage VVA symptoms. Women in Europe were more likely to use over-the-counter treatments than prescription (62.2% vs 13.9%). In a US study comparing women with and without VVA, 9.6% vs 6.4% ($p<0.001$) were hospitalized in a 12-month period, respectively. **Conclusion:** To date, this is the first systematic review to evaluate the burden of symptomatic VVA. Global studies suggest symptomatic VVA is prevalent among postmenopausal women and is associated with clinical and humanistic burden. Data suggest that many cases of VVA may go undiagnosed, and prevalence estimates may be lower than the reality. Limitations of this SLR include variation of diagnostic criteria and instruments in different studies, and lack of reporting in some areas.

Sources of Funding: Allergan plc

P-24.

TX-004HR Improved Moderate-to-Severe Dyspareunia and Vaginal Dryness Associated with Vulvar and Vaginal Atrophy (VVA) in Postmenopausal Women

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Objective: TX-004HR is an investigational, rapidly dissolving, vaginal softgel capsule containing a low dose of solubilized 17β-estradiol. In the 12-week, phase 3 REJOICE trial (NCT02253173), TX-004HR significantly improved percentages of superficial and parabasal cells, vaginal pH and dyspareunia compared with placebo in postmenopausal women with vulvar and vaginal atrophy (VVA) and moderate-to-severe dyspareunia. The objectives of these analyses were to assess the levels of improvement in the severity of dyspareunia and vaginal dryness and the proportion of women who achieved complete symptomatic resolution. **Design:** Postmenopausal women with VVA and moderate-to-severe dyspareunia received 4-µg, 10-µg, or 25-µg TX-004HR or placebo for 12 weeks. Dyspareunia and vaginal dryness were self-assessed using a 4-point scale (0=none; 1=mild; 2=moderate; and 3=severe); moderate and severe symptoms could change by -3 points/levels (severe to none) to +1 point/level (from moderate-to-severe). Changes from baseline in severity of dyspareunia and vaginal dryness were evaluated at week 12. Complete resolution (score of 0=none) and substantial improvements (by 2 to 3 levels) were determined for dyspareunia and vaginal dryness. Meaningful improvements (by at least 1 level) in dyspareunia and concurrent dyspareunia and vaginal dryness were also determined in women with vaginal dryness at baseline. **Results:** REJOICE's modified intent-to-treat population consisted of 747 women with moderate-to-severe dyspareunia at baseline. Of these, 733 (n=98.1%) also had mild, moderate or severe vaginal dryness, with most having moderate-to-severe vaginal dryness (n=698 [95.2%]). All doses of TX-004HR compared with placebo significantly improved dyspareunia and vaginal dryness severity from baseline to week 12 ($P<0.05$ for all). Dyspareunia severity substantially improved (by 2 to 3 levels) in 41.4-55.4% of women treated with TX-004HR vs 35.8% with placebo at week 12 ($P<0.05$ for all). Complete resolution of dyspareunia (score of 0) at week 12 was also observed in more women using TX-004HR than placebo; 10 µg and 25 µg reached statistical significance. In women with moderate-to-severe vaginal dryness at baseline (n=698), vaginal dryness severity also substantially improved in 41.3-51.1% of women receiving TX-004HR vs 30.9% with placebo at week 12 ($P<0.05$ for all). Complete resolution of vaginal dryness at week 12 was observed in significantly more women treated with TX-004HR than with placebo ($P<0.001$ for all). For women who had mild, moderate or severe vaginal dryness at baseline (n=733), significantly more had a clinically meaningful improvement (of ≥1 level) in dyspareunia with all TX-004HR doses (83.8–88.1%) compared with placebo (74.1%) from baseline to week 12 ($P<0.05$ for all). Many of these women (73-79%) treated with TX-004HR had concurrent clinically meaningful improvement of at least one level in both dyspareunia and vaginal dryness compared with 65% in the placebo group after 12 weeks ($P<0.05$ for all). **Conclusion:** TX-004HR improved both dyspareunia and vaginal dryness; the two most commonly reported VVA symptoms. Moderate-to-severe dyspareunia and vaginal dryness improved to none or mild in approximately half of postmenopausal women using TX-004HR for 12 weeks, with complete resolution occurring in more women using these low doses of estradiol compared with placebo. This was achieved with negligible to low systemic 17β-estradiol absorption.

Sources of Funding: TherapeuticsMD

P-25.

An Open-label Phase 2a Study to Evaluate the Efficacy of IZN-6NVS Cream for the Treatment of Vulvovaginal Atrophy (NCT02313545)

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Objective: Management of vulvovaginal atrophy (VVA), now encompassed by the new terminology genitourinary syndrome of menopause (GSM), remains an unsolved therapeutic challenge for women unable or unwilling to be treated with estrogen. IZN-6NVS is a proprietary blend of botanical extracts (*Echinacea purpurea*, *Sambucus nigra* and *Centella asiatica*) in a cream formulation that has demonstrated the capacity to reduce inflammation and promote tissue repair in inflamed tissue in preclinical in vitro studies, and in clinical trials for gingival inflammation and non-healing diabetic foot ulcers. Conceptually, this blend of botanical extracts would also have the potential to reduce mucosal inflammation and promote tissue repair of the vaginal mucosa, and thereby fulfill a critical unmet medical need for a non-hormonal alternative to estrogen for the treatment of VVA. IZN-6NVS facilitates wound healing by reducing production of pro-inflammatory mediators such as TNF, IL-1b, and PGE2 and by promoting fibroblast production of IL-11, collagen deposition and production of TIMP-3. The objective of this Phase 2a open label study was to determine the efficacy of IZN-6NVS Cream for treatment of VVA. Efficacy was measured using a quality of life questionnaire that assessed VVA symptom severity and the impact on sexual function, and by measuring changes in vaginal pH and the vaginal maturation index (VMI). **Design:** Patients were

screened using a VVA symptom questionnaire, vaginal pH, transvaginal ultrasound and VMI. Entry criteria included the subjective experience of at least one symptom of VVA to a moderate or severe extent. A total of 21 patients with VVA were assigned to treatment with IZN-6NVS Cream based on symptom severity and pH >/= 4.5 after baseline screening. Patients completed the VVA symptom questionnaire and were examined after two weeks of daily treatment with the vaginal cream, and after an additional 4 weeks of treatment 3 times/week. At the follow-up visit 6 weeks after end of treatment, patients again completed the questionnaire, vaginal assessments and ultrasound. Patients were asked to avoid sexual activity during the first two weeks of treatment. Dyspareunia and avoidance of sexual activity due to pain were assessed in the questionnaire at baseline, at the 6 week treatment visit and at the follow-up visit. **Results:** Subjective improvement was measured by a visual-analog scale (VAS) in response to the question "to what extent do the vaginal symptoms disturb you on a daily basis?" and by a composite score of the severity of individual VVA symptoms (dryness, discomfort/irritation, itching, discharge, and malodor). Improvement in the symptoms of VVA compared to baseline was evident in the VAS and the composite score at two weeks of treatment ($p<0.0001$), and continued to improve throughout the 6 week treatment period ($p<0.0001$). At the 6 week follow-up visit, despite no treatment for 6 weeks, the VVA symptoms remained significantly improved as compared to baseline ($p=0.0012$ for the VAS, and $p<0.0001$ for the composite vaginal symptom score). The composite score of sexual symptoms significantly improved after 6 weeks of treatment ($p=0.0037$) and at the follow-up visit ($p=0.001$). Treatment did not significantly impact upon the vaginal pH, however the VMI demonstrated a significant shift to more mature cell types that was evident at the end of treatment visit ($p=0.0057$). No effect was noted on endometrial thickness as assessed by transvaginal ultrasound. **Conclusion:** The results indicate that treatment with IZN-6NVS Cream significantly improved the symptoms of VVA, and impacted upon the maturation of the vaginal epithelium. With further clinical testing, IZN-6NVS Cream may offer an excellent alternative to currently available hormonal therapies.

Sources of Funding: Study sponsored by Izun Pharmaceuticals Corp, USA

P-26.

REJOICE Trial: TX-004HR Consistently Improved Vaginal Dryness in Subgroups of Postmenopausal Women with Vulvar and Vaginal Atrophy (VVA) and Dyspareunia

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Objective: TX-004HR is an investigational, muco-adhesive, rapidly dissolving, vaginal softgel capsule containing low doses of solubilized 17β-estradiol (4 μg, 10 μg, and 25 μg). In the phase 3 REJOICE trial (NCT02253173), TX-004HR significantly reduced vaginal dryness in postmenopausal women with VVA and concurrent moderate-to-severe dyspareunia as early as 2 weeks (10 μg and 25 μg; 6 weeks 4 μg) and maintained this improvement up to 12 weeks with negligible to very low systemic absorption. The objective of these analyses was to assess the effects of patient characteristics on reductions in vaginal dryness with TX-004HR. **Design:** The randomized, double-blind, placebo-controlled, multicenter REJOICE trial was powered to evaluate TX-004HR in all randomized, postmenopausal women (40-75 years) with VVA and the most bothersome symptom of moderate-to-severe dyspareunia. Descriptive analyses of subgroups based on patients' age (56 years or less, 57-61 years, 62 years or greater), BMI (24 kg/m^2 or less, 25-28 kg/m^2, 29 kg/m^2 or greater), uterine status, prior pregnancy, and number of vaginal births were performed on the change in vaginal dryness severity from baseline to week 12 with TX-004HR. **Results:** Baseline differences in the percentages of parabasal cells and vaginal pH varied significantly between the age subgroups, with both being greater among women aged ≥62 years relative to the youngest group. Significant baseline differences were also observed between BMI subgroups with higher percentages of parabasal cells and vaginal pH in women with the lowest BMI compared with women with higher BMI. Over 12 weeks, 4-μg, 10-μg, and 25-μg TX-004HR reduced vaginal dryness from baseline in all subgroups, with several subgroups having significantly greater improvement compared with placebo (Table). **Conclusion:** This study demonstrated that TX-004HR reduced vaginal dryness concurrent with moderate-to-severe dyspareunia, regardless of patient's age, BMI, uterine status, prior pregnancy, and number of vaginal births, even though the power for analyzing subgroups was low. All three TX-004HR doses demonstrated a robust, consistent effect for reducing vaginal dryness compared with placebo with negligible to very low systemic absorption.

Sources of Funding: TherapeuticsMD

Change in vaginal dryness severity from baseline to week 12 based on patient demographics and reproductive factors.

	Placebo (n=187)		TX-004HR 4 μg (n=186)		TX-004HR 10 μg (n=188)		TX-004HR 25 μg (n=186)	
	n	LS Mean±SE	n	LS Mean±SE	n	LS Mean±SE	n	LS Mean±SE
Age, years								
≤ 56	56	-0.97±0.12	52	**-1.40±0.12** [a]	67	**-1.69±0.11** [d]	70	**-1.66±0.11** [d]
57-61	58	-1.05±0.11	58	-1.06±0.11	55	**-1.47±0.12** [b]	49	**-1.53±0.12** [b]
≥ 62	60	-0.88±0.12	61	**-1.33±0.11** [b]	51	-1.21±0.13	57	**-1.22±0.12** [a]
BMI, kg/m^2								
≤ 24	61	-0.74±0.11	68	**-1.25±0.11** [c]	63	**-1.49±0.11** [d]	56	**-1.48±0.12** [d]
25-28	61	-1.15±0.12	47	-1.31±0.13	57	-1.39±0.12	65	-1.41±0.11
≥ 29	52	-1.03±0.12	56	-1.27±0.12	53	**-1.52±0.12** [b]	55	**-1.54±0.12** [b]
Uterine Status								
Intact	108	-0.96±0.08	93	**-1.40±0.09** [c]	95	**-1.43±0.09** [c]	95	**-1.52±0.09** [d]
Non-intact	66	-0.97±0.11	78	-1.12±0.10	78	**-1.51±0.10** [c]	81	**-1.42±0.10** [b]
Prior Pregnancy								
n = 0	19	-0.89±0.20	22	-1.17±0.19	22	1.29±0.19	16	-1.25±0.22
n ≥ 1	155	-0.98±0.07	149	**-1.29±0.07** [b]	151	**-1.49±0.07** [d]	160	**-1.49±0.07** [d]
Vaginal Births								
n = 0	30	-0.94±0.16	25	-1.40±0.18	33	**-1.50±0.15** [a]	34	**-1.58±0.15** [b]
n ≥ 1	125	-0.99±0.08	124	**-1.27±0.08** [a]	118	**-1.49±0.08** [d]	126	**-1.47±0.08** [d]

LS: least squares; SE: standard error.
[a]$P<0.05$; [b]$P<0.01$; [c]$P<0.001$; [d]$P<0.0001$ vs placebo.

P-27.

FDA 510 K Medical Clearance for Vaginal Lubricants: Issues and Answers

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Objective: Vaginal moisturizers and lubricants have become under greater scrutiny with the consumer awareness campaign that has focused on additives and potential chemical irritants or carcinogens in these products. Acid base status, osmolality, and chemical ingredients are now of paramount concern for the female consumer particularly those who suffer from genitourinary syndrome of menopause (GSM) or chronic medical conditions that impact the delicate vaginal mucosal lining. For a personal lubricant to be distributed and marketed within the United States, the FDA requires all products to have a Class II Medical Device 510(k) clearance. This 510(k) is a premarket submission, made directly to the FDA that has sufficient evidence to demonstrate that the lubricant/device is at least as safe and effective, that is, substantially equivalent, to a legally marketed device that is not subject to premarket approval. 510(k) clearance means that a company has done its due research as well as its due diligence with testing the product according to FDA guidelines and specifications. There is a disconnect between achieved 510(k) clearance and marketing materials on consumer friendly home pages. We conducted this survey to investigate whether a) consumers were aware if the lubricant they were using was 510(k) Cleared Device and b) to investigate if companies were actively marketing this clearance on their home consumer web-internet page. **Design:** We reviewed the official FDA site and retrieved information concerning 50 lubricants (30 water based; 20 silicone based products). In addition, also preformed a systematic review of these products websites and surveyed whether or not they illustrated the concept of 510(k)/FDA clearance on their home page. If the product did not have its own business website then we reviewed amazon.com, adamandeve.com, cheaplubes.com. In addition, we surveyed 50 consecutive patients who were seen in a sexual medicine clinic by a specialized sexuality gynecologist were asked if they were aware if their personal lubricant was 510(k) cleared by the FDA as well as if they were aware what this clearance specifically meant **Results:** A total of 50 lubricants (30 water based; 20 silicone based products) were assessed for this project. 50% (15/30) water based lubricants were deemed to be 510(k) cleared by the FDA whereas only 14% of those mentioned this designation on their website. 50% of the silicone lubes (10/20) were 510(k) Cleared and only 5% of them mentioned their clearance on their websites. An average of 3 minutes (1-5 minutes) was spent per lubricant evaluation. The home page as well all other tabs were assessed. Common terms found on the lubricant websites included: medical grade, all natural, organic, vegan friendly, no chemicals, non-irritating, medically approved, high quality formulated, infused with natural products, doctor approved. Fifty women, who are current users of lubricant with a mean age 48 (range 28 to 77) were asked if they were aware if their lubricant was 510(k) cleared by the FDA, and if they knew the meaning of 510(k) clearance. 96% of the women were not aware if their lubricant was 510(k) cleared, 4% or 2 patients felt that their lubricant was not 510(k) cleared. 96% of women (n=48) nor did have any concept of what the 510(k) clearance specified. One women felt that 510K(k) clearance meant "uncovered by insurance" another felt it meant that " there were no adverse effects" from the lubricant. **Conclusion:** Most women are not aware of the 510(k) designation nor are they familiar with its significance and meaning. Companies are remiss in educating women and men about this important safety, efficacy and product designation and should include a more detailed discussion of the 510(k) clearance process on their web pages.

Sources of Funding: None

P-28.

Acceptability and Tolerability of an Intravaginal Ring (IVR) in Postmenopausal Women

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Objective: Medications can be administered through various routes. The vaginal route can be advantageous due to proximity to target tissue, rich pelvic vascularity, and obviating both first pass hepatic metabolism and potential gastrointestinal side effects. Ideally, a vaginal drug delivery product should be easily self-administered and offer long-term controlled drug release. An ethylene vinyl acetate copolymer IVR drug delivery system was developed, 2 rings with 54 mm outer diameter and cross-sectional diameters of 4 mm and 6 mm were tested. While the IVR will eventually be used to provide long-term controlled release of a medicinal product, the use of unmedicated IVRs in this study eliminated potential confounding with respect to outcomes. Assessments included ease of use and tolerability during a 7-day period, general acceptability, and human factors. **Design:** Following informed consent, subjects were randomized (ratio 1:1) to open-label 4 mm or 6 mm IVR. Baseline pelvic examination (with speculum) and dipstick urinalysis were performed. Following comprehension assessment of instructions for use, subjects who correctly inserted, removed, and reinserted the IVR at the clinic were sent home to wear the IVR continuously for 7 days and to complete a daily diary. Subjects returned to the site for post IVR use pelvic examination with visualization of the vagina and cervix and dipstick urinalysis. A Tolerability and Acceptability Questionnaire was completed, evaluating ease of use, adverse events, comfort, and acceptability. **Results:** Forty-four healthy female post-menopausal women, average age 58.2 years, BMI 29.4 kg/m^2 were randomized. No subject reported previous IVR use. There were no meaningful differences between the groups with respect to baseline characteristics. Thirty-two subjects (72.7%) successfully followed instructions for correct insertion, removal, and re-insertion of the IVR, suggesting that more training might be needed for some before they can insert an IVR correctly. Twelve (28%) were discontinued from the study due to inability to correctly insert or remove IVR. Higher BMI was associated with inability to correctly insert and remove the IVR. Ninety percent of subjects responding reported that if a medicine that they take now could be administered through an intravaginal ring and they would only need to change the ring once every week, it would make their use of medications easier. When subjects were asked about their preferred interval for changing the ring, 37.5% reported once-weekly, 21.9% reported every two weeks, and 40.6% reported monthly. Further, 87.6% of subjects reported that they would be very likely or somewhat likely to use an IVR for a condition/disease related to Women's Health, while 81.3% of subjects responding reported they would be very likely or somewhat likely to use an IVR for a condition or disease that was NOT related to Women's Health (eg, to treat hypertension or diabetes). A total of 96.9% of subjects strongly agreed or agreed the IVR was comfortable when worn and that the IVR was convenient to use, while 93.7% agreed that the IVR works with their lifestyle. Ring expulsion occurred in 1 of 32 (3.1%) evaluable subjects (subject had history of surgical vaginal prolapse); 5 subjects reported mild and transient vaginal symptoms (eg, irritation) over the diary period. Use of the IVR did not result in untoward findings on pelvic examination or on vaginal integrity characteristics. **Conclusion:** This study demonstrated that an IVR drug delivery system in post-menopausal women is practical and the device itself would not result in tolerability issues that might limit its use. IVR sizing did not appear to be associated with any differences in outcomes. The IVR was well-accepted by an IVR treatment naïve population. The high acceptability and tolerability as observed offers the promise and potential that the vaginal route of administration can enhance adherence to chronic drug therapy for women and improve health outcomes.

