ABSTRACT PRESENTATIONS

THURSDAY CONCURRENT SESSION #1

S-1.

Odanacatib Efficacy and Safety in Postmenopausal Women with Osteoporosis: 5-Year Data from the Extension of the Phase 3 Long-term Odanacatib Fracture Trial (LOFT)

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Objective: Odanacatib (ODN) is a selective oral inhibitor of cathepsin K in development for the treatment of osteoporosis. The randomized, double-blind, placebo (PBO)-controlled, event-driven, Phase 3 Fracture Trial (Long-Term Odanacatib Fracture Trial [LOFT]; NCT00529373) evaluated efficacy and safety of ODN in postmenopausal women with osteoporosis. In a planned double-blind extension to LOFT, eligible patients continued on their originally assigned treatment for up to 5 years. We present efficacy and safety data for the entire 5-year double-blind period. **Design:** Women ≥65 years of age with BMD T-score ≤–2.5 at total hip (TH) or femoral neck (FN), or with radiographic vertebral fracture (VFx) and T-score ≤–1.5 at TH or FN, were randomized (1:1) to ODN 50 mg/week or PBO. All received vitamin D_3 (5600 IU/week) and calcium as required. Endpoints included morphometric VFx, hip fracture, non-VFx, clinical VFx, and safety and tolerability. Specific adverse events (AEs) were adjudicated. **Results:** Of 16,071 patients (8043 ODN, 8028 PBO) in LOFT, 12,290 (6092 ODN, 6198 PBO) completed the study. Among these, 8,257 (4297 ODN, 3960 PBO) who were eligible and consented entered the extension and 6,047 (3432 ODN, 2615 PBO) completed it. Mean (SD) age at randomization was 72.8 (5.3) years, 46.5% had prior VFx, and mean BMD T-scores were lumbar spine (LS) –2.7, TH –2.4, and FN –2.7. Mean (SD) follow-up was approximately 44 (18) months. Compared with PBO, ODN treatment over 5 years resulted in relative risk reductions of 52% for morphometric VFx, 48% for hip fracture, 26% for non-VFx, and 67% for clinical VFx (all p<0.001). Compared with PBO, ODN treatment led to progressive mean percent increases (95% CI) in BMD of 10.9% (10.5, 11.2) at LS and 10.3% (10.0, 10.6) at TH (both p<0.001) at 5 years. Incidences of AEs and serious AEs overall were balanced for ODN vs PBO (88.3 vs 88.2% and 30.3 vs 30.4%, respectively). Deaths reported in patients being followed on study were 378 (4.7%) vs 327 (4.1%), ODN vs PBO, respectively (HR 1.12 [95% CI: 0.97, 1.30]); more complete ITT analysis of deaths among all patients, including those who discontinued from study, showed 682 (8.5%) vs 660 (8.2%), respectively (HR 1.04 [95% CI: 0.93, 1.16]). Delayed fracture union occurred in 18 patients in each group. Femoral shaft fractures occurred more often with ODN (26 patients [0.3%] vs 7 [0.1%]), of which 10 (0.1%) on ODN and none on PBO met criteria for atypical femoral shaft fractures (AFFs). No cases of osteonecrosis of the jaw (ONJ) were confirmed. Morphea-like skin lesions occurred more often with ODN (13 [0.2%] vs 3 [<0.1%]), most with onset within 2 years and all improved or fully recovered. Systemic sclerosis occurred in 2 (<0.1%) with ODN vs 1 (<0.1%) with PBO. Independent adjudication of CV events is ongoing and will be presented. **Conclusion:** Consistent with the results of LOFT, treatment with ODN for up to 5 years reduced the risk of hip, vertebral and non-vertebral fractures. Overall incidence of AEs, including serious AEs, was generally balanced between ODN and PBO. Femoral shaft fractures, including AFFs, and morphea-like skin lesions were uncommon but more frequent with ODN.

Sources of Funding: This study was sponsored by Merck & Co., Inc., Kenilworth, NJ, USA

S-2.

Women's Health Initiative Clinical Trials: The Interactive Effect of Calcium and Vitamin D Supplementation with Hormonal Therapy on Cardiovascular Events and Venous Thromboembolism