Sources of Funding: Juniper Pharmaceuticals, Inc

P-29.

Safety of nonhormonal vaginal lubricants and moisturizers

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Objective: Nonhormonal vaginal lubricants and moisturizers are recommended as a first-line therapy for symptomatic vulvovaginal atrophy related to menopause. These products are effective in relieving pain and dryness and are good alternatives to vaginal estrogen products. In 2013, The North American Menopause Society (NAMS) released a position statement on the management of symptomatic vulvovaginal atrophy. At the time of the statement, NAMS recognized that there were few published clinical trials on the efficacy of nonhormonal vaginal lubricants and moisturizers. Vaginal lubricants and moisturizers are widely available over the counter yet there are few published articles that investigate the safety of these products. The FDA clears vaginal moisturizers and lubricants as medical devices and lists them in the 510(k) database. The purpose of this abstract aims to identify the published safety data and reported adverse effects of vaginal lubricant and vaginal moisturizers since the last NAMS position statement. **Design:** The literature search was conducted exclusively through PubMed using combinations of the key words vaginal, lubricant, moisturizer, safety, and cytotoxicity from 2013 to present. There were no other filters placed on the search. Articles that solely evaluated vaginal suppositories, vaginal lubricant use in diabetes, and vaginal lubricant effect on condom use were excluded from the results. Additionally, one article that discussed a lubricant unavailable in the United States was excluded. From the remaining results, only articles that discussed safety and/or cytotoxicity of vaginal moisturizers and lubricants were included. A separate search was conducted using the FDA Manufacturer and User Facility Device Experience (MAUDE) database from 2013 to present. The search included all lubricant categories for patient and personal use. **Results:** The PubMed search yielded four articles published between 2013 and 2016 that met our criteria. All articles included use of vaginal lubricants and moisturizers for postmenopausal vulvovaginal atrophy. One study was an in vitro study, one was a randomized control trial, and two were review articles. The results included data on vaginal lubricant and moisturizer pH, osmolality, cytotoxicity, vital signs, reported side effects, and laboratory examinations of the vaginal microecosystem. Overall, the results demonstrate several common vaginal lubricants and moisturizers that have a pH outside the normal vaginal pH range and an osmolality outside the range recommended by the World Health Organization. However, there were very few reported side effects beyond local vaginal irritation. The FDA MAUDE database search was limited to seventy total results. The most commonly reported adverse effects were irritation and burning. **Conclusion:** Nonhormonal vaginal moisturizers and lubricants are widely used as successful first-line therapies for vaginal symptoms in women with vulvovaginal atrophy. There are well established testing and reporting methods in place for these products. However, there are limited published studies since the 2013 NAMS statement that relate to safety for this wide variety of products. Patient and provider education regarding the benefits and potential risks will improve awareness of these readily available management options for symptomatic vulvovaginal atrophy and will potentially improve the symptomatology at the population health level.

Sources of Funding: None

P-30.

Concerns with Long-Term Estrogen Exposure, Inconsistent Treatment Use, and Reduced Quality of Life in Postmenopausal Women With Symptoms of Vulvar and Vaginal Atrophy

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Objective: Vulvar and vaginal atrophy (VVA)—a feature of genitourinary syndrome of menopause (GSM)—is a chronic medical condition caused by decreased levels of estrogen, which may impact women's quality of life. Postmenopausal women with VVA have a variety of symptoms, including vaginal dryness, irritation, and dyspareunia. These symptoms often impact sexual function and may affect other activities of daily life. This study builds on current knowledge of women's experiences with and perceptions of VVA symptoms by clarifying the journey of patients with VVA as well as understanding the burden and impact of VVA on women's lives (physiological, quality of life, self-image, and relationships). The study also aims to understand the benefits and limitations of current agents, unmet needs, and preferences for treatment. **Design:** An online survey was conducted among women in the US aged 45-75 from GfK's KnowledgePanel®, a 56,000-member probability-selected internet panel projectable to the overall US population. The sample was augmented by users of prescription treatments from online opt-in consumer panels. A total of 3,031 postmenopausal women completed the survey, including women who self-reported as having been diagnosed with VVA and women who are undiagnosed but have experienced symptoms of VVA. **Results:** Survey results indicated that VVA interferes with many aspects of women's lives (somewhat/very interfering) including enjoyment of sex (71%), sexual spontaneity (64%), and ability to be intimate (61%), even more so among women who have had an intimate partner in the past year. Quality of life was also affected, including sleep (33%), temperament (31%), and enjoyment of life (28%), more so among women who have not had a sexual partner in the past year. Despite having experienced a variety of symptoms, only 42% of postmenopausal women with VVA are currently using treatments: over-the-counter (OTC) only (30%), OTC + prescription (5%), and prescription only (7%); treatments included both estrogen and non-estrogen-based options. Of the VVA symptoms experienced, the most common were dryness (61%), pain associated with sexual intercourse (52%), and irritation (31%). Half of all study participants voiced safety concerns regarding long-term use of products containing estrogen, even if dosage of estrogen was small. Furthermore, 32% are very/extremely concerned (score of 6 or 7 on a 7-pt scale), and 42% are somewhat concerned (score of 3, 4, or 5 on a 7-pt scale) about the amount of estrogen in vaginal prescription treatments. The level of concern is highest among women who have never used prescription treatments (36% [score of 6 or 7 on a 7-pt scale]). Overall, 34% of study participants agree/strongly agreed they are interested in trying a treatment with the lowest amount of estrogen. Concerns about long-term safety and hormone exposure, along with inconvenience, were the top reasons why women discontinued using prescription treatments. Among users of prescription creams, only 45% of women reported using the treatments consistently. **Conclusion:** Due to safety concerns about estrogen use and hormone exposure, postmenopausal women with symptomatic VVA may discontinue treatments or use them inconsistently, which can lead to under-treatment. This may result in chronic vaginal health complaints—such as dryness and dyspareunia—which have the potential to negatively impact sexual health, intimacy, and overall quality of life. Evidence-based package labeling may address these concerns and might lead to higher utilization of low-dose estrogen.

Sources of Funding: Allergan plc

P-31.

Efficacy of vaginal misoprostol before diagnostic hysteroscopy in postmenopausal women: a randomized double-blind placebo-controlled clinical trial

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Objective: To evaluate the efficacy and safety of prior use of misoprostol or placebo for postmenopausal women undergoing diagnostic hysteroscopy. **Design:** Randomized double-blind placebo-controlled clinical trial of 158 postmenopausal women who received either 200μg of misoprostol or placebo by vaginal route before diagnostic hysteroscopy. Indication for the exam, duration of the procedure, need for additional cervical dilatation, pain intensity, complications and adverse effects were studied. **Results:** Abnormal bleeding and endometrial thickening were the most common indications of the exam in both groups (p=0.4974). The duration of hysteroscopy was similar in both groups (p=0.43). Additional cervical dilatation was needed in 11 women in misoprostol group *versus* 9 in placebo group (p=0.6323). In both groups, there was no significant difference in pain intensity and complications. Adverse effects were reported by 25.3% of women using misoprostol and were vaginal bleeding in 11.3%, cramping in 12.6% and diarrhea in 2.5% while one reported both vaginal bleeding and cramping. In the placebo group, only 2.5% of women presented adverse effects (p=0.0001). **Conclusion:** Misoprostol does not reduce duration of the procedure, need for additional cervical dilatation, pain intensity and causes more adverse effects when used in postmenopausal women prior diagnostic hysteroscopy.

Sources of Funding: Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP), Brazil.

P-32.

Intravaginal testosterone provides efficacy and safety for postmenopausal vaginal atrophy treatment: a randomized controlled trial.

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Objective: To evaluate the metabolic, hormonal and endometrial safety after the use of estrogen, testosterone and polyacrylic acid used for the treatment of vaginal atrophy in postmenopausal women and compared to a control group. **Design:** This was a randomized controlled clinical trial on 80 postmenopausal women between 40 and 70 years of age with follow-up at the Menopause Clinic of the CAISM, State University of Campinas. The women were randomized to treatment with topical vaginal estrogen, testosterone, polyacrylic acid, or water lubricant alone, three times a week for a period of 12 weeks from November 2011 to January 2013. In all four groups, data were collected at baseline and after 6 and 12 weeks of use of the respective medication. To examine the hormonal and metabolic safety, it was measured the endogenous levels of FSH, LH, 17-estradiol, estrone, androstenedione, DHEA, DHEA sulphate, SHBG and metabolites: total cholesterol, HDL, LDL, triglycerides, AST, ALT, GGT. Transvaginal sonography was performed to evaluate endometrial thickness at baseline and after 6 and 12 weeks of treatment. **Results:** Topical estrogen, testosterone and polyacrylic acid in comparison with lubricant after 12 weeks of treatment showed no significant laboratory and endometrial alteration. Treatment with vaginal estrogen presented with elevation of serum estradiol values after 12 weeks in only 3 women. There were no statistically significant differences in endometrial thickness between the four groups at baseline and after 6 and 12 weeks of treatment. **Conclusion:** The vaginal use of testosterone and estrogen for treatment of post menopause vaginal atrophy demonstrated hormonal, metabolic and endometrial safety when compared to the lubricant.

Sources of Funding: None

P-33.

Research and Evidence on Lubrication Toxicity

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Objective: To present the research and the latest evidence on the safety, efficacy, and acceptability of personal lubricants and reached a common understanding of the science behind the products (osmolality, ingredients, and formulations) and the physiological effects of different types of lubricants. This presentation will educate the medical community about the importance of recommending iso-osmatic lubricant formulas for their patients, especially patients with compromised vaginal thinning walls. **Design:** Abstract: Most of the widely used vaginal lubricants in the U.S. and Europe are strongly hyper-osmolal, formulated with high concentrations of glycerol, propylene glycol, polyquaternary compounds or other ingredients that make these lubricants 4 to 30 times the osmolality of healthy vaginal fluid. Hyper-osmolal formulations have been shown to cause marked toxicity to human colorectal epithelia in vivo, and significantly increase vaginal transmission of genital herpes infections in the mouse/HSV model. They also cause toxicity to explants of vaginal epithelia, to cultured vaginal epithelial cells, and increase susceptibility to HIV in target cells in cell cultures. Here, we report that the osmolality of healthy vaginal fluid is 370±40 mOsm/Kg, and that a well-characterized three-dimensional human vaginal epithelium tissue model demonstrated that vaginal lubricants with osmolality greater than 4 times that of vaginal fluid (>1500 mOsm/Kg) cause disruption of epithelial barrier properties and structural damage. Four out of four such lubricants caused disruption in the parabasal and basal layers of cells as observed by histological analysis and reduced barrier integrity as measured by trans-epithelial electrical resistance (TEER). No epithelial damage to these layers was observed for hypo- and iso-osmolal lubricants (N=4) with osmolality of <400 mOsm/Kg. The results confirm extensive reports of safety concerns of hyper-osmolal lubricants and the usefulness of in vitro reconstructed vaginal tissue models for assessing safety of lubricants. The results strongly suggest that the regulatory agencies review the toxic effects of currently marketed vaginal lubricants. **Results:** The results confirm extensive reports of safety concerns of hyper-osmolal lubricants and the usefulness of in vitro reconstructed vaginal tissue models for assessing safety of lubricants. The results strongly suggest that the regulatory agencies review the toxic effects of currently marketed vaginal lubricants. Fortunately, the FDA is highly encouraging a validation study to determine whether three-dimensional human vaginal epithelium tissue models can replace the rabbit vaginal irritation test in the assessment of personal lubricant biocompatibility. **Conclusion:** Sexual lubricants have been associated in several studies with increased risk of episodes of BV (Hassan, Ellender et al. 2007, Hassan, Lavreys et al. 2007, McClelland, Richardson et al. 2008, Brotman, Ravel et al. 2010, Marrazzo, Thomas et al. 2010, Brown, Hess et al. 2013), and most sexual lubricants are hyper-osmolal with respect to the osmolality of healthy vaginal fluids (370 mOsmol/Kg as reported here). Hyper-osmolal vaginal lubricants disrupted the barrier functions of the basal and parabasal layers and shedding of the apical layers. These results clearly suggest osmolality-induced toxic effects may be the mechanism by which use of vaginal lubricants is associated with the risk of bacterial vaginosis (Marrazzo JM, Thomas KK et al. 2010) and may increase susceptibility to sexually transmitted infections. Both of these hypotheses are in need of clinical testing. The broad range of results to date on the toxicity of hyper-osmolal lubricants, should encourage manufactures of vaginal lubricants to devise iso- or hypo- osmolal formulations that do not disrupt the barrier properties of the vaginal epithelium. Moreover, the regulatory agencies should insist on toxicity testing in more appropriate, human- relevant models than the rabbit vagina. A study to validate the use of reconstructed human vaginal epithelium models, including EpiVaginal, as a replacement for the rabbit vaginal irritation test is currently being organized for this purpose.

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P-34.

Vaginal symptoms and microbioty in postmenopausal women

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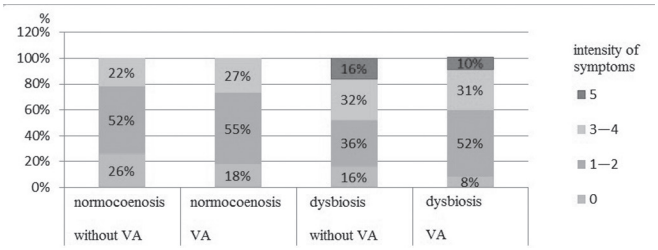
Objective: To evaluate the relationship between the state of the vaginal microbiota in postmenopausal women with vaginal symptoms. **Design:** 136 postmenopausal women with postmenopause duration from 1 to 20 years. Methods of the study included questioning of patients, assessment of the intensity of the symptoms (D. Barlow),cytologic screening of vaginal paries with further assessment of maturation index (MI) (MI = 0.5 x number of intermediate cells(%)+1 x number of surface cells(%),(N - ≥65) PCR diagnosis of vaginal flora. Exclusion criteria: sexually transmitted infections, use of vaginal systemic and/or local MGT within the last 6 months, systemic and local antibiotic therapy within 1 month prior to the start of the study. Comparisons between groups were carried out using the Mann-Whitney U test.In the study it was found that total bacterial mass(TBM) in postmenopausal women was $10^{6.5\ (5.0\text{-}7.5)}$ GE/sample. The postmenopausal women's microflora of the vagina was represented by *Lactobacillus spp*.($10^{5.0(0.0\text{-}7.3)}$GE/sample);, *Streptococcus spp.*,*Prevotella bivia/Porphyromonas spp.*,*Eubacterium spp.*,*Megasphaera spp./Veillonella spp./Dialister spp.*,*Mobiluncus spp./Corynebacterium*. **Results:** The essential group (group1) comprised 84 patients (62%) who had diagnosis "Vulvovaginal atrophy", the control group (group2)- 84 (62%) of patients accordingly. Dryness to be the most frequent complaint mentioned by 63 % of respondents (tab.1).For women with VVA, the predominance of obligate-anaerobic conditionally pathogenic microflora (CPM), progressing with increasing duration of menopause, is characteristic. At half of women without VA lactobacilli prevailed even 15 years after the onset of menopause.Since there are no criteria for a "normal" vaginal flora for postmenopausal women, we used a classification for women of reproductive age, depending on the percentage of lactobacilli in the TBM and 2 groups were formed: 1 - *Lactobacillus spp.*>80% - conditionally "normocenosis", 2-*Lactobacillus spp.*≤80% conditionally vaginal flora.We compared the intensity of vaginal symptoms with the D. Barlow's 5-point system. Patients with "normocoenosis" had fewer complaints compared with patients with "dysbiosis" We observed symptoms with the greatest intensity exclusively in patients with "dysbiosis" (Pic.1). We carried out Pearson's correlation analysis between the intensity of all symptoms, the lactobacilli fraction of TBM and the maturation index. The highest dependence was observed between the intensity of symptoms and lactobacilli fractions from TBM (part of lactobacilli: R^2=0.224 **,p=0.008,maturation index: R^2 = -0.075,p=0.388). **Conclusion:** The intensity of vaginal symptoms mainly depends on the state of the vaginal flora, and not on the presence or absence of VVA.

Sources of Funding: None

Distribution of vaginal symptoms in observation groups

Indicators	Group № 1 (n=84)	Group № 2 (n=52)	p-level	Groups № 1 и № 2 (n=136)
Pruritus	38 (45,2%)	20 (38,5%)	0,439	58 (42,6%)
had stinging and pin sensation	43 (51,2%)	21 (40,4%)	0,222	64 (47,1%)
Pain	23 (27,4%)	9 (17,3%)	0,180	32 (23,5%)
Irritation	32 (38,1%)	20 (35,1%)	0,966	52 (38,2%)
Dryness	58 (69,0%)	28 (53,8%)	0,075	86 (63,2%)
discharges from reproductive tracts	18 (21,4%)	14 (26,9%)	0,465	32 (23,5%)
discharges from reproductive tracts have foul smell	21 (25,0%)	14 (26,9%)	0,804	35 (25,7%)



Pic. 1 Distribution of intensity of symptoms in the observation groups by D. Barlow

P-35.

Improvement in Quality of Life (QoL) and satisfaction rate with a new disposable home-use vaginal device in the management of Pelvic Organ Prolapse (POP) in women

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Objective: A new disposable vaginal device for the management of POP was developed. The device is inserted vaginally in small dimensions within an applicator, by the user herself, at her home environment. Within the vagina the device opens to become a ring (various sizes, up to 91 mm). Following insertion, the applicator is removed and discarded and the device may remain in the vagina for up to seven days, when the user pulls a string and the device collapses and is comfortably removed from the vagina in small dimensions, for disposal. The user may insert the next device immediately or later, at her will. This part of the study evaluated overall improvement in QoL and satisfaction while using this new vaginal device. **Design:** Study was prospective, multi clinic, single arm, open label, hypothesis driven and statistically powered, home use performance study. Following screening and size fitting (visits 1-3) subjects were requested to use the device during 28-45 days, through visit 5. During that time subjects were allowed to use as many devices as they wished, for a period of 1-7 days each. Two validated pelvic floor QoL questionnaires (modified PFDI-20 & PFIQ-7) were used, comparing results from visits 1 & 5. Four almost identical device models were tested sequentially along 3 identical parts of the study (parts A, B, C), where Part C was the pivotal study, with the final finished version of the device. Statistical analysis was conducted on results from the pivotal study (part C) and from All Parts (A, B & C). **Results:** 52 subjects completed the study in 3 clinics. 24 completed one part of the study, 14 completed 2 parts, and 14 completed 3 parts, altogether 94 usage cycles in which 1431 devices were used over 3530 usage days (parts A, B & C). 41/52 subjects completed the pivotal study (part C, 41 usage cycles) using 591 devices over 1556 usage days. Age range was 33.2-80.3 (mean 60.4), mean BMI was 25.3, and 80.9% were postmenopausal. At study end, while using the device, in the All Parts group, 90 subjects (97.8%) had complete reduction of the prolapse while 2 subjects (2.2%) had POP-Q stage 1 prolapse. 100% of subjects had at least 2 POP-Q stages reduction and 97% of subjects with stage 3 prolapse (64/66) had 3 stages reduction. Subjective assessment was carried out using an author compiled symptom scoring system which showed improvement of the mean total score from 29 to 2.7 (of 100) ($p<0.0001$). For the PFDI-20 & PFIQ-7 QoL modified questionnaires, a decrease in score implies improvement in QoL. Table 1 shows mean scores for each of the questionnaires, before and while using the device, for both Part C and All Parts. Statistical analysis shows significant difference in the scores with all p-values <0.0001. Table 2 shows percentage of subjects who scored specific questions as "having no complaint at all", with significant increase while using the device. McNemar's tests for each item separately showed statistically significant differences for all items. Satisfaction was assessed using an author compiled questionnaire at study end. Complaints, specific to the use of the device, with emphasis on ability to insert and remove the device (to exclude hand movement limitation), were recorded in details. Responses to the satisfaction questionnaire were highly favorable with scores of "not at all" given by 77.7%-100% of women in All Parts group and between 87.8% and 100% in Part C. **Conclusion:** The new disposable, self-use POP vaginal device was found to substantially increase QoL, as scored with validated pelvic floor questionnaires, with very high satisfaction rate through all phases of usage. The device was suitable for elderly women as well, who quite easily self-inserted and removed the device.

Sources of Funding: ConTIPI Medical Ltd funded the study

Table 1

Modified PFDI-20 Mean Score				Modified PFIQ-7 Mean Score			
All Parts		Part C		All Parts		Part C	
Pre study	Study end	Pre study	Study end	Pre study	Study end	Pre study	Study end
33.6	5.1	33.6	2.1	24.9	0.7	23.7	0.2
p<0.0001		p<0.0001		p<0.0001		p<0.0001	

Table 2

PFDI-20 percentage of subjects who had no complaints in specific items (scored them as "not at all")				PFIQ-7 percentage of subjects who had no complaints in specific items (scored them as "not at all")			
All Parts		Part C		All Parts		Part C	
Pre study	Study end	Pre study	Study end	Pre study	Study end	Pre study	Study end
5.3-76.6	80.6-98.9	7.3-70.7	87.8-100	33-81.9	95.7-100	36.6-78	97.6-100
p<0.05 for all items		p<0.004 for all items		p<0.0001 for all items		p<0.007 for all items	

HEALTH SERVICES AND SURVEYS POSTER PRESENTATIONS

P-36.

Clinical, demographic, and physician-related factors associated with women's adherence to Premarin® (conjugated estrogens) Vaginal Cream: findings from a large, US based, observational, real-world database

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Objective: Vulvar and vaginal atrophy (VVA), a common condition in post-menopausal women, is associated with vaginal dryness, irritation or itching, dysuria, and dyspareunia, which may negatively impact not only sexual functioning, but also health-related quality of life. Premarin® (conjugated estrogens) Vaginal Cream (PVC) is indicated for the treatment of atrophic vaginitis and kraurosis vulvae and moderate to severe dyspareunia, a symptom of vulvar and vaginal atrophy, due to menopause. The aim of this study was to identify clinical, demographic, and physician-related factors associated with women's adherence to Premarin® Vaginal Cream, to aid prescribers in identifying women at risk of low adherence. **Design:** The study took an observational, retrospective approach using real-world data. The data were obtained from the Decision Resources Group Real-World Evidence repository, linking medical claims, prescription claims and electronic health records to provide longitudinal patient-level data covering the majority of the US healthcare system. The inclusion criteria specified women aged ≥18 years with at least one pharmacy prescription claim for PVC between March 1, 2014 and December 31, 2015. Each patient was classified into one of three adherence groups, based on their use of PVC within the study period: adherent repeat users (>1 prescription, with ≤8 months between first and second prescription), one-time users (only 1 prescription, with no refill), and non-adherent repeat users (>1 prescription, with >8 months between first and second prescription). To classify each patient correctly, for any woman with a prescription of PVC between March 1, 2014 and December 31, 2015, prior and subsequent prescriptions of PVC were also searched within the time windows July 1, 2013 - February 28, 2014 and January 1, 2016 - August, 31 2016. Seventeen potential explanatory variables were extracted and a regression-based approach was taken to identify associated factors. Univariate multinomial logistic regression models were fitted for each explanatory variable, and those with a statistically significant ($p<0.05$) effect on adherence were assessed in a multivariate approach. Stepwise backwards selection was then performed, sequentially removing covariates with p values >0.1 to yield the final model. **Results:** Data from 140,118 women with a prescription of PVC were available for analysis; women were characterized as adherent repeat users, one time users and non-adherent repeat users. The mean age of women across groups was 64.4 years. Adherent and non-adherent repeat users (65.1 and 65.4 years, respectively) were significantly older than one time users (63.3 years)($p<0.01$). The final regression model included age, region, number of prior VVA diagnoses (identified by ICD-9 code 627.3 or ICD-10 code N95.2), number of prior dyspareunia diagnoses (identified by ICD-9 code 625.0 or ICD-10 code N94.1), number of inpatient visits, number of co-medications, health plan membership, sex of prescribing physician and years' experience of prescribing physician as significant independent predictors ($p<0.05$) of adherence group membership. The probability of being a one-time user compared to an adherent repeat user decreased with: increasing patient age ($p<0.001$), increasing number of prior VVA and/or dyspareunia diagnoses ($p<0.001$ and $p=0.031$, respectively), increasing number of co-medications ($p<0.001$) and increasing number of prescribing physician's years of experience ($p<0.001$); the probability decreased when a prescription was issued by a male physician ($p<0.001$). **Conclusion:** This study based on a large, real-world data database has identified clinical, demographic, and physician-related characteristics associated with adherence to Premarin® Vaginal Cream. Understanding factors with the potential to impact a woman's adherence to PVC treatment may enable prescribers to better identify those patients at risk of low adherence and develop strategies to proactively address their individual needs.

Sources of Funding: Pfizer Inc.

P-37.

Women- and health practitioner-generated technological solutions to support women experiencing menopause

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Objective: To understand the technological needs of women and health practitioners to support women experiencing menopause. **Design:** This cross-sectional, descriptive study used participatory design (PD), a focus-group like method that involves potential end-users early in the design of technologies. Two 4.5-hour PD sessions were held with women in Seattle, WA. Three facilitators guided women through: Creating affinity diagrams of positive/negative aspects of menopause; thinking expansively about technologies to address aspects; using crafting materials (markers, color paper, pipecleaners, etc.) to describe their technology ideas; and sharing ideas. Three 0.5-2.5-hour PD sessions were held in the western USA with health practitioners who support women through menopause and included most tasks completed by the women during their sessions. Sessions were audio-recorded and transcribed. **Results:** Women in the two sessions

(n=4, 4) varied in education (less than high school to college graduate) and self-identified ethnicity (e.g., Black, Asian, South American, White). Health practitioners in the three sessions (n=10, 3, 5) included Nurse Practitioners, Medical Doctors, and complementary health and wellness practitioners. Women suggested technological solutions to support prediction of symptoms, provide guidance on what to do to manage/prevent symptoms, and provide treatment. Practitioners suggested solutions to track and manage symptoms. Examples of women's and practitioners' convergent ideas for technological solutions included wearable devices (e.g., watch, bracelet, patch) that monitor physiology and behavior, alert women when a symptom will occur soon, provide suggestions on how to stop/minimize symptoms, and/or provide treatments (e.g., engage cooling mechanisms). **Conclusion:** Innovative technological solutions have the potential to support women experiencing symptoms during the menopausal transition. These include integrating predictive analytics, artificial intelligence, and decision-support systems with sensors and other devices. These solutions could meet the needs of women experiencing menopause, including anticipating symptom onset and engaging in behaviors or with devices to temper symptoms and the disruptions they cause in their daily lives.

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P-38.

The Many Menopauses: Searching the cognitive research literature for menopause types

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Objective: Clinicians are becoming more concerned with understanding the different types of menopause - and with good reason, since for close to a quarter of women, menopause will occur either earlier than the normative age range (primary ovarian insufficiency or early menopause) and/or as a result of the removal of the ovaries (induced menopause). In 2014, the North American Menopause Society (NAMS) released clinical guidelines for best practice in treating health risks related to the menopause transition, acknowledging that there is no single pathway to the end of menses and emphasizing individualised treatment. Taking the type of menopause into consideration takes on added importance in light of recent evidence suggesting that early or induced menopause increases the risk for dementia. Given the potential for different cognitive outcomes due to menopause types, it is important that current clinical research on menopause and cognition distinguish between types. The aim of this project was to determine whether research on menopause and cognition published since the NAMS guidelines considers different menopause types. Publications from 2016 were reviewed. **Design:** MEDLINE, EMBASE, and PsychINFO were searched using keywords and MESH terms for menopause and cognition, limiting to studies published between January 1, 2016 and January 25, 2017. Reviews were excluded. Any analytic paper which reported a cognitive measure in a menopausal human population was included. Two independent reviewers analysed whether or not the different types of menopause were distinguished during study design, reporting, and/or analysis. Distinction between the types of menopause was defined by four categories: no distinction, demographic distinction (type reported but not analysed), partial distinction (multiple types included; some but not all types analysed) and full distinction (different types factored into analysis or recruitment of only one type). **Results:** A total of 232 journal articles were found. After removing duplicates, 215 were examined in more detail based on title and abstract. Of these, 157 were excluded because they did not study cognition or humans. The remaining 61 were read in full: 5 articles were further excluded, leaving 56 for full assessment. Distinction was distributed as follows: no distinction in 55% (31 articles), demographic distinction in 14% (8), partial distinction in 22% (12), and complete distinction in 9% (5). Importantly, the few studies that separated and compared menopause types found worse visual and semantic memory in women with induced menopause compared to natural menopause, dependent on age at surgery. **Conclusion:** This review revealed that, while clinical guidelines advocate for distinguishing between the many menopauses in clinical decision making, few clinical research studies on cognition have taken up these guidelines. Understanding the effects of menopause on cognition and subsequent treatment can depend on the type of menopause, thus this lack of uptake in the research community effects the relevance of findings to clinical practice. Furthermore, when menopause types are distinguished, the differing cognitive outcomes of each type are underscored. Current menopause research on cognition must incorporate the NAMS guidelines to produce the best clinical evidence, which in turn will be able to inform best clinical practice for treating all women.

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P-39.

Development and Implementation of a Menopause Specialty Clinic: Improving the Quality of Menopause Education in an Academic OB/GYN Residency Program

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Objective: Previous research has shown that US OB/GYN residents are lacking in menopause training. Our objective was to develop and implement a menopause specialty clinic and accompanying curriculum for University of North Carolina OB/GYN residents. Secondary objectives included conducting a baseline needs assessment to evaluate resident confidence and knowledge in management of menopause, and assessment of the efficacy of the intervention via a menopause knowledge assessment tool. **Design:** Using the Kern model of curriculum development, a menopause curriculum was created. The menopause clinic was integrated as a single session per week into the PGY3 ambulatory care rotation (7 weeks total). A web based knowledge and confidence survey (KCS) was emailed to all UNC OB/GYN residents in May 2016. Results of this were used to develop a targeted 6 session curriculum addressing core topics (Diagnosis and Physiology of menopause, Hormone Therapy, Non-hormonal treatments and Selective Estrogen Receptor Modulators, Osteoporosis, Vulvar and Genitourinary disease, Menopausal Preventative Health). The curriculum included independent review of information prior to clinic, 30 minutes of teaching and case vignette review in clinic with attending and experiential learning in clinic. Prior to curriculum implementation, a 16 item knowledge assessment tool (KAT) was administered to PGY3 residents. In April 2017, one year after curriculum implementation, the KAT and 28 item KCS were again administered to the PGY3 class. **Results:** 23 residents (PGY1-4) completed baseline KCS. Average knowledge rating was 3.08 and confidence was 2.89 on a scale of 1-5 (1=poor, 3= barely sufficient, 5= no need for further learning). The lowest scoring areas were HRT, SERMs, Non-hormonal pharmacologic management, Osteoporosis treatment and prophylaxis, and Vulvar dystrophy. Menopause clinic was started in July 2016. Six PGY3 residents participated in clinic, completing between 1-5 sessions. No resident completed the entire curriculum. Mean PGY3 score on the KAT were 9.8 and 10.8 pre and post-curriculum. KCS ratings also improved with mean knowledge rating increasing by 0.41 and mean confidence rating increasing by 0.5. Eighty-five percent (6/7) of PGY3 residents felt that participation in Menopause clinic helped them to be more comfortable with management of menopausal patients. **Conclusion:** A clinic based Menopause curriculum can be successfully implemented into a busy academic residency program. Participation resulted in observed improvement in resident subjective menopause knowledge and confidence ratings, as well as objective knowledge. These results are not significant and limited due to small sample size. The positive response to this piloted curriculum has supported its continuation as a component of resident education and has prompted similar efforts in other subspecialty areas.

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P-40.

2016 NAMS Annual Meeting May Have a Significant Impact on Hormone Therapy Prescribing Patterns

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Objective: Due to lack of definitive recommendations and evidence based data for complex and controversial case scenarios, hormone therapy (HT) prescription patterns among providers may vary significantly. While prescription patterns can be affected by multiple factors, the objective of the current study was to assess whether the 2016 NAMS Annual Meeting, where the draft of the NAMS 2017 HT Position Statement focused on appropriate dosing, regimen, duration, and route of administration was presented and discussed, had any impact on providers HT prescribing behaviors. **Design:** An anonymous survey with 11 case scenarios was sent to all NAMS members before and after the 2016 NAMS Annual Meeting. Pre and post-meeting responses were pooled into a single cohort, for those who responded to both surveys (matched population), only post-meeting survey responses were included in the cohort. Controversial questions were first identified in this cohort if 30%-70% of responders answered "Yes" to the question. Paired responses to those controversial questions were further compared between pre-meeting and post-meeting surveys, in matched population who either attended the NAMS Annual Meeting (study arm) or did not (control arm), to assess impact of the 2016 NAMS Annual Meeting on HT prescription patterns. McNemar's test was applied to analyze paired responses using SAS statistical software, with $p<0.05$ being considered statistically significant. **Results:** A total of 1,786 NAMS members were surveyed before and after the 2016 NAMS Annual Meeting, 234 (13%) completed pre-meeting survey, 166 (9%) completed post-meeting survey, and 52 completed both surveys. Of the 52, 27 attended the meeting and 25 did not. Pooled cohort contains 348 responses with a 20% response rate, and 74% responses came from providers with more than 20 years in practice. Six complex case scenarios were identified and reexamined in the study and control arm, respectively. In the study arm, significant changes towards being more likely to prescribe HT in appropriate cases were noted in 4 out of 6 cases, however, significant change in HT use was not seen in any of 6 complex cases in the control arm. For example, for a 45 year old woman with a history of MI and migraine with severe vasomotor symptoms (VMS) not relieved with nonpharmacological therapy, 12% on the pre-meeting vs. 35% on the post-meeting survey considered prescribing HT (P=0.014). For a 40 year old woman with severe VMS, who is BRCA1+ and underwent prophylactic bilateral salpingooophorectomy with uterine conservation 6 months ago, 72% at pre-meeting vs. 88% at post-meeting considered prescribing HT (P=0.04). **Conclusion:** After the 2016 NAMS Annual Meeting where the NAMS 2017 HT Position Statement was presented and discussed, for those challenging and complex clinical situations (history of MI, DVT, BRCA1, ER+ Breast Cancer), significantly more practitioners changed their prescription patterns toward being more likely to prescribe HT in appropriate cases.

Sources of Funding: None

P-41.