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Objective: Evidence from limited data suggests that calcium and vitamin D (CaD) at moderate to high doses may reduce cardiovascular disease (CVD) risk. Using randomized trial data we analyzed if the effect of menopausal hormone therapy (HT) on various cardiovascular disease events is enhanced by calcium and vitamin D (CaD) supplementation. **Design:** A prospective, randomized, double-blind, placebo controlled trial was implemented among Women's Health Initiative (WHI) postmenopausal women. A total of 27,347 women were randomized to the HT trials (0.625 mg/d of conjugated equine estrogens [CEE] alone for women without a uterus or 0.625 mg of CEE in addition to 2.5 mg of medroxyprogesterone acetate daily [CEE+MPA] for women with a uterus versus placebo). After 1 year, 16, 089 women in the HT trial were randomized to the CaD trial to receive either 1,000 mg of elemental calcium carbonate plus 400 IU of vitamin D3 daily or placebo. The mean (SD) duration of follow-up after CaD randomization were 6.2(1.3) and 4.6(1.1) years, respectively. CVD events analyzed in this subgroup analysis include coronary heart disease (CHD), stroke, pulmonary embolism, all-cause mortality, plus select secondary endpoints (total myocardial infarction, coronary revascularization, deep venous thrombosis, cardiovascular death, and all CVD events). The time-to-event methods were used and models were fit with a Cox proportional hazards regression model. **Results:** In the CEE trial, CaD did not significantly modify the effect of CEE on most CVD outcomes but did modify its effect on cardiovascular death (p-interaction = 0.03). In the CaD-placebo group, the effect of CEE on cardiovascular death was somewhat harmful (HR [95%CI] = 1.47[0.86, 2.53]); in the CaD-supplement group, the effect of CEE was somewhat beneficial (HR [95%CI] = 0.57[0.29, 1.10]), see figure 1. Similar results were found for CHD deaths, which account for the majority of the cardiovascular deaths (52 of 92; p-interaction=0.04). We did not observe significant CEE x CaD interactions for CHD, total CVD events, or any of the remaining endpoints. Contrary to the CEE trial, there was no evidence that the effect of CEE+MPA on cardiovascular death or other CVD endpoints was modified by the CaD-supplementation (p-interaction = 0.24), see figure 2. Moreover, hazard ratios were in the opposite direction of those observed in the CEE trial. **Conclusion:** Calcium and vitamin D supplementation did not consistently modify the effect of CEE therapy on CVD events, but did appear to modify its effect on CVD death. The effect of CEE (active vs. placebo) on CVD death was favorable among women randomized to CaD supplement use but unfavorable among those randomized to CaD-Placebo. While CaD significantly modified the effect of CEE on cardiovascular death (p-interaction = 0.03), these differences were not individually significant. CaD did not significantly modify the effect of CEE+MPA on CVD death or any CVD events. Additional research on potential interactions between CaD and HT is warranted.

Sources of Funding: None

S-3.

Early Age at Natural Menopause is a Risk Factor for Type 2 Diabetes: The Rotterdam Study

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Objective: Early onset of natural menopause has been associated with adverse cardiometabolic health, but little is known about the association between age at natural menopause and the risk of type 2 diabetes (T2D). We aimed to examine the association between age at natural menopause and the risk of T2D. **Design:** Data of 3234 postmenopausal women participants of the Rotterdam Study (RS), a prospective population based cohort, were available. Age at natural menopause was self-reported. T2D events were diagnosed on the basis of medical records. Relative risks (RRs) and 95% Confidence Intervals (CIs) were calculated using Cox proportional hazards models. **Results:** During a median follow-up of 10.9 years, we identified 319 incident cases of T2D in the RS. After adjustment for age, hormone replacement therapy, socioeconomic status, smoking, alcohol intake, total cholesterol levels, blood pressure and prevalent cardiovascular disease, hazard ratios (HRs) of T2D were 2.29 (95% CI 1.35–3.88), 1.49 (1.06–2.11) and 0.70 (0.41–1.21) for women with premature (<40 years), early (40-44 years) and late menopause (>55), respectively, relative to those with normal age at menopause (45–55 years). The HR per SD (4.4 years) younger age at natural menopause was 1.20 (1.09-1.33). Further adjustment for body mass index, insulin, glucose,

C-reactive protein and sex hormone levels did not affect these associations. **Conclusion:** Early age at natural menopause is associated with increased risk of T2D independent of intermediate risk factors and sex hormone levels. Future studies are needed to identify the underlying mechanisms so that novel prevention strategies for midlife women can be considered.

Sources of Funding: Metagenics.Inc

S-4.