Trends of breast cancer in Korean women and the mortality rate of breast cancer and cardiovascular disease in postmenopausal women in Korea

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Objective: To describe the trend of breast cancer in Korean women and reveal the relatively low risk comparing the mortality of breast cancer with mortality of cardiovascular disease in postmenopausal women. **Design:** Using data of Ministry of Health & Welfare and Cancer registry of National Cancer Cancer, we analyzed the incidence rate, survival rate and mortality of breast cancer. Also we assessed the mortality of cardiovascular disease in postmenopausal women in Korea. **Results:** Breast cancer has become one of the most common cancer in Korean women in recent years, with continuously increased incidence rates attributed to westernized life styles. However, epidemiologic evidence suggests that Korean women have still lower incidence of breast cancer than Caucasian women. Age-standardized incidence rate of breast cancer in Korea was 52.1/100,000, Whereas US was 92.9/100,000 in 2012. The age distribution of breast cancer incidence in Korea showed marked difference compared to western countries. The age-specific incidence rate of breast cancer increased with age in western countries. On the other hand, the most frequent age group in Korea was the fourth decade and there was no significant difference between premenopausal women and postmenopausal women (47.9% vs 52.1%). The five-year survival rate of breast cancer in Korea was 83.2 percent in 1996-2000, but increased by 5 percent in 2001-2005 to 88.5 percent. In Recent years (2008-2012), It recorded a steady growth rate of 91.3 percent, and recorded the highest level of survival in the world. Also, age-standardized mortality was 6.1 per 100,000 in 2012 and it ranked in the lowest among the OECD countries. Meanwhile, cardiovascular disease remained the leading cause of death in Korea, with crude mortality rates for women exceeding those of men since 1992, although CVD mortality rate have been decreasing steadily over the past 3 decades. The cause of highest mortality rate in women over 45 years old was cardiovascular disease (172.7/100,000), and the second cause was cancer-related mortality (114.4/100,000) in 2015 in Korea. Particularly, breast cancer showed a low mortality rate with 9.2/100,000 among other cancers. **Conclusion:** The incidence rate of breast cancer in Korean women was increased continuously, but the incidence and mortality rate was lower compared with western countries. In perspective of mortality rate, cardiovascular disease has higher risk than breast cancer in postmenopausal women in Korea.

Sources of Funding: None

P-42.

Knowledge about the climacteric syndrome and use of hormone therapy among Brazilian women – a population-based household survey.

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Objective: To evaluate knowledge about the climacteric syndrome, prevalence of hormone therapy use among Brazilian women and the factors associated with its use. **Design:** A cross-sectional population-based household survey of 749 women aged between 45 to 60 years was conducted in the metropolitan region of Campinas/Brazil. The dependent variable was current or previous use of menopausal hormone therapy. The independent variables were sociodemographic data, health-related problems and knowledge about the climacteric syndrome assessed using a score developed with a questionnaire on various aspects of the menopause. Statistical analysis was carried out by $\chi 2$ test and Poisson regression. **Results:** The mean age of women was 52.5 (± 4.4) years. Regarding the menopausal status, 16% were premenopausal, 16% perimenopausal and 68% postmenopausal. Of all women included, 19.5% reported current or previous use of menopausal hormone therapy. In the final multivariate Poisson regression, being postmenopausal (PR 2.76; 95%CI 1.74-4.38), receive information about menopause from medical and health services (PR 2.73; 95%CI 1.91-3.89), having a higher knowledge about menopause (PR 1.12; 95%CI 1.05-1.19), history of bilateral oophorectomy (PR 2.18; 95%CI 1.49-3.17), and need to stop working due to hot flushes (PR 1.44; 95%CI 1.03-2.01) were associated with a higher frequency of use of menopausal hormone therapy. **Conclusion:** The level of knowledge about the climacteric syndrome and how this knowledge is acquired are associated with the prevalence of use of hormone therapy. Educational actions promoted by healthcare systems can increase the use of menopausal hormone therapy in women who have indications for treatment.

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P-43.

In People Living with HIV (PLWH), Symptom Burden is Worse in Women and Excaberated by Menopause: Results from an On-line Survey

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Objective: Objective: We examined the influence of self-reported sex and menstrual bleeding status on symptom profiles and burden in people living with HIV (PLWH) using combination antriretroviral therapy (cART) for the following reasons: * although cART has allowed PLWH to live well past midlife with a chronic illness, they are more likely to be affected by comorbid conditions such as diabetes and cardiovascular disease (Cook et al, 2011) * the prevalence of HIV in women has escalated in the US such that sex and gender differences in disease progression, complications and treatment outcomes are emerging, with women now facing a 3-year higher mortality rate vs men with HIV (CDC Report, 2015) * PLWH report fatigue, depression, poor sleep and difficulty concentrating as the most frequent and debilitating HIV symptoms, but much of the research is dated, restricted to single site studies, based on old symptom indices and focused mostly on men (The Antiretroviral Therapy Cohort C. 2008). **Design:** A cross-sectional study was conducted that included both a sex-based analysis of previously reported symptom characteristics of 1373 respondents to an anonymous, online survey (Schnall et al, under review) and a follow-up, on-line survey of menstrual bleeding status in eligible females from the respondent pool. Eligibility for the parent survey included 18 yrs of age or older, a diagnosis of HIV and treated with combination antiretroviral therapy (cART), experiencing symptoms in the last 4 weeks, not currently pregnant, resident of the US, able to read and respond electronically in English, and willing to participate in an online survey. A modified version of the Memorial Symptom Assessment scale was used to measure 27 HIV-associated symptoms (yes/no) and burden (difficulty with day-to-day activites in the last 30 days) on a scale from 0-no impact to 4 - very much. (Auizerat et al, 2009). For the sex-based analysis, only data were used from respondents with concordant sex at birth and current gender identity. For the follow-up female survey, respondents had to be willing to be re-contacted and not currently pregnant. Descriptive statistics, bivariate correlations and linear mixed models were used to characterize the role of sex and menstrual status as predictors of HIV symptom burden in PLWH. **Results:** There were 957 males and 385 females who reported concordant sex at birth and gender identity.Females were more likely to be Black (46% vs 20%, p=<0.01), heterosexual (91% vs 4%, p =<.01), and with less education and lower income (p = <0.01) compared to males. Although younger on average (47±11 yrs vs 50±12 yrs, p=<0.01), females were heavier (BMI = 33±9 vs 28±5, p = <0.01) and reported a longer duration of HIV infection (16±9 yrs vs 14±10yrs, p = 0.05) and more comorbid conditions (1.06±1 vs 0.86±0.9, p = <0.01). In both men and women, fatigue, muscle aches/pains and depression were the most common of the 27 HIV symptoms assessed, but in females, mean symptom burden scores were higher (worse) for fatigue, muscle aches/pains, shortness of breath, nausea and thirst, after adjusting for covariates (p = ≤0.05). In the follow-up online female survey (n = 222), those reporting amenorrhea due to natural menopause or hysterectomy (= menopause group; n = 104) did not differ on BMI or by race, sexual orientation, income/eduation or smoking features compared to those still menstruating at least once in the past 11 months (= menstruating group; n = 118), but the menopause group was older (54±7 vs 39±9 yrs, p=<.01) with longer duration of HIV (18±8 vs 13±9 yrs, p = <0.1) and more comorbid conditions (1.3±1 vs .65±.9, p = <.01). After adjusting for these covariates, the estimate of difference in burden scores remained higher for fatigue (p= 0.03), difficulty falling asleep (p = .04) and muscle aches and pains (p = .05) in the menopause group. **Conclusion:** Two of the most common symptoms in PLWH – fatigue and muscle aches/pains - invoke additional burden in women compared to men. This symptom burden may be exacerbated once menses ceases, suggesting a greater role for menopause management in women with HIV.

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P-44.

Crowding of behavioral risk factors for chronic non-communicable diseases in climacteric women

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Objective: The decrease of serum estrogen levels during menopause is associated with increased risk for some diseases. In this age group, there is a recognized trend towards a higher incidence of chronic non-communicable diseases (CNCD). Certain behaviors considered harmful may act synergistically for the occurrence of such diseases. In this study, the goal was to verify the crowding prevalence of behavioral risk factors for CNCD in a sample of climacteric women assisted by Primary Health Care teams in a medium-sized city in Southeastern Brazil. **Design:** A cross-sectional, analytical, population-based study carried out in 2014 and 2015, with a random sample of climacteric women registered in 73 health units of the town's Primary Health Care teams. Behavioral risk factors for CNCD and factors associated with crowding (three or more) of risk factors were investigated. The independent variables evaluated were: age, color/race, marital status, schooling, family income, premenopausal or postmenopausal stage, body mass index, intensity of climacteric symptoms, sleep disturbances (Pittsburg Scale), Anxiety and Depression (Beck Inventory). The association between variables was analyzed using the chi-square test and the variables that were associated up to the level of 20% were analyzed jointly by means of Poisson regression, with robust variance, being assumed in the final model only the associated variables up to the level of 5%. **Results:** We evaluated 810 women aged between 40 and 65 years, being 27.4% premenopausal, 29.8% perimenopausal and 42.8% postmenopausal. The prevalence of risky behaviors for CNCD was 83.5% for habitual intake of meat with apparent fat; 1.9% for high intake of salt in meals; 64.4% for low fruit intake; 11.4% for high intake of soft drinks; 87.2% for sedentarism; 7.3% for alcohol abuse and 9.6% for smoking. The prevalence of crowding of behavioral risk factors for CNCD was 33.7%. Demographic and socioeconomic variables were not associated with a higher prevalence of crowding of risk factors for CNCD. After multiple analysis, the variables that remained associated with a higher prevalence of crowding of risk factors were: anxiety (PR = 1.47, CI 95% = 1.04-2.06), depression (PR = 1.95, CI 95% = 1.25-3.04) and premenopausal stage (PR = 1.62, CI 95% = 1.17-2.25). **Conclusion:** Climacteric women with higher scores for anxiety and depression and those in the premenopausal stage present higher prevalence of crowding of behavioral risk factors for CNCD. These characteristics should serve as a warning for professionals and health managers, considering that the synergy of risk factors increases the probability of the CNCD emergence. Educational interventions for this group are necessary and can help reduce the risks for climacteric women and costs for health services.

P-45.

Hormone Therapy: An Assessment of OB/GYN Resident Knowledge and An Effective Case-based, Self-learning Module

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Objective: OB/GYNs are often presented with women who are experiencing bothersome vasomotor symptoms at the onset of menopause. The comfort level of providers with prescribing hormone therapy (HT) and alternative treatments vary, depending on degree of exposure to HT and alternative therapies during residency training. However, research is lacking on feelings of preparedness or comfort concerning issues and problems related to the topic of HT amongst OB/GYN residents. The objective of this study is to assess resident knowledge of HT and their comfort level with prescribing HT, and to evaluate the effectiveness of a computerized case-based teaching tool. **Design:** A pre-test survey using SurveyMonkey was sent out to all 15 OB/GYN residents at a university-affiliated hospital evaluating resident knowledge, comfort level, and practice habits regarding HT. After voluntary completion of a pre-test, computer-based teaching materials including case-based presentations and targeted educational information, based on the NAMS 2017 Hormone Therapy Position Statement, were sent out for the participants to complete independently. Two weeks later, a post-test was administered, evaluating resident knowledge and the effectiveness of the teaching tool. Analysis was performed using SAS and McNemar's test to compare pre and post-test responses. **Results:** 14 residents completed the survey. At pre-test, all respondents reported that they rarely (n=9) or never (n= 5) prescribe HT and none of the 14 respondents felt completely comfortable prescribing HT. Reasons identified for not feeling comfortable included lack of adequate education (78.6%), limited patients with this complaint (64.3%), unsure about different options, routes, and dosages (85.7%), unsure about relative risks and contraindications (57.1%) and unsure about special populations (71.4%). Of participants, 42% reported that they do not always routinely screen perimenopausal and postmenopausal patients for menopaus symptoms. The post-test revealed 100% of participants felt our educational materials were an effective tool to teach information on HT with 8 respondents saying it was very effective (57.1%), 6 somewhat effective (42.9%) and 0 respondents reporting that it was not effective. Of respondents, 100% felt they are more likely to screen perimenopausal and postmenopausal patients for menopause symptoms after completing this module. Of residents, 85.7% replied they felt more comfortable prescribing HT after this module. In addition, 100% of residents reported that they think rotating in a clinical setting where HT is prescribed frequently (like a midlife clinic) would make them feel more comfortable prescribing HT. In regard to resident knowledge, there was improvement in the number of responders who answered questions correctly. Comparing pre and post-test data, significantly more residents correctly identified symptomatic otherwise healthy younger women as candidates for HT and identified the best primary therapy (64% pre-test, 100% post-test, p=0.03). More residents recognized all the various options including newer therapies for treating menopause symptoms, including conjugated estrogens plus bazedoxifene, after our module (7% pre-test vs 57% post-test, p=0.01). There was higher recognition that HT is an option for primary bone or fracture protection and that a higher systemic dose may be needed in a patient who enters early natural menopause or has POI (7% pretest, 57% post-test, p=0.01). **Conclusion:** The study demonstrates that there is a need and desire among residents for further education on HT management. Our study suggests that our educational tool is effective in increasing the knowledge and comfort level with HT among our residents. To validate our findings, two additional sites have been identified and are in progress to utilize the pre and post-test and educational module. If similar results are found, we plan to use this module and the results from the testing to craft an educational package for residency programs across the country.

Sources of Funding: None

P-46.

Perspectives and Decision Making about Menopausal Therapies in Women Who Had an Early Surgical Menopause: A Focus Group Study

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Objective: To explore the process of decision-making about menopausal treatments in women who have had an early surgical menopause (<50 years). **Design:** We used a descriptive qualitative research design. Women who had an early surgical menopause were purposefully selected from the Edmonton Menopause Clinics. Focus groups were held, each with 6 to 9 participants and lasted for 1.5 hours. All sessions were audio-recorded and transcribed verbatim. Data was analysed using qualitative content analysis. **Results:** We conducted five focus groups from Jun 30 to Jul 21, 2016 (N = 37). One-third of the women had the surgery within the last 5 years. Women mainly performed the surgery for benign ovarian conditions such as endometriosis and ovarian cysts (75%), and/or cancer prevention (32%). Almost all women had a concurrent hysterectomy (97%) and were current users of hormone therapy (HT) (70%), and close to half were taking anti-depressants with or without HT. Four main themes identified were: "perceptions of surgical menopause", "perceptions of support", "being my own advocate", and "concept of adequate support". Women described their menopausal experience as sudden, severe and worse than their expectations. They shared unique perceptions of inadequate support received before and during their menopausal experience, such as lack of preparation and adequate information, lack of guidance and engagement in decision-making and lack of social support. Women had to "be their own advocates" and seek support from within the health care system and outside, to cope with their health issues. To make an informed decision about treatments post-surgery, women expressed a need to learn more about the symptoms of surgical menopause, treatment options, resources, avenues for support and stories of similar experiences, preferably before the surgery. **Conclusion:** Despite being severely impacted by the experience, women who have had an early surgical menopause have a strong sense of ownership towards their menopausal health and treatment decisions; although, at times, they may not have the adequate support to act upon this feeling. Patient decision aids can serve as an ideal source of support and guidance to these women as it will offer them with the education, resources, and skills to manage decision-making.

Sources of Funding: The study was supported by the Women's and Children Health Research Institute (WCHRI) clinical seed grant.

HORMONE THERAPY POSTER PRESENTATIONS

P-47.

Efficacy and Safety of Transdermal Estrogen and Intermittent Progesterone: A Retrospective Study

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Objective: Women with an intact uterus using menopausal hormone therapy (MHT) require progestogens to reduce the risk of endometrial cancer. Epidemiological data suggests that the progestogen component of MHT may be responsible for the increased risk of breast cancer, as observed in the combination arm of the 2002 Women's Health Initiative. We therefore propose an optimal regimen that would confer a satisfactory safety profile for both the breast and the endometrium while maintaining the vascular benefits of transdermal therapy, the relief of vasomotor symptoms and the promotion of bone health. The proposed therapy is a low-dose transdermal estrogen combined with intermittent progesterone. The objective of this study is to assess patient satisfaction, bleeding profile, endometrial safety and breast effects on this regimen. **Design:** This was a retrospective cohort study reviewing outcomes of women using a regimen of transdermal estrogen and intermittent progesterone. Following approval from our institutional review ethics board, we reviewed the charts of postmenopausal women in a specialized menopause clinic. All included participants were using transdermal 17-B estradiol 37.5 or 25 micrograms through a twice-weekly patch or daily gel as well as intermittent micronized progesterone 100 mg 3 to 5 times per week. **Results:** The health records of 237 patients were reviewed. The mean age of menopause of participants was 49 years old with the average start of MHT at 52. The majority were on 37.5 micrograms of transdermal estrogen (68.3%) and micronized progesterone 5 times per week (59.1%). Oral administration of progesterone (89.9%) was the preferred route. After at least one year of follow-up, 39.7% of women required an adjustment in the dose or form of estrogen they were on, and 31.6% required an adjustment in the dose or form of progestogen. Breakthrough bleeding occurred in 11.0% of patients. All available endometrial biopsies were negative for hyperplasia or endometrial cancer. Endometrial lining was measured in 66.2% of women after the start of MHT and averaged 4.2 ± 2.3 mm. Median endometrial lining measurements for women on patches of 37.5 and 25 micrograms were 4.02 and 4.74 mm; the distributions in the two groups did not differ significantly (Mann-Whitney $U = 796.5$, n1 =67, n2=31, P>0.05 two-tailed). None of the mammograms performed at least one year after the start of MHT showed evidence of lesions suspicious for malignancy. **Conclusion:** The use of 37.5 mcg or 25 mcg of transdermal 17-B estradiol and micronized progesterone 5 times per week is an acceptable regimen for postmenopausal women. The safety profile for the endometrium and the breast were maintained. It remains that prescribing MHT is an art and adjustments are frequently required for individual needs.

Sources of Funding: None

P-48.