Estrogen-alone Therapy and Invasive Breast Cancer Incidence by Dose, Formulation, and Route of Delivery: Findings from the WHI Observational Study

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Objective: In the WHI clinical trial, conjugated equine estrogens (CEE-alone) was not associated with an increase in invasive breast cancer but possibly protective (RR 0.79, 95% CI 0.65-0.97). Relations between this finding and other doses or formulations of estrogen-alone are unexplored. Using the large-scale WHI observational study (WHI-OS), we analyzed the relationship between different estrogen doses, routes of delivery and formulations of hormone therapy (HT) in postmenopausal women with a hysterectomy in relation to risk of invasive breast cancer. **Design:** The WHI-OS is a large multi-center prospective cohort study at 40 US sites. 93,676 postmenopausal women, aged 50-79 years were recruited between September 1993 - December 1998, with annual follow-up through September 2005. Women with a history of breast cancer or no mammogram within 2 years of baseline were excluded. Breast cancer events were defined as invasive breast cancer confirmed by physician adjudicators. Information about HT was obtained by self-report. Statistical analysis was performed using Cox regression and adjusted for age, race or ethnic group, smoking, physical activity, treated diabetes, oophorectomy (no, partial, bilateral), education and household income, alcohol consumption, parity, cumulative frequency of mammography, Gail score for breast cancer, prior HT use. **Results:** At baseline, 26,525 (44%) of the study sample had a hysterectomy and of those 16,627 (63%) were using estrogen-alone. At baseline, 12,812 (77%) of women were using oral CEE of which, 846 (2%) was low-dose (<0.625mg), 1,126 (7%) women were using oral estradiol and 1,134 (7%) using transdermal estrogen. Average follow up was 8.2 years. Overall, the absolute risk of invasive breast cancer was 43 per 10,000 person-years. For CEE users, no difference was observed between low-dose CEE compared to conventional-dose CEE (0.625mg) for breast cancer events [HR 0.99 (95% CI 0.65, 1.48)]. Compared to conventional-dose CEE, transdermal estrogen was associated with a non-significant lower risk of invasive breast cancer [HR 0.75 (0.47, 1.19)]. Power was limited for this comparison as well as for a comparison of oral estradiol to conventional-dose of CEE [HR 1.20 (95% CI 0.84, 1.39)]. **Conclusion:** Our results indicate that invasive breast cancer risk did not differ appreciably when comparing low-dose to conventional-dose CEE. We did not observe differences in invasive breast cancer risk between oral estradiol or transdermal estradiol compared to conventional-dose oral CEE but power was limited. Future analyses will include longer follow-up and evaluate differences by time since menopause and duration of estrogen use.

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S-5.

Arterial stiffening across the stages of the menopause transition is associated with menopausal symptoms, depression, and quality of life

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Objective: The menopause transition is associated with multiple somatic symptoms and greater rates of depression which can affect quality of life and increase the risk of cardiovascular disease (CVD). The menopause transition is also associated with an acceleration in large elastic arterial stiffening, an antecedent to CVD. We sought to determine whether depression, menopausal symptoms and quality of life are associated with arterial stiffening across the stages of menopause in healthy women. **Design:** Participants included 123 women (19-70 years) classified as premenopausal (n=35, 34±8 years; mean ± SD), early perimenopausal (n=25, 49±3 years), late perimenopausal (n=24, 50±4 years) or postmenopausal (n=39, 58±5 years). Arterial stiffness (compliance) was measured via carotid artery ultrasound. Questionnaires included the Menopausal Symptom List (frequency and severity of psychological, vasosomatic and general somatic symptoms), Center for Epidemiologic Studies Depression Scale (CES-D), and Utian Quality of Life Scale (occupational, health-related, emotional, sexual, and total). **Results:** Psychological, vasosomatic, general somatic and depressive symptoms, and health-related, sexual and total quality of life differed across menopausal stages (all p<0.05). Compared to premenopausal, early perimenopausal and postmenopausal women, late perimenopausal women reported the most frequent and severe menopausal symptoms, highest depressive symptoms, and lowest qualify of life. Vasosomatic and general somatic symptoms were inversely correlated with carotid artery compliance (r = 0.23-0.30; p <0.05), whereas health-related, sexual and total quality of life were positively correlated with carotid artery compliance (r = 0.19-0.27; p<0.05). CES-D scores were not correlated with carotid artery compliance (r = -0.14; p=0.14). **Conclusion:** The menopause transition appears to be a vulnerable period for somatic and psychosocial symptoms, particularly in the late perimenopausal stage. These somatic and psychosocial symptoms were associated with large artery stiffening (i.e. reduced carotid artery compliance) across the stages of menopause that could contribute to increased CVD risk in women. Potential mechanisms underlying these associations such as inflammation and oxidative stress should be explored in future studies.

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THURSDAY CONCURRENT SESSION #2

S-6.