Changes in endometrial thickness after conversion from tamoxifen to aromatase inhibitor in postmenopausal breast cancer patients

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Objective: The effect of postmenopausal tamoxifen treatment appears to be its proliferative effect on the endometrium, provoking a high rate of endometrial pathologies including hyperplasia, polyps, carcinoma and malignant mixed mesodermal tumors. Lately, tamoxifen treatment is being challenged by third-generation aromatase inhibitors (AIs) that have demonstrated improved disease-free survival in a variety of adjuvant settings for early breast cancer. AIs inhibit aromatase enzyme function and thus, block the conversion of androgens to estrogens, leading to suppressed estrogen synthesis. Thus, it may be speculated that AIs might prevent endometrial thickening and the formation of endometrial pathologies in postmenopausal breast cancer patients. The purpose of this study is to estimate the effect of AIs on endometrial thickness in postmenopausal breast cancer patients previously having long-term tamoxifen treatment. **Design:** Twenty-six postmenopausal breast cancer patients who had received adjuvant tamoxifen 20mg/daily were replaced by AIs. The last endometrial thickness measurement taken before stopping of tamoxifen treatment was prospectively compared with further transvaginal ultrasonography evaluations, performed following aromatase inhibitors up to 3 years.

Results: The mean duration of tamoxifen treatment before AIs was 29.6±17.9months. The last mean endometrial thickness was 5.5±3.3mm before stopping of tamoxifen treatment decreased to a mean value of 2.9±1.1mm after 6 months since replacement treatment with AIs (P<0.001). A second ultrasonographic measurement performed in 25 patients after 12 months since replacement treatment with AIs showed further decline of mean endometrial thickness to 2.6±1.0mm (P<0.001). Also, there was a significant decrease in endometrial thickness after 24 months since replacement treatment with AIs compared with the last mean endometrial thickness before stopping of tamoxifen treatment in 18 patients (P<0.001). After 36 months since replacement treatment with AIs, there was a significant decrease in endometrial thickness compared with the last mean endometrial thickness before stopping of tamoxifen treatment in 11 patients (P=0.001). **Conclusion:** Conversion from tamoxifen AIs treatment in postmenopausal breast cancer patients may lead to a reduction in endometrial thickness.
Sources of Funding: None

P-49.

Hormone Replacement Therapy in Adult Turner 's Syndrome Patients: A Retrospective Analysis

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Objective: Turner's Syndrome (TS) is defined as complete or partial monosomy of an X chromosome in phenotypically female patients, often accompanied by gonadal dysgenesis and short stature. These patients are prescribed hormone therapy (HT) to achieve secondary sex characteristics and growth potential. After achieving their final height and induction of secondary sexual characteristics, these patients are often discharged to the community. There is limited data on their long-term outcomes as it relates to premature menopause. We aim to understand the challenges associated with HT use in this population, especially given the paucity of literature. Through a retrospective chart review of TS patients seen in an adult multidisicplinary (gynecology/endocrinology) clinic, our objective is to describe the medical comorbidities, HT regimens, and longterm outcomes in adult TS patients as they approach mid-life. **Design:** A retrospective chart review was performed on all patients attending a multidisciplinary gynecology and endocrinology adult TS clinic at an academic ambulatory hospital. Subjects included adult women with karyotype-proven complete or partial monosomy X who had been exposed to sufficient exogenous or endogneous sex steroids to develop secondary sexual characteristics and menses. Charts from 2012-2015 were reviewed for demographics, evidence of medical comorbidities, HT regimens, and experiences related to HT. **Results:** There were 82 women with TS included. The median age of the cohort was 38.5 years (range 21-71 years). Almost half the cohort (N=35) were older than 40 years. Available karyotypes showed 41.4% had complete monosomy X and 32.9% partial. The median age for starting HT was 16. Ten (12.2%) of women had stopped HT, 4 of whom were over 50 years of age. The average age for stopping HT was 38.9y. In the duration of the study, 32 women (39%) took a single regimen of HT, whereas 10 (12.2%) took no HT. Forty women (48.8%) had their HT regimen changed at least once. The most common HT regimen was oral estradiol with oral progesterone, taken by 24 (29.2%) followed by extended use oral contraceptives (n=16, 19.5%). Of the oral estradiol/progesterone combinations, the most common regimen taken by eight women (9.8%) was estradiol 2mg with cyclic progesterone 200mg. There were three pregnancies resulting in three live births, one of which was conceived with donor egg. Chronic medical conditions were identified in 79% of the cohort, including 26 (31.7%) with reduced bone density, and 57 (69.5%) with structural or functional cardiovascular disease. There were no breast cancers. **Conclusion:** The adult TS population has unique challenges with regard to HT beyond pubertal induction. It is unclear until what age this cohort should be treated given the high prevalence of cardiovascular morbidity. Common reasons to change HT regimens in this population include abnormal bleeding, headaches, and decreasing estrogen exposure with aging. Further studies are needed to best determine the optimal HT regimen in older women with TS.
Sources of Funding: None

P-50.

Pellet vs. FDA approved Hormonal Therapy in postmenopausal women: Preliminary safety findings from a retrospective cohort study

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Objective: Pellet Therapy (PT) is a non-FDA approved Hormonal Therapy (HT) method of treating menopausal symptoms with limited research on safety and efficacy. The objective of this study was to assess the safety of PT vs. FDA approved HT (FDA-HT). **Design:** A retrospective cohort study was designed to compare two cohorts, women treated with PT and women treated with FDA-HT. A total of 11,862 postmenopausal women were identified through the Reading Hospital Electronic Medical Record System by pharmacy coding, including 10,801 in FDA-HT and 1,061 in PT (estradiol and/or testosterone pellets). Of 11,862 women, 337 were randomly selected for further investigation. Data on patient histories, demographics, initial symptoms (e.g. hot flash, vaginal dryness, decreased libido), side effects (e.g. abnormal uterine bleeding [AUB], mood swing, anxiety, breast tenderness, change in hair pattern, acne, weight gain), and treatment duration were extracted from medical records. Chi-Square test was applied to assess the difference in incidence of side effects between the two cohorts, and a logistic regression model was fit with covariates, including age at the initiation of HT, Body Mass Index, duration of HT treatment, HT type (FDA-HT vs. PT), to assess risk profile of individual covariate. All statistical analyses were conducted with SAS 9.3 at the 0.05 significance level. **Results:** Women on PT (n=183) were significantly younger than those in FDA-HT group (n=154), with mean age (SD) of 51.03 (7.30) and 60.62 (9.26), respectively (p<.0001). Mean (SD) duration of HT treatment in years was significantly longer in PT group (3.60 [2.67] vs. 2.37 [1.60], p<.0001). The incidence of side effects was significantly higher in PT group while compared with FDA-HT (117 [63.9%] vs. 15 [10.6%], p<.0001, odds ratio [95% CI] =14.7[7.93-27.25]). A total of 81 (53.6%) women on FDA-HT had a hysterectomy prior to the initiation of HT, which was significantly higher than the 75 (41.2%) on PT (p=0.024). When examining women with an intact uterus prior to HT initiation, 62.6% (67/107) on PT vs. 17.7% (12/68) on FDA-HT had at least one episode of AUB (p<.0001, odds ratio [95% CI] =5.46[2.49-11.98]). Furthermore, significantly higher proportion of women on HT (38.1% [40/107]), compared with 10% (7/70) on FDA-HT, had a hysterectomy even though HT in both cohorts included a variety of progestational agents for endometrial protection (p<.0001, odds ratio [95% CI] =3.20[1.26-8.15]). **Conclusion:** When compared with women on FDA-HT, women on PT had a significantly higher incidence of side effects including AUB and subsequent hysterectomy. These preliminary findings raise concern about the safety of PT. Further clinical research is warranted to investigate utilization of PT for treating menopausal symptoms.
Sources of Funding: None

P-51.

The Effects of Acute Tryptophan Depletion on Emotional Stroop in Midlife Women Receiving Estrogen-based Treatment: An fMRI study

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Objective: Objective: Dysregulation in the serotonergic system may modulate changes in estrogen levels and symptoms related to menopause transition. Serotonin availability can be temporarily manipulated with exposure to the acute tryptophan depletion (ATD) paradigm. Etkin et al. (2006) introduced an Emotional Conflict Task, demonstrating differences between two types of emotional Stroop stimuli: **Conflict Generation** and **Conflict Resolution**. Manipulation of serotonin availability may influence the brain response to emotional Stroop. We hypothesized that this Conflict Generation/ Resolution of emotionally-valenced stimuli may vary in ATD compared to sham conditions. To date no study has examined the effect of ATD on emotional Stroop in a group of midlife women receiving estradiol. **Design:** Twenty-one midlife women (mean age 52 ± 4 years) receiving estradiol were included in the analysis. In a repeated measures design, participants were assigned to ATD or sham in an fMRI session. Order of conditions was randomized and the participants were blind to condition. Brain blood oxygen level dependent (BOLD) activity was measured with functional magnetic resonance imaging (fMRI) data collected in a 3T MRI, while participants completed the Emotional Conflict Task. The Emotional Conflict Task was comprised of 148 happy or fearful faces with the word "HAPPY" or "FEAR" superimposed on happy or fearful faces, counterbalanced for equal numbers of congruent (affect and word match) and incongruent (affect and word do not match) presentations. FMRI data was preprocessed and analyzed using SPM12 software. Statistical analyses included a second level random effects General Linear Model comparing ATD and sham conditions applying conflict generation and conflict resolution as contrasts of interest. **Results:** Significant differences in conflict generation trials between ATD and sham conditions indicated greater activity in the ATD condition in right Brodmann Area (BA) 8, left fusiform gyrus, and left BA 6. Similarly, activation on conflict resolution trials indicated significantly greater activity in the ATD condition compared to sham in the right BA 8 (all results, p<0.001 unc). **Conclusion:** A comparison of BOLD activation on an Emotional Conflict Task indicated significantly greater activity in the ATD compared to sham conditions. Since the ATD paradigm depletes serotonin in the brain, these results may indicate that the serotonergic system is implicated in processing Emotional Stroop in prefrontal and temporal cortical regions.
Sources of Funding: Canadian Institute of Health Research

P-52.

Then and Now: Expert Insights on Understanding the Women's Health Initiative Hormone Therapy Trials

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Objective: Introduction: More than a decade following the abrupt cessation of the Women's Health Initiative (WHI) clinical trials for hormone therapy (HT), there remains a perception in the medical community that HT is unsafe for postmenopausal women. Published evidence from the WHI suggests otherwise for the majority of symptomatic menopausal women under age 60 years who are within 10 years postmenopause. Objectives: (i) To uncover knowledge gaps of clinicians who treat postmenopausal

women prior to an educational intervention about HT; and (ii) to evaluate the potential requirements for future educational programming. **Design:** A continuing medical education program (30-minute expert interview) discussed the accurate interpretation of published data from the WHI trials. Immediate pre- and post-activity tests, which included case-based scenarios, tested participants' knowledge of WHI trial data and the appropriate and recommended use of HT in postmenopausal women. Test answers from both time points were evaluated to assess improvements in knowledge, as well as potential additional learning gaps. **Results:** 34,501 individuals engaged with the program to date (July 1, 2016 – March 22, 2017), of whom 1,087 participants completed the activity (completers). Learners included physicians (50% of participants), nurse practitioners (NPs) (18%), and physician assistants (PAs) (12%). Here we report the results for obstetrician/gynecologists (ob/gyns), and NPs and PAs who work in an ob/gyn setting. Among ob/gyns, the average percentage of participants who correctly answered test questions related to outcomes of the WHI trials was 57% pre-activity and 70% post-activity; for NPs, the average percentage of those who answered correctly was 49% pre-activity and 68% post-activity, and for PAs, 52% and 70%, respectively. Percentage of correct responses increased from pre- to post-activity tests for all 3 groups on questions about attributes of new menopausal medications (ob/gyns, 39% to 58%; NPs, 36% to 62%; PAs, 50% to 77%) and appropriate application of clinical guidelines (ob/gyns, 81% to 92%; NPs, 84% to 88%; PAs, 70% to 97%). For most of the case-based questions, the increase in percentage of correct responses was minimal for all 3 groups, although PAs scored better for all but one of four questions. Knowledge gaps identified pre-activity included primary objectives of the WHI trials and differences in outcomes such as breast and colon cancer between estrogen alone or with progestin. There was improvement post-test in understanding that the WHI results were not stratified by age or time since menopause and that further analysis showed significant differences depending on timing of initiation of HT. Limitations: Direct comparisons between pre- and post-activity test answers could not be made because more learners completed the post-activity test than the pre-activity test. **Conclusion:** There was an expectation that obstetrician/gynecologists would demonstrate better results in both the pre- and post-activity tests than what was recorded. Improvements were seen in some key areas but our data suggest that there remains uncertainty about HT risks, differences between findings for estrogen alone or with progestin, the interpretation of WHI follow-up studies, and the benefits and risks of newer menopausal medications. Future educational interventions are warranted to reinforce the appropriate treatment of symptomatic menopausal women according to the 2017 NAMS Hormone Therapy Position Statement.
Sources of Funding: Pfizer

P-53.

The Benefit of Postpartum Hormone Therapy in Turner Syndrome

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Objective: Hormone therapy is imperative in managing complications related to the hypergonadic state in Turner Syndrome (TS). The objective of this study was to describe the use of hormone therapy for postpartum mood disturbances and it's role in treating severe postpartum depression in a patient with Turner Syndrome. **Design:** We present a case of severe postpartum depression (PPD) with psychotic features in a patient with TS, which presented at four weeks following the birth of her first child via egg donation. A review of relevant literature was completed. **Results:** A previously well 32-year old patient with an 46 X, i(Xq) karyotype developed a severe postpartum depression and required intensive inpatient treatment, including electroconvulsant therapy (ECT) for persistent infanticidal and suicidal ideation. It was hypothesized that an estrogen depleted state secondary to POI and lactation, may have been more pronounced during her postpartum course. In attempt to buffer the dramatic drop in sex steroid levels postpartum, she was immediately started on estrogen and progesterone replacement after the birth of her second child, and did not experience any change in mood or similar psychiatric disturbance. Four years later from the PPD episode, her mood remains stable. **Conclusion:** The complex interplay between ovarian steroids, depletion of their levels and psychiatric sequelae is highlighted in this case. The postpartum period represents a particularly vulnerable time for patients with POI, that requires very close monitoring and early hormone replacement.
Sources of Funding: none

P-54.

Hormone Replacement Therapy has a Beneficial Effect on Hypertensive Postmenopausal Women: Results from the KNHANES 2010-2012

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Objective: Hypertension is the most important risk factor of cerebrovascular diseases in Korea. The relative risk of cardiovascular diseases after menopause is greater than premenopausal period. The relationship between hypertension and hormone replacement therapy (HRT) has not been clearly determined. Therefore, we examined the effects of HRT on hypertension in Korean postmenopausal women. **Design:** The data were acquired from the Fifth Korean National Health and Nutritional Examination Survey conducted from 2010 to 2012. Questionnaires were used to collect a medical history about women's health and cardiovascular diseases. Each woman also had her blood pressure (BP) taken and provided a blood sample for risk factor assessment. **Results:** This study involved 2,260 postmenopausal women. The participants in stage 4 hypertension showed lower propor! tion of HRT than other groups (P for trend = 0.027). After adjustment of several lifestyle factors and cardiovascular risk factors, the HRT group showed lower systolic blood pressure (SBP) and diastolic blood pressure (DBP). Hormone replacement therapy was independently related to the control rate of hypertension. Longer duration of HRT led to lower BP and better control rate of hypertension. The proportion of participants with stage 4 blood pressure decreased from 4.3% in the non-HRT group to 0.4% in the long HRT group. **Conclusion:** The hormone therapy group showed lower BP, and presented greater hypertensive control rate. Longer duration of hormone therapy led to lower BP and higher hypertensive control rate. These data suggest that HRT in hypertensive postmenopausal women may be helpful for controlling BP.
Sources of Funding: None

P-55.

Low-dose local hormonal therapy for VVA in postmenopausal women

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Objective: Up to 57% of postmenopausal women are concerned about the symptoms of vaginal atrophy (VVA), such as dryness, burning, itching, vaginal discomfort, dyspareunia and spotting during sexual intercourse. The gold standard for the treatment of VVA symptoms is the use of local hormone therapy (HT) with estrogens. At present, European countries tend to use low doses of local estrogens.The aim of this research was to study the dynamics of atrophic changes in the vaginal mucosa during the treatment of low-dose regimens of local hormonal therapy in patients with postmenopausal VVA. **Design:** For the study, 44 patients with vaginal atrophy were selected. The duration of the follow-up was 3 months. Using block randomization, the participants were divided into 2 groups of 22 people each. In the first group it was used a drug containing estriol in a dose of 0.5 mg, in the second group – a drug containing a lyophilized culture of lactobacilli L. casei rhamnosus Doderleini - 341 mg; estriol - 0.2 mg; progesterone - 2.0 mg. Treatment regimens were created for patients in both groups with the same dose of estriol 9.8 mg (Group A: 0.5 mg of estriol every other day for 3 weeks, followed by 0.5 mg once a week for 9 weeks; Group B: lyophilized culture of lactobacilli L. casei rhamnosus Doderleini - 341 mg, estriol - 0.2 mg, progesterone - 2.0 mg daily for 2 weeks, then every other day for 10 weeks). Methods of the study included of cytological examination of the vaginal wall with subsequent evaluation of the epithelial maturation index (EMI = 0.5 x number of intermediate cells (%) + 1 x number of surface cells (%) (N ≥ 65%)), ph-metrics of the vaginal secretion, determination of the Index of Vaginal Health (IVH), PCR diagnostics of the vaginal. **Results:** The full course of treatment was completed by 91% of women in group 1 and 95.5% in group 2. Initially, the EMI and vaginal pH were 54.6 ± 4.4 and 6.0 ± 0.66 in group A and 54.45 ± 4.7 and 6.2 ± 0.8 in group B ($p = 0.05$). Patients of both groups were comparable in age, BMI, and differed in the duration of postmenopause (group A - 8.9 ± 5.7, group B - 5.2 ± 3.8, $p = 0.029$). After the therapy patients of both groups noted relief of vaginal symptoms. In the treatment groups, patients were comparable in the frequency of occurrence of complaints both before and after treatment. According to the D. Barlow's analysis of complaints, a statistically significant decrease in symptom intensity was observed only in group B (group A: symptom intensity initially - 2.05 ± 1.3, after treatment 1.57 ± 1.3 ($p = 0.135$), group B: Initially - 2.04 ± 1.43, after treatment - 0.95 ± 1.32 ($p = 0.013$)). At the end of the treatment, a statistically significant decrease in the pH of the vagina and EMI were noted in two groups ($p < 0.0001$). However, in group A 25% of women retained a mild degree of VVA, while in the second group it was achieved a 100% treatment effect. Initially, vaginal flora of the mucous membrane of the vagina in women in treatment groups was characterized by a sharp decrease in the number of lactobacilli (group A - 0.0% (0.0-89.9), group B - 0.0% (0.0 - 2.8). After the treatment course, there was an increase in the number of lactobacilli (group A - 17.9% (0.0-99.9) ($p = 0.178$), group B - 86% (8.0 - 99.2)) ($p = 0.014$). By the end of the treatment course, the frequency of detection of normocenosis increased (the proportion of *Lactobacillus spp*.> 80% of the total bacterial mass (TBM)) in the study groups. In the first group, the incidence rate of normocenosis increased by only 10%, and it increased by almost 40% in group 2. **Conclusion:** The use of a combined preparation containing estriol, lactobacilli and progesterone was accompanied by a more pronounced decrease in the intensity of vaginal symptoms ($p = 0.013$) and an increase in the proportion of lactoflora of TBM as compared with estriol alone.
Sources of Funding: None

MENOPAUSE SYMPTOMS POSTER PRESENTATIONS

P-56.

A Pooled Analysis of 5 Treatments for Menopausal Hot Flashes

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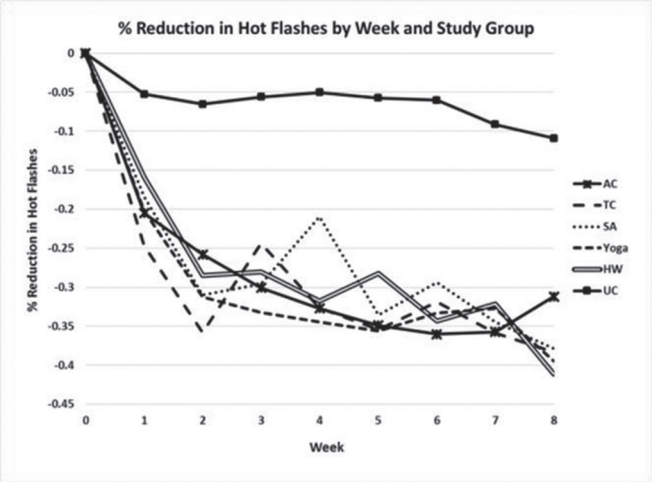
Objective: To compare 3 active treatments for menopausal hot flashes (HF) with 2 attention control groups and 3 usual care groups across 3 randomized studies on % reduction in HF. **Design:** Study #1 randomized 56 women to one of 3 groups: true acupuncture (TA); sham acupuncture (SA), an attention control; and usual care (UC). The true and sham acupuncture groups received 2 treatments per wk for 8 wks. Study #2 randomized 54 women to one of 3 groups: yoga; health and wellness classes (HW), an attention control; and waitlist (WL). Yoga and HW classes were weekly for 8 wks. Study #3 randomized 209 women to acupuncture (AC) or waitlist. The AC group received up to 20 treatments over 6 mos., though our pooled analysis used 8 wk data only for consistency across studies. All 3 studies recruited peri or postmenopausal women aged

44-60 experiencing at least 4 hot flashes/day. Participants completed daily HF diaries over the course of all 3 studies. There were no significant differences among the 3 studies in average number of HF at baseline. We used mixed repeated measures models to estimate reductions in HF, by group, controlling for age, race, and menopausal status. Study week was included as a categorical (rather than ordinal) variable to allow for detection of nonmonotonic trends in hot flashes over the 8 wks. **Results:** Estimated average % reduction in daily HF reported over the entire 8 wks for the 5 intervention groups were: TA: 32%, SA: 29%, Yoga: 33%, HW: 30%, AC: 31%. Corresponding average reductions for the 3 UC groups were: 3%, 18%, and 4%. There was no significant differences among the 3 UC groups (p=0.36) and they were combined into a single passive control group. Controlling for age, race, and menopausal status, there was a significant effect for wk (p<.0001) and treatment (p<0.0001). This significant overall treatment effect was largely confined to a significant difference between all 5 treatments and UC (p<0.0001 for contrast of average of 5 groups vs pooled passive control group). There were no significant differences among the 5 treatments (p=0.99). **Conclusion:** The 3 active treatment groups and 2 attention control groups showed statistically similar trends in % reduction in HF over 8 wks and all 5 groups were significantly better than usual care. Results suggest that yoga and acupuncture are equally effective in reducing HF and also show that the attention control groups were as effective as the active treatment groups. We conclude that these control groups were actually active treatments and/or the non-specific effects of patient-provider interactions are sufficient to reduce hot flashes.
Sources of Funding: NIH Grants R21CA104427, R21AT004234, R01AT005854



P-57.

Patient Satisfaction with the Use of Relizen to Treat Menopausal Symptoms

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Objective: A national survey study was conducted to determine the extent of patient satisfaction on the efficacy of Relizen®† for the relief of hot flashes and other symptoms associated with menopause. Relizen is a non-hormonal, non-estrogenic, purified pollen extract with clinical efficacy in treating vasomotor symptoms (VMS) and improving quality of life. Relizen is plant-based and made from a unique blend of pollen extract from flowers grown in Sweden. The allergenic husk is removed to improve absorption and efficacy. There is scientific data substantiating the safety and efficacy of Relizen as an effective option for the treatment of menopausal symptoms. In a randomized, double-blind, placebo-controlled clinical trial, Relizen significantly reduced hot flashes compared to placebo. Relizen does not have any estrogenic activity, as shown by having no effect on the MCF-7 cell line used for the study of estrogenic compounds, or on estrogen receptors. Additionally, uterine weights in rats remained stable when exposed to Relizen. In an *in vitro* study, Relizen was shown not to inhibit the CYP2D6 metabolic pathway used to metabolize tamoxifen, providing evidence that it may be a safe option for patients taking tamoxifen but also suffering from vasomotor symptoms. The activity of Relizen is thought to be mediated by a serotonergic pathway, acting on the hypothalamus to reduce vasomotor symptoms and improve overall quality of life. A survey study was conducted to gather patient experience data on Relizen for the relief of menopausal symptoms. **Design:** An optional, rolling online survey was emailed to Relizen patients who had been taking Relizen consistently for at least 3 months. Survey data was collected from 2,304 patients between January 2015 and January 2017. Patients who completed the survey were compensated with a $10 gift card for their opinions about Relizen. The survey results were pooled and analyzed by an independent statistician. **Results:** Major survey findings reflecting the real-world opinions of patients taking Relizen for at least 3 months: 78% responded that Relizen reduced the frequency of hot flashes; 75% responded that Relizen reduced the intensity of hot flashes; 69% responded that Relizen reduced the frequency of night sweats; 68% responded that Relizen reduced the intensity of night sweats; 58% responded that Relizen improved their quality of life; 47% responded that Relizen improved their quality of sleep. In addition, 89% would recommend Relizen to any friends or family members who are experiencing menopausal symptoms and 88% planned to continue using Relizen for their menopausal symptoms. **Conclusion:** This survey demonstrated Relizen's positive patient experience and level of patient satisfaction with this non-hormonal option for the treatment of menopausal symptoms. The objective findings of previously published Relizen studies are in line with the subjective opinions expressed by the patients in this survey.
Sources of Funding: This study was funded by JDS Therapeutics, LLC. †Relizen® is known in other countries under different registered trade names: Sérélys®, Femal®, Femalen®

P-58.

Gabapentin for the Treatment of Hot flushes in Menopause : A Meta-analysis

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Objective: Estrogen replacement therapy is the most effective treatment for vasomotor symptoms (VMS) among postmenopausal women. Other hormones and non-hormonal and non-medical treatments have been considered for VMS among postmenopausal women. Gabapentin could be used for the treatment of VMS in postmenopausal women with contraindications to hormonal therapy or those who prefer alternatives to hormonal therapy. To investigate the efficacy and tolerability of gabapentin for the treatment of menopausal hot flushes, a meta analysis was performed **Design:** Reviews and original articles were searched in the MEDLINE, PubMed and EMBASE databases and in the Cochrane Central Register for Controlled Trials (CENTRAL) in the Cochrane Library up to October 2015. A combination of the following search terms was used: 'menopause', 'hot flushes', 'vasomotor symptoms', 'gabapentin', and 'non-hormonal therapy'. Mean difference (MD), odd ratio (ORs) and their 95% confidence intervals (95% CIs) were calculated by standard meta-analysis techniques **Results:** A meta-analysis of the 7 RCTs that compared single-agent gabapentin with placebo for the treatment of menopause hot flashes was performed. In this meta-analysis, 789 individuals who had gabapentin, 637 individuals were enrolled in placebo group. Among the 4 studies for which data were available, women assigned to gabapentin treatment reported significantly greater percent reductions in the frequency (SMD=0.437, 95% CI, 0.302 to 0.573; P<0.000). Among 4 studies for which data were available, women assigned to gabapentin treatment reported significantly greater percent reduction in the composite score (SMD = 0.479, 95% CI, 0.338-0.620, P<0.000). (Figure 3C) Heterogeneity was low across the studies (P= 0.202 and I^2 =31.14%). Dropouts due to adverse events were more frequent in women randomized to gabapentin than in women in the control groups. (OR=0.928; 95% CI 0.632-1.364, P=0.704). The relative risk of the clustering of dizziness and unsteadiness also was significant higher in the women treated with gabapentin than in the controls. (OR=3.994; 95% CI 2.512-6.350, P=0.000). **Conclusion:** These results indicate that Gabapentin could be used for the treatment of VMS in postmenopausal women with contraindications to hormonal therapy or those who prefer alternatives to hormonal therapy. Further studies should investigate the lowest effective dose of gabapentin to minimize its adverse effects.
Sources of Funding: none

P-59.

Subjective pain complaints across the menopausal transition: a daily diary study of the Daily Hormone Sub-Study (DHS) of the Study of Women's Health Across the Nation (SWAN)

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Objective: Alterations in ovarian hormones have been implicated in susceptibility to developing chronic pain disorders. It is uncertain whether pain is more common during the menopausal transition (MT), a time of dynamic and changing reproductive hormone activity. Past studies suggest that perimenopause is associated with increased prevalence of some pain disorders (migraine, musculosceletal pain), however the effect of menopausal transition stage on the frequency of subjective pain complaints in midlife women has not been explored. Headaches are known to be hormonally regulated and often precipitated by change in hormones, while aches and pains are indicative of musculoskeletal pain which tends to worsen with age. Furthermore, while age is known to be a risk factor for musculoskeletal pain, relationship of age to stage of MT on pain is unknown. The goal of this study was to characterize the distribution of common subjective pain complaints (headache and "aches and pains") in community dwelling women, in relation to menopausal status. Design: A secondary analysis of annual collections of daily diary symptoms for a period of at least a month per year, collected for a median of 4 annual visits per woman in the Daily Hormone sub-Study (DHS) of the Study of Women's Health across the Nation (SWAN). Self-reported pain measures of "headache" and "aches and pains" derived from the daily symptom diary were completed using the frequency categories 1-4 days per month (dpm), 5-9 dpm, 10-14 dpm, and ≥15 dpm,. Separate longitudinal random effects ordinal or multinomial logistic regressions for 1) number of headache days and 2) number of days with aches/pains were estimated and interactions of concurrent menopausal status with age tested. Results: Participants (n= 862, 3867 collections), were on average aged 47.4+ 2.6 (SD) years at the first collection. Subjective pain complaints were common with 20.9% of women experiencing 15 or more days of headaches per month and 55.9 % experiencing 15 or more days of "aches and pains" per month. For headache

frequency, premenopausal visits had the lowest headache frequency, followed by postmenopausal visits. Headache frequency was highest in early perimenopausal visits. Frequency of "aches and pains" was also lowest in premenopausal visits, but in contrast to headache frequency postmenopausal visits had the highest frequency, although the association is not statistically significant after adjusting for concurrent age (0.1109). Conclusion: Subjective pain complaints are common in midlife and their frequency increases in perimenopause. While frequency of headaches increases in the early and late stages of perimenopause and decreases post-menopause, complaints of musculoskeletal pain continue to increase post-menopause. Further correlation of DHS hormones with pain may clarify this relationship. Better understanding the temporal occurrence of pain as a function of the stage of the menopausal transition can help optimize the timing of pain treatment for prevention and ultimately for aborting progression to chronic pain.
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 U01NR004061; U01AG012505, U01AG012535, U01AG012531, U01AG012539, U01AG012546, U01AG012553, U01AG012554, U01AG012495).

P-60.

Impact of microbiota on use and effects of isoflavones in the relief of climacteric symptoms and additional benefits in menopausal women

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Objective: The efficacy of equol in several health benefits and especially in menopause related problems is the objective of this review. In addition to the hormonal effect that directly affects the relief of menopausal symptoms, isoflavones have been associated with beneficial effects on human health, mainly because of its antioxidant capacity, including reduction of the risk of cardiovascular disease, lower risk of cancer and reduces the risk of osteoporosis. Phytoestrogen therapy is well accepted among women who can not or do not wish to use hormone therapy and demonstrate scientific evidence that it can effectively be an alternative treatment for menopausal women. **Design:** A review of the current literature. For the realization of this review we searched articles in electronic data bases, PUBMED, MEDLINE, The Cochrane Library, Scielo, published in English or Portuguese until April 2017. Were also used the lists of references of the selected articles. This review examined the efficacy of isoflavones therapy for menopause. While not an exhaustive review, it focused on those therapies cited most frequently in recent recommendations or guidelines from national organizations, systematic reviews, and meta-analyses. **Results:** The potential benefits of isoflavones on menopausal women s health have attracted great attention, not only because it is an alternative to hormonal therapy in the improvement of climacteric symptoms, but also because it is able to act in the prevention of diseases that is more prevalent in this stage of life, such as cardiovascular disease, breast cancer and osteoporosis. Gut microbiota is essential for the metabolism and subsequent clinical effect of the isoflavones. The functionality of isoflavones depends on their bioavailability and their conversion within the intestinal tract to metabolites more active than the aglycones forms, as equol (metabolite produced from daidzein), for this is important variability of the intestinal microorganisms. Therefore, supplying suitable equol-producing probiotic bacteria can optimize the estrogenic action of isoflavones and their metabolites, to promote health improvements complementary to the usual relief of climacteric symptoms, as reduced incidence of hormone-dependent and aging-associated diseases such as osteoporosis, cardiovascular diseases and cancer. **Conclusion:** The dietary supplements, soy and soy isoflavones have the strongest evidence for being effective in reducing frequency and severity of hot flushes. Dietary soy or soy isoflavones (S-equol-containing supplements) may be recommended for vasomotor symptoms.
Sources of Funding: Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP), Brazil.

P-61.

Clinical efficacy of an ammonium succinate-based dietary supplement in women with menopausal symptoms: a pooled analysis of two randomized, multicenter, double-blinded placebo-controlled clinical trials.

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Objective: To evaluate the efficacy of an ammonium succinate-based daily dietary supplement (AS; Amberen™) for the relief of climacteric symptoms in menopausal women. **Design:** A pooled analysis of data from two randomized, multicenter, double-blinded placebo-controlled clinical trials. Both studies evaluated an ammonium succinate-based daily dietary supplement (AS) versus a daily placebo for a 3-month study duration. The designs of both trials were identical, thus allowing for pooling of demographic and outcome data to carry out outcome analyses. The studies enrolled healthy postmenopausal women (12 months amenorrhea) between 42 and 60 years of effects of study supplement and placebo on vasomotor and psychosomatic climacteric symptoms. Body mass, BMI and waist circumference, levels of follicle stimulating hormone (FSH), luteinizing hormone (LH), estradiol, leptin, apolipoproteins A1 and B were evaluated as secondary endpoints. All laboratory measurements of both trials were conducted using the same test kits and on the same equipment. **Results:** A total of 227 women, aged 42–60 years, were recruited for the two studies with 114 women in the treatment group and 113 women in the placebo group. Analysis of the Greene Climacteric Scale results showed a statistically significant ($p<0.05$) reduction in 16 out of 21 menopausal symptoms, including hot flashes, night sweats and lack of sex drive, in the treatment group compared to placebo users who showed no such reductions. State-Trait Anxiety Inventory showed that AS supplementation resulted in a significant decrease in anxiety compared to placebo ($p<0.0001$). Over the course of the AS treatment and by the end of the study, the patients showed significant ($p<0.0001$) increase in the levels of estradiol compared to the baseline (from 35.7 to 58.0 pg/ml). Levels of FSH and LH decreased slightly in both groups, without significant differences between the groups. No significant differences were observed in the anthropometric parameters (weight, BMI, waist circumference) in the groups at study initiation; however, analysis of the anthropometric changes demonstrated statistically significant reductions in the weight, BMI and waist circumference changes among AS users. Average leptin levels within the groups did not differ significantly between the baseline and end of the study; however, by the conclusion of the trial, leptin levels were significantly lower in the Amberen group compared to the placebo group ($p=0.027$). For those with initial leptin levels above the reference range, levels decreased significantly in the AS group compared to the baseline (from 16.5 to 14.1 ng/ml, $p<0.0001$) and to placebo ($p=0.027$). There were no significant differences in levels of apolipoproteins between the two groups. **Conclusion:** A daily dietary supplement containing ammonium succinate has been shown to relieve climacteric symptoms in menopausal women and to improve overall quality-of-life. In addition, our study surprisingly shows that users of AS were more likely to show beneficial changes in anthropometric characteristics than placebo users. Further study is needed to characterize longer term use of AS as well as the duration of benefits.
Sources of Funding: Supported by Lunada Biomedical, Inc.

REPRODUCTION POSTER PRESENTATIONS

P-62.

Pregnancy after age 50: A meta-analysis

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Objective: There has been an increased incidence of births to post-menopausal women. The goal of this study is to compare health outcomes in the United States (US) and the international community for pregnant post-menopausal women. **Design:** We identified studies reporting on women who achieved pregnancy after the age of 50 using assisted reproductive techniques (ART) through a database search. We excluded studies that were not in English and those published before 1995. We abstracted study characteristics including methodological quality and generalizability. Study results from the US were compared with results from international studies. Meta-analyses were performed to evaluate singleton pregnancies, cesarean section (C/S) in singleton pregnancies, the development of gestational diabetes, and the proportion of patients requiring antenatal hospitalization between the US and the international community. **Results:** In total, 925 births in 11 studies reporting on women 50 and older with pregnancy were identified. Five were from US sources and six were international. The studies were published between 1995 and 2017. The mean age of women was similar. In the US it was 52.3 years and internationally 52.7 years. When comparing the proportions having a singleton, the US group had a weighted percentage of 67% (95% confidence interval: [61%, 73%]), as compared to the international group which had a weighted percentage of 77% (95% confidence interval: [66%, 88%]). The difference of 10% was not statistically significant (P=0.11). When comparing the proportions having C/S for a singleton, the US group had a weighted percentage of 76% (95% confidence interval: [64%, 89%]), as compared to the international group which had a weighted percentage of 81% (95% confidence interval: [59%, 100%]). The difference of 5% was not statistically significant (P=0.71). When comparing the proportions of gestational diabetics, the US group had a weighted percentage of 20% (95% confidence interval: [15%, 25%]), as compared to the international group which had a weighted percentage of 20% (95% confidence interval: [14%, 26%]). The difference of 0.1% was not statistically significant (P=0.98). When comparing the proportions of maternal complications requiring hospitalization, the US group had a weighted percentage of 2.7% (95% confidence interval: [0%, 6.7%]), as compared to the international group which had a weighted percentage of 49% (95% confidence interval: [36%, 62%]). The difference of 46% was statistically significant (P<0.0001). In the 11 articles, one maternal death was described. **Conclusion:** Available studies suggest that health outcomes in the US and the international community for post-menopausal women undergoing pregnancy are similar. There is no difference in the two groups between singletons, the number having a cesarean section for singleton pregnancies, or development of gestational diabetes. There is a difference between US and international patients in antenatal hospitalizations. The reason for this difference is not obvious from the comparison of outcomes. We speculate this may be a result of pre-existing co-morbidities in the post-menopausal women achieving pregnancy or a variation in reporting.
Sources of Funding: None

P-63.

The inflammatory markers in gonadal failure association with chromosomal abnormalities and autoimmune antibodies

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Objective: Gonadal failure in young women is related with genetic factor and autoimmunity, however, most of cases are unknown of etiology. The role of autoimmunity in primary ovarian insufficiency (POI) and the presence of autoimmune oophoritis were demonstrated. The inflammatory markers studied in chronic disorders is a paucity in gonadal failure. The aim of this study was to investigate the inflammatory markers in gonadal failure and compared regarding to chromosomal abnormalities and autoimmune antibodies. **Design:** Total 128 women complained of amenorrhea were enrolled in this cross sectional study. One hundred four women having hypergonadotropic hypogonadism diagnosed as gonadal failure, and evaluated the chromosomal abnormalities, autoimmune antibodies such as antithyroglobluin antibody, antimicrosomal antibody, antinuclear antibody, rheumatic factor, anti-smooth muscle antibody, and anti-acetylcholin receptor antibody. Twenty four women with hypogonadotropic hypogonadism were also included as control. The inflammatory markers were leukocyte count, neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), and red cell distribution width to platelet ratio (RPR). **Results:** Mean age of women with gonadal failure was 22.34±4.55, and FSH and AMH were 66.22±33.61 mIU/mL, and 0.24±0.86 ng/mL separately. Gonadal failure group had higher RPR than those of controls (0.06±0.03, 0.04±0.01, p=0.04). Leukocyte count, NLR, and PLR were similar between two groups. Among 104 women with gonadal failure, 73 women were diagnosed as POI and 31 women had chromosomal abnormalities such as 45 X, 46 X Del(X)(q22q26), etc. In women with POI, leukocyte count, neutrophil count, lymphocyte count, NLR, PLR, and RPR were not different with those of gonadal failure related with chromosomal abnormalities. Twenty two women (30.1%) of POI and 8 (25.8%) women of gonadal failure related with chromosomal abnormalities had autoantibodies. Regarding the presence of autoantibodies, leukocyte count, NLR, PLR, and RPR were not different. AMH, FSH, or estradiol were not correlated with inflammatory markers either. **Conclusion:** RPR was increased in gonadal failure. However, NLR, PLR, and RPR were not different by POI or presence of autoantibodies. The inflammatory markers were not correlated with ovarian reserve either. Further larger studies are needed.

Sources of Funding: none

demographic data and results

	Gonadal failure (n=104)	Hypogonadotropic Hypogoandism (n=24)	p-value
Age	22.34±4.55	20.25±5.43	0.49
Parity	0.09±0.34	0.04±0.20	0.63
SA	0.03±0.17	0.04±0.20	0.75
FSH	66.22±33.61	2.49±2.33	<0.01
LH	21.71±12.62	1.68±1.46	<0.01
E2	36.81±40.73	30.44±17.3	0.99
AMH	0.24±0.86	6.62±3.47	<0.01
WBC	5913.73±1663.81	6317.85±1544.38	0.37
Leutrophil	3159.84±1476.37	3693.74±1600.54	0.46
Leutrophil %	54.36±11.83	58.99±13.81	0.34
Lymphocyte	1943.34±610.84	1875.08±921.29	0.31
Lymphocyte %	34.62±9.79	31.11±0.77	0.55
Platelet(x103)	253.57±68.90	270.25±847.50	0.47
RDW	13.45±2.91	13.20±0.77	0.61
NLR	1.79±0.86	2.61±1.88	0.50
PLR	137.78±49.23	188.08±130.11	0.29
RPR	0.06±0.03	0.04±0.01	0.04

SEXUAL HEALTH POSTER PRESENTATIONS

P-64.

Sexual dysfunction in postmenopausal women with metabolic syndrome: What's the most important component?

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Objective: To evaluate the diagnostic component of MetS with greater impact as cause sexual dysfunction (SD) in postmenopausal women. **Design:** A total of 1100 women were interviewed after a menopause at the FCMSCSP Ambulatory and HMLMB. Of these, 221 women, aged between 40 and 65 years, who met the inclusion criteria, were selected and a case-control study was performed. We were considered to be postmenopausal women with amenorrhea ≥ 1 year and FSH ≥30mUI / mL. The diagnosis of MetS was determined following the guidelines defined by the ATP III (Adult Treatment Panel): (1) abdominal circumference (AC) ≥88cm; (2) HDL-cholesterol ≤50mg / dL; (3) triglycerides ≥ 150 mg / dL; (4) blood pressure (SAH) ≥130 / 85mmHg; And (5) fasting glycemia ≥110mg / dL. The women considered to be carriers of MetS were those with at least three of the components described. The evaluation of sexual function was performed through the FSFI questionnaire. **Results:** All scores in FSFI domains, excluding pain scores, were statistically lower in women with altered triglycerides ($p < 0.05$), considered the most important fator impact. The FSFI scores, arousal, lubrication, and total score were statistically lower in women with SAH ($p < 0.05$). There was no association of dysfunctions with alteration in AC or HDL ($p > 0.05$). All domain scores and FSFI total were statistically lower in women with MetS, except for the pain score. The lubrication, orgasm, and total FSFI scores were statistically lower in women with altered glycemia ($p = 0.004$, $p = 0.025$ and $p = 0.028$, respectively). The sexual dysfunction was statistically higher in women with altered glycemia ($p = 0.025$) when we used cut off of 23 (Silva et al 2013). The diagnosis of Hypoactive sexual desire disorder were statistically higher in women with MetS ($p < 0.05$). **Conclusion:** Women with a diagnosis of MetS had a negative influence on sexual function. The factor with the greatest impact on the sexual response was the increase in triglycerides.

Sources of Funding: None

P-65.

Study of sexual function in postmenopausal women with obesity

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Objective: To evaluate the sexual function of postmenopausal women with a body mass index (BMI) greater than 30 kg / m2. **Design:** A total of 1100 postmenopausal women were interviewed at the Ambulatory of Climatério of the Faculty of Medical Sciences of Santa Casa de São Paulo and the Unit of Management Assistance (UGA) IV Leonor Mendes de Barros Maternity Hospital (HMLMB). Of these, 221 women, aged between 40 and 65 years, were selected and a case-control study was performed. The diagnosis of obesity was given according to the BMI, obtained by dividing the weight (in kilograms) by height (in meters) squared. Body weight was obtained on an electronic scale (accuracy of 0.1 kg), with the bladder empty and the woman wearing only underwear. The stature was obtained in a wall stadiometer with the woman barefoot and with an accuracy of 0.5 cm. In this way, the body mass index (BMI = weight / height2) was calculated, as recommended by the WHO to assess nutritional status. In our study, women were grouped according to their body mass index (BMI) in 3 groups: Group 1: BMI between 18.5 and 24.9 kg / m2 (IMC Normal Group), Group 2: BMI between 25 and 29.9 kg / m2 (Overweight Group); Group 3: BMI between 30kg / m2 and 34.5kg / m2 or more) (Obesity Group). All the women signed the Term of Free and Informed Consent (TCLE). The sexual function was assessed by completing the Female Sexual Function Index (FSFI), a questionnaire validated for the Portuguese language (Brazil) with 19 items for measuring female sexual function (Rosen et al 2000). We considered 23 (Silva et al 2014) and 26.5 (Rosen et al 2000) as a cutoff point for the diagnosis of Sexual Dysfunction according to the American Psychiatric Association Manual, Diagnostic and Statistical Manual of Mental Disorders, 4th edition, Revision text (DSM -IV-TR), criteria of duration> 24 weeks. A score of 5 or less in the combination of items composing the desire domain is used for the diagnosis of Hypoactive Sexual Desire Disorder (HSDD) in postmenopausal women (Gerstenberger et al 2010).The diagnosis of sexual dysfunctions was made by a doctor with a background in sexology with experience and trained in the diagnosis of female sexual disorders through a structured clinical interview. All women underwent standardized anamnesis by our service. We measured blood pressure (BP), waist circumference (WC) and calculated body mass index (BMI), submitted to gynecological examination and cytology sampling for Pap smears. After laboratory tests (total cholesterol and fractions, triglycerides and fasting glycemia), bilateral mammography and transvaginal ultrasonography were requested, according to the basic propaedeutics of our service. The protocol was approved by the Ethics Committee of the Faculty of Medical Sciences of Santa Casa de São Paulo and Leonor Mendes de Barros Maternity Hospital. **Results:** The desire, excitation, arousal, and total FSFI scores differed statistically among the BMI categories ($p < 0.05$). The HSDD (hypoactive desire) presented association with the categories of BMI ($p = 0.003$). The desire and arousal scores were statistically higher in women of the normal weight group than in the women in the obesity group ($p = 0.028$ and $p = 0.043$, respectively). The satisfaction score was statistically higher in women with normal weight than in the overweight and obesity groups ($p < 0.05$). The diagnosis of HSDD was statistically lower in women of the normal weight group than in women in the overweight and obesity groups ($p = 0.034$ and $p = 0.002$, respectively). The FSFI total score, although statistically different between BMI categories (Table 2, $p = 0.027$), it was not possible to identify between the categories of BMI a difference ($p > 0.05$), however, it suggests a lower score in women with overweight and obesity than in women with normal weight ($p = 0.060$). The FSFI score is slightly higher in women with normal BMI than in the other categories, but mainly in obese women. **Conclusion:** In our study we observed that obese and overweight menopausal women had a higher index of desire dysfunction, arousal and less sexual satisfaction when compared to normal weight women. There was no relation to orgasm and pain scores.

Sources of Funding: None

P-66.

Effect of Flibanserin on Sexual Functioning in Postmenopausal Women: An Analysis of Female Sexual Function Index Domains

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Objective: Flibanserin, a 5-HT_{1A} agonist and 5-HT_{2A} antagonist, is approved by the US Food and Drug Administration (FDA) for the treatment of acquired, generalized hypoactive sexual desire disorder (HSDD). Although flibanserin is approved only for premenopausal women, it has also been studied in postmenopausal women with HSDD. In a randomized, placebo-controlled study of naturally postmenopausal women with HSDD (study name, SNOWDROP), significantly greater improvement in sexual desire and sexual distress was obtained with flibanserin 100 mg qhs compared with placebo (Simon JA, et al. *Menopause*. 2014;21(6):633-640). The Female Sexual Function Index (FSFI) is

a validated self-report questionnaire comprising 6 domains of sexual functioning: desire, arousal, lubrication, orgasm, satisfaction, and pain. This post hoc analysis evaluated the effect of flibanserin treatment across the 6 FSFI domains in postmenopausal women. **Design:** FSFI data were obtained from this 24-week, double-blind, placebo-controlled study of flibanserin 100 mg once daily (qhs) in naturally postmenopausal women with HSDD (SNOWDROP). Change from baseline to week 24 (last observation carried forward [LOCF]) on FSFI domain and total scores was compared between the flibanserin and placebo groups using analysis of covariance. **Results:** This analysis included 895 women (flibanserin, n=432; placebo, n=463) who had at least 1 on-treatment efficacy assessment. The least-squares mean differences (standard error of the mean) in change scores from baseline to week 24 (LOCF) for flibanserin versus placebo were 0.3 (0.1) for the FSFI desire domain (P<0.0001), 0.3 (0.1) for the arousal domain (P=0.003), 0.2 (0.1) for the lubrication domain (P=0.044), 0.2 (0.1) for the orgasm domain (P=0.044), 0.3 (0.1) for the satisfaction domain (P=0.004), 0.2 (0.1) for the pain domain (P=0.099), and 1.5 (0.5) for the total score (P=0.01). **Conclusion:** In this post hoc analysis of data from a randomized, placebo-controlled study of postmenopausal women, treatment with flibanserin produced significant improvement not only in the FSFI desire domain (a key outcome in clinical trials of HSDD) but also across most other domains of sexual function assessed by the FSFI. Flibanserin is approved by the FDA only for the treatment of premenopausal women with acquired, generalized HSDD.

Sources of Funding: Boehringer Ingelheim; Valeant Pharmaceuticals North America, LLC.

SLEEP AND MOOD POSTER PRESENTATIONS

P-67.

Association of Menopausal Symptoms and Risk of Sleep Apnea in Midlife Women: Results from the Data Registry on Experiences of Aging, Menopause and Sexuality (DREAMS)

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Objective: Poor sleep is reported by 38-46% of women during the menopause transition. The incidence of obstructive sleep apnea (OSA) increases around menopause. OSA contributes to poor sleep, daytime tiredness, and cardiovascular risk; however this condition remains underdiagnosed and undertreated in women. Vasomotor symptoms (VMS-hot flashes and night sweats), occurring in up to 80% of women during the menopausal transition, also disrupt sleep. VMS and OSA may coexist in midlife women with sleep disturbances, hindering the diagnosis of OSA. The objective of this study was to determine the association of self-reported menopausal symptoms with risk of OSA in midlife women. **Design:** All women presenting for consultation in the Mayo Clinic Women's Health Clinic (WHC) in Rochester, MN between May 1, 2015 and December 31, 2016 completed the Menopause Rating Scale (MRS) and the STOP BANG questionnaires. In the MRS, menopausal symptoms and severity were assessed with 11 questions, rated on a scale of 0-4 for severity (0 = none; 1 = mild; 2 = moderate; 3 = severe; 4 = very severe). In addition to total MRS score, the questions assessing episodes of hot flashes/sweating and sleep problems (difficulty falling asleep, difficulty sleeping through the night, waking up early) were reviewed individually. OSA risk was calculated based on the STOP BANG scale as low risk: yes to 0-2 questions; intermediate risk: yes to 3-4 questions; high risk: yes to 5-8 questions or yes to 2 or more of STOP questions and self-reported body mass index (BMI) > 35 kg/m^2. BMI, education, relationship status, employment status, and race/ethnicity were obtained from the electronic medical record. Current tobacco use was assessed as present/absent (yes/no). Women between the ages of 40 and 65 years who completed the two questionnaires and provided authorization for use of their medical records were included in the study. **Results:** Of the 1691 women meeting inclusion criteria, 147 (8.7%) had STOP BANG scores representing high risk for OSA and 274 (16.2%) had intermediate risk scores. Total MRS scores were significantly higher for those with intermediate/high risk for OSA compared to those with low risk (mean (SD): 16.8 (8.0) vs 12.9 (7.0), p<0.001). After adjusting for age, BMI, and smoking status, the odds of having intermediate/high risk for OSA increase 1.08 (95% CI: 1.06-1.10, p<0.001) times for every additional point on the MRS. On subanalysis of menopausal symptoms, severe/very severe hot flashes (26.6% vs 15.0%) and sleep problems (41.0% vs 27.3%) were significantly associated with intermediate/high risk for OSA (p<0.001). Based on ICD codes, 23% of the women with an intermediate/high OSA risk had a diagnosis of OSA prior to the visit, and an additional 11.7% received the diagnosis within 2 years of being seen in the WHC. The remaining 65.3% did not have a diagnosis of OSA up to 2 years after being seen in WHC. Women at intermediate/high OSA risk were more likely to be older, have less education, have a history of hypertension or BMI >35 kg/m^2, and were less likely to be married or employed. **Conclusion:** In women participating in the Data Registry on Experiences of Aging, Menopause and Sexuality (DREAMS), severity of menopausal symptoms was significantly associated with intermediate/high risk for OSA. About one-quarter (24.9%) of midlife women presenting to our menopause and sexual health clinic were at intermediate/high risk for OSA, but 65% remained without a diagnosis up to 2 years after the visit. These results underscore the need to screen women presenting with bothersome menopausal symptoms for OSA as it is underdiagnosed and undertreated.

Sources of Funding: None

P-68.

Assessment of the Psychological Factors Related to Menopause

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Objective: Although menopause is part of the normal and natural aging process, many women report symptoms that range from minimal to debilitating and these can last a variable number of years before and after the end of menstrual periods. Menopause symptoms, such as hot flashes, can have a significant negative impact on daily functioning and quality of life.[1,2] Hot flashes (including night sweats) occur in up to 75 to 80% of all women in the US.[3,4] The most effective treatment of hot flashes is hormone replacement therapy (HRT)5, yet there is a palpable hesitation and skepticism towards its routine use by both patients and physicians. There is lack of comprehensive data and studies which examine female beliefs and attitudes toward menopause in general and HRT specifically. **Design:** The present study examined perceptions of menopause, hot flashes, and associated treatments in female participants by using a standardized survey which was distributed at a community health fair. **Results:** The survey was completed by141 female volunteers (mean age = 65; SD = 10.69). 75% reported being post-menopausal and 66% reported having experienced a hot flash. Among the many findings, participants reported being significantly less willing to use HRT for hot flashes than exercise, diet, herbal supplements, acupuncture, and meditation ($p < 0.001$). Although participants strongly agreed that hot flashes could be reduced through HRT ($p < 0.05$), they were significantly less likely to use HRT for improvement of hot flashes than exercise, diet, herbal supplements, acupuncture, and meditation ($p > 0.15$). **Conclusion:** Our findings suggest that women are less willing to use the most empirically validated treatment for hot flashes than the alternative treatment options mentioned. Also, their confidence in successful treatment outcomes was not greater for HRT than the other treatment options. Our study introduces several areas for future research including perception modification and the formulation of appropriate, theory-based psychological interventions with the intent of enhancing effectiveness of therapy.

Sources of Funding: None.

P-69.

Psychosocial Factors Linking Depressive Symptoms to Stress Eating in Postmenopausal Women

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Objective: Women in midlife are at risk for the development of obesity. Hormonal and emotional fluctuations experienced during the menopause transition contribute to mood symptoms, which influence health behaviors that contribute to weight gain. Consequently, the menopausal transition is a particularly vulnerable stage for the development of obesity. Previous work has demonstrated that specific subsets of midlife women (i.e., postmenopausal women) are prone to engage in stress eating when experiencing depression, thus contributing to poor weight outcomes. Specifically, postmenopausal women experiencing depressive symptoms and hormonal changes (i.e., lowered estrogen levels) are more likely to stress eat. While physiological factors linking mood symptoms to eating behavior and obesity are known, limited knowledge exists concerning psychosocial factors that connect depressive symptoms to subsequent eating behavior. Recently, well-being has been identified as a factor leading to stress eating in this population. As depressive symptoms contribute to decreases in well-being (e.g., feelings of loss of relatedness, decreased autonomy, and reduced competence), it is possible that lower mood affects eating choices via decreased social support, control, and competency. As stress eating leads to poor weight outcomes such as obesity, and obesity is a prevalent and preventable health condition in this population, identification of targets for preventative interventions is a priority. Thus, the aim of the current study is to explore the connection between depressive symptoms and stress eating in postmenopausal women by investigating how specific factors resulting from depressive symptoms (i.e., decreases in relatedness, autonomy, and competence) may influence subsequent stress eating. Results can inform intervention and prevention efforts to influence positive health outcomes in this population. **Design:** An archival analysis was performed of data from the Midlife in the United States-II study (MIDUS-II), Project 1. The sample consisted of 432 postmenopausal women between the ages of 40-60 (M=56.69, SD=4.64). Postmenopausal status was defined as not having a period in the last 12 months due to menopause. Depressive symptoms were measured with the World Health Organization Composite International Diagnostic Interview–Short Form (CIDI-SF). Autonomy, competence, and relatedness were measured by three subscales of a psychological well-being questionnaire. Stress eating was measured via a coping inventory. **Results:** A Hayes PROCESS mediation analysis was performed to assess the study aim. After controlling for selected covariates, depressive symptoms were directly associated with stress eating (95% CI [.0098, .2088]). Additionally, competence served as a significant mediator of depressive symptoms and stress eating relation (95% CI [.0507, .1500]). While depressive symptoms were associated with relatedness (95% CI [-.9881, -.2262]), relatedness did not serve as an indirect pathway between depressive symptoms and stress eating (95% CI [-.0468, .0025]). Autonomy was not associated with

depressive symptoms (95% CI [-.7900, .0323]) and did not serve as a significant mediator between depressive symptoms and stress eating (95% CI [-.0008, .0393]). **Conclusion:** Results from the current study highlight the importance of competence in the relation between depressive symptoms and stress eating. Among a sample of postmenopausal women, depressive symptoms predicted decreases in competence, which then predicted greater stress eating. While it is known that the combination of depressive symptoms and hormonal changes specific to postmenopause interact to impact stress eating, the current study highlights an additional psychological factor which may aid in identifying who among postmenopausal women is at risk for the development of stress eating and poor weight outcomes. Future work should continue to explore the impact of psychosocial influences on eating behavior in this population in addition to known physiological factors, which contribute to poor weight outcomes.

Sources of Funding: MIDUS I was supported by the John D. and Catherine T. MacArthur Foundation Research Network on Successful Midlife Development. MIDUS II was supported by a grant from the National Institute on Aging (P01-AG020166) to conduct a longitudinal follow-up of the MIDUS I investigation.

P-70.

Sex as a moderator in the relation between sleep and well-being in midlife

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Objective: Inadequate sleep duration and poor sleep quality in midlife have both been shown to produce negative physiological and psychological health outcomes. One psychological health outcome associated with poor sleep quality and duration is decreased well-being. Although well-being is associated with poor outcomes in its own right, it is also associated with additional negative health outcomes including cardiovascular disease and poor metabolic health outcomes. Hence, there is a need to explore the connection between sleep variables and well-being. While the association between sleep and well-being has been investigated, few studies have attempted to include sex differences when exploring this association. Sex differences are important to explore given that midlife brings a disparate set of psychosocial stressors to males and females. Women in particular experience many physiological and psychosocial changes during this time period, which impact both sleep and psychological health. As such, there is a need to explore how specific sleep factors associated with poor health outcomes may differentially impact well-being across sex. The current study was conducted to examine the possible moderation of sex differences in the relation between sleep and well-being. **Design:** The study is an archival analysis of data from the Midlife in the United States-II study (MIDUS-II), Project 4. The sample consisted of 785 adults between the ages of 34–84, including 427 women (M=55.2, SD=11.3) and 358 men (M=56.91, SD=11.9). Measures include the Pittsburgh Sleep Quality Index and a subjective well-being scale. **Results:** A Hayes PROCESS moderation analysis was performed to assess study aims. After controlling for selected covariates (race, overall physical health, BMI, level of education, and age), sleep duration was not significantly associated with well-being for males (b = -.15, p = .08) and females (b = -.10, p = .19). However, sleep quality was significantly associated with well-being for males (b = .51, p < .05) and females (b = .24, p < .05). Upon closer inspection, there was a significant interaction between sex and sleep quality, where the association between sleep quality and well-being was stronger for males compared to females (b = -.28, p < .05). **Conclusion:** Although sleep duration did not predict well-being in men or women, there was a positive association between sleep quality and well-being in both sexes. Upon closer inspection, the relation between sleep quality and well-being was shown to be stronger for men compared to women, highlighting that sleep quality influences well-being to a greater extent in this population. This finding indicates that while sleep quality may aid in explaining well-being outcomes for men across midlife, there are likely other important factors to explore regarding well-being outcomes for women across this time period. While sleep quality is an important variable to consider in terms of well-being outcomes in midlife women, this study emphasizes that other health factors may contribute to well-being in this population, given the wide range of biopsychosocial changes that women experience during midlife. As the current study highlights that sleep quality is an important factor impacting well-being for males and females in midlife, further work should examine precipitating factors that may predict sleep quality deficiencies, in order to ascertain measures by which sleep quality can be improved. Future research should also explore other health factors which may differentially contribute to well-being outcomes in men and women during midlife.

Sources of Funding: MIDUS I was supported by the John D. and Catherine T. MacArthur Foundation Research Network on Successful Midlife Development. MIDUS II was supported by a grant from the National Institute on Aging (P01-AG020166) to conduct a longitudinal follow-up of the MIDUS I investigation.

P-71.

Effects of Tryptophan Depletion on Mood, Vasomotor Symptoms and Sleep in Midlife Women on Estrogen Therapy: Double Blind Placebo-Controlled Crossover Trial

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Objective: Estrogen therapy (ET) is known for its efficacy for vasomotor symptoms, its positive effects on perceived sleep quality/efficiency, and for the alleviation of depressive symptoms. It is unclear, however, whether these benefits are mediated primarily by ET effects on the serotonergic (5-HT) system. A better understanding of distinc pathways for the effects of ET could lead to the development of more precise treatment alternatives. This study examines the effects of Acute Tryptophan Depletion (ATD) paradigm (Figure 1) on mood, VMS and sleep in women treated with transdermal estradiol (E2). **Design:** Symptomatic midlife women (N=23) on ET (transdermal estradiol [E2],100µg/day) for 8 weeks were then randomized to ATD or sham drink. Sleep (Pittsburgh Sleep Quality Index [PSQI]), Mood (Profile of Mood States [POMS]), and vasomotor symptoms (Hot Flash Related Daily Interference Scale [HFRDIS]) were assessed pre- and post-ATD or Sham. Actigraph was employed for 72 hours post-test. Measurements were repeated (crossover fashion) after a washout period. **Results:** Subjects were in midlife years (mean age= 51.9 [SD 4.1] years), mostly Caucasian (73.9%), and peri-postmenopausal based on menstrual history and FSH levels (mean FSH= 59.0, SD 33.2). Use of ET resulted in improved mood, as well as reduction of VMS (84.9%, p<0.001) and sleep improvement (39.6%, p<0.001). Mood symptoms were slighlty affected by ATD. Neither VMS nor sleep patterns showed significant changes. Actigraph measures for sleep onset latency, sleep efficiency and WASO also did not reveal differences between ATD and sham. **Conclusion:** There was a slight worsening of mood after ATD, consistent with the hypothesis that ET might be 'beneficial' to mood through its modulatory effects on 5-HT synthesis, metabolism, and receptor density/activity. The benefits of ET for VMS and sleep were not adversely affected by ATD. These findings suggest that the positive effects of estradiol on VMS and sleep might be exerted through other, distinct pathways other than 5-HT system. Ongoing research using the acute phenylalanine/tyrosine depletion (APTD) will clarify potential roles of dopamine and norepinephrine in this process.

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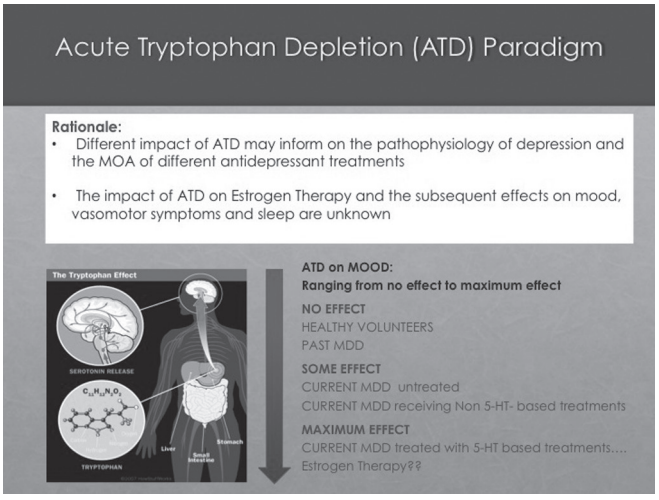

P-72.

Cortisol Response to Acute Stress in Midlife Women with Vasomotor Symptoms

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Objective: Hot flashes and night sweats, or vasomotor symptoms (VMS), have been linked with altered diurnal cortisol secretion patterns in midlife women. These patterns are similar to those observed in individuals with insomnia. While resting-state cortisol levels have been investigated in women with VMS, previous studies have not examined if the presence of VMS also leads to perturbed cortisol release in response to acute stressors. Individuals with underlying chronic stress conditions (such as PTSD and depression) have been found to have both abnormally blunted and hyper-reactive cortisol release related to experimentally induced stress. Because women with significant VMS have more psychological distress and report more stress, we examined whether women with VMS also experience abnormal cortisol release patterns in response to an acute experimental stress paradigm compared to women without VMS. We also investigated if abnormal cortisol response was intensified by the presence of insomnia as these conditions are frequently linked. **Design:** 37 midlife women completed the Montreal Imaging Stress Task (MIST), a stress paradigm derived from the Trier Mental Challenge Test that includes a computerized arithmetic task combined with a social evaluative threat. 27 (73%) women reported VMS (mean 12.9 VMS events per 24hr) during screening and 10 (27%) reported none or <1 VMS event per 24 hours. All subjects completed questionnaires assessing insomnia (ISI), depressive (PHQ-8), and anxiety symptoms (HAM-A). Before and after completing the task, salivary cortisol, blood pressure, heart rate, and acute psychological responses (frustration, stress, anxiety, pain, comfort, calm, confidence) on a Visual Analog Scale (VAS) were measured. Within-person change in each of these measures was compared between those with and without VMS using Student's t-tests. To examine the impact of comorbid insomnia (defined as ISI>=14, threshold score for clinical insomnia), we also examined differences between subjects without VMS (n=10), with VMS but no insomnia (n=16), and with both VMS and insomnia (n=11) using the non-parametric test for trend between the 3 groups. **Results:** Women with VMS had a smaller cortisol change in response to the MIST stress task compared to women without VMS (mean: 0.02 μg/dl, 54% increase vs 0.07 μg/dl, 83% increase, p=0.039, respectively). Mean baseline cortisol did not differ between those with and without VMS (0.1 μg/dl vs. 0.09 μg/dl; p=0.74). Time of day, and time from wake had no significant effect on baseline cortisol or cortisol response. Women with VMS had a diminished stress response on all VAS items, particularly on domains of confidence (p=0.08) and calm feelings (p<0.01) compared to women without VMS. When the VMS group was divided according to the presence or absence of insomnia symptoms, women with both VMS and insomnia had the smallest cortisol elevation in response to the acute stressor (mean cortisol increase 0.01 vs. 0.03 vs. 0.07 μg/dl for VMS plus insomnia vs. VMS but no insomnia vs. no VMS/no insomnia, respectively; p=0.09). Women with VMS also reported higher depressive (PHQ-8, p<0.01) and anxiety symptoms (HAM-A, p<0.01). No group differences were observed in cardiovascular responses to the task. **Conclusion:** Results of this study show that women with VMS have a blunted acute response to a cognitive and social stressor task. This association was more pronounced when VMS were comorbid with insomnia symptoms. These findings suggest that chronic exposure to VMS is associated with an abnormal adrenal acute stress response, similar to that observed in people with other chronic stress conditions such as PTSD.

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P-73.

Lipoperoxide levels increase and superoxide dismutase decreases, as oxidative stress biomarkers, with hot flashes severity after menopause

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Objective: To determine the relationship among different oxidative stress biomarkers and the hot flashes severity in postmenopausal women. **Design:** We carry out a cross-sectional study with 90 postmenopausal women of Mexico City, 48-57 yr (52.2±3.5 yr). We measured plasma lipoperoxides (LPO) by the TBARS assay, erythrocyte superoxide dismutase (SOD) and glutathione peroxidase (GPx), and total plasma antioxidant status with Randox kits, all as oxidative stress biomarkers. The hot flashes were evaluated by Hot Flush Weekly Weighted Score, developed and evaluated by Sloan J et al., and strengthen the concepts pictorially. In this test, the amount and intensity of the hot flashes in 24 hours, during 1 week, were registered by each woman. For the evaluation, we classified 5 categories of hot flashes intensity (0= no, 1= mild, 2= moderate, 3= severe and 4= very severe), we added the total of hot flashes per day, and then we multiplied each category by the number of times that was presented to the week. After, we obtained the scores and it was stratified into 3 groups per the intensity of the hot flashes as: mild (<17), moderate (17-59) and severe ≥60). **Results:** A positive correlation between LPO and hot flashes score was observed (r=0.342, p<0.05) [Figure A] and, a negative correlation between SOD and the test score (r=-0.286, p<0.05) [Figure B]; other oxidative stress markers were not related. LPO levels increase with hot flashes severity (mild 0.309±0.06, moderate 0.351±0.07 and severe 0.372±0.06 μmol/L, p<0.05) and SOD activity diminished (mild 1.29±0.13, moderate 1.19±0.11 and severe 1.16±0.07 U/gHb, p<0.05). **Conclusion:** Our findings suggest that LPO levels increase and SOD activity decreases with the severity of hot flashes, showing high oxidative stress in postmenopausal women with severe hot flashes.

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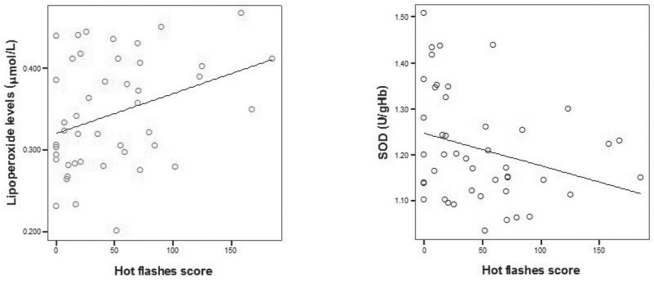

Figure. A. Correlation between lipoperoxides levels and hot flashes score; B. SOD and hot flashes score.