TX-004HR Improves Vaginal Physiology and Dyspareunia with Negligible Systemic Absorption

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Objective: TX-004HR, an investigational, applicator-free, low-dose vaginal softgel capsule containing solubilized 17β-estradiol (E2), was designed to rapidly and effectively treat symptoms of VVA without increasing serum E2 levels and to provide easy insertion and complete dissolution, thus minimizing vaginal discharge. The primary objective of this analysis was to assess the effect of patient characteristics (i.e., age, BMI, and uterine status) on the efficacy of TX-004HR. **Design:** The REJOICE trial was a randomized, double-blind, placebo-controlled, multicenter, phase 3 study of 4 µg, 10 µg, and 25 µg TX-004HR in postmenopausal women (40-75 years) with VVA and a self-identified most bothersome symptom of moderate-to-severe dyspareunia. Each dose was compared with placebo for change from baseline to week 12 in the percentages of vaginal superficial cells and parabasal cells, vaginal pH, and severity of dyspareunia (co-primary endpoints). The proportion of responders (defined as women with ≥2 of the following at week 12: vaginal superficial cells >5%, vaginal pH <5.0, ≥1 category improvement from baseline dyspareunia score) was compared in TX-004HR groups vs placebo. Pre-specified subgroup analyses of co-primary endpoints were analyzed by age (≤56 years, 57-61 years, and ≥62 years), BMI (≤24 kg/m^2, 25-28 kg/m^2, and ≥29 kg/m^2), uterine status, parity, and vaginal births. Pharmacokinetic (PK) parameters were compared with placebo in a sub-analysis of the main study. **Results:** The proportion of responders was significantly higher for all TX-004HR dose groups vs placebo (p<0.0001 for all). All TX-004HR doses vs placebo significantly improved percentage of superficial and parabasal cells, vaginal pH, and severity of dyspareunia at 12 weeks. Subgroup analyses showed generally similar results for percentage of superficial and parabasal cells and vaginal pH irrespective of age, BMI, uterine status, parity, and vaginal births. Severity of dyspareunia was significantly reduced at 12 weeks with all TX-004HR doses vs placebo in most subgroups (Table). The PK sub-analysis (n=72) found AUC and C_{avg} parameters for E2 and estrone (E1) with 4 µg and 10 µg TX-004HR to be similar to placebo. Increases occurred in E2 AUC and C_{avg} with 25 µg vs placebo but remained within the normal postmenopausal range. E2 levels at day 84 were similar between the TX-004HR groups and placebo, indicating no systemic drug accumulation. **Conclusion:** All doses of TX-004HR were associated with robust efficacy and demonstrated a statistically significant difference vs placebo for increasing superficial cells, decreasing parabasal cells and vaginal pH, and reducing the severity of dyspareunia. Age, BMI, uterine status, parity and vaginal births generally did not affect TX-004HR efficacy. These results occurred with negligible systemic absorption of TX-004HR estradiol doses of 4 µg, 10 µg, and 25 µg. Together, the subgroup and responder analyses demonstrate a consistency of TX-004HR's effect with up to 12 weeks of treatment.

Sources of Funding: TherapeuticsMD

Table. Change from baseline to week 12 in the severity of dyspareunia (LS mean change ± SE).

Key clinical factors		Placebo (n=187)		TX-004HR 4 µg (n=186)		TX-004HR 10 µg (n=188)		TX-004HR 25 µg (n=186)	
Age, years	≤56	n=52	-1.25 ± 0.119	n=50	-1.58 ± 0.122	n=61	-1.77 ± 0.112†	n=65	-1.86 ± 0.108‡
	57-61	n=53	-1.39 ± 0.118	n=50	-1.42 ± 0.121	n=49	-1.63 ± 0.121	n=47	-1.79 ± 0.125†
	≥62	n=58	-1.19 ± 0.122	n=51	-1.52 ± 0.126	n=44	-1.66 ± 0.138†	n=47	-1.38 ± 0.135
BMI, kg/m^2	≤24	n=56	-1.14 ± 0.115	n=58	-1.48 ± 0.113†	n=56	-1.6 ± 0.117†	n=51	-1.72 ± 0.123‡
	25 to 28	n=57	-1.48 ± 0.118	n=45	-1.51 ± 0.131	n=52	-1.78 ± 0.124	n=58	-1.77 ± 0.117†
	≥29	n=50	-1.21 ± 0.125	n=48	-1.56 ± 0.125	n=46	-1.71 ± 0.129†	n=50	-1.57 ± 0.124*
Uterine status	Intact	n=101	-1.35 ± 0.086	n=82	-1.66 ± 0.095*	n=84	-1.74 ± 0.095†	n=85	-1.81 ± 0.094‡
	Non-intact	n=62	-1.15 ± 0.115	n=69	-1.35 ± 0.108	n=70	-1.63 ± 0.108†	n=74	-1.55 ± 0.107*
Pregnancy status	Pregnancy = 0	n=16	-1.18 ± 0.220	n=17	-1.28 ± 0.217	n=19	-1.26 ± 0.209	n=13	-1.64 ± 0.257
	Pregnancy ≥ 1	n=147	-1.28 ± 0.073	n=134	-1.55 ± 0.075*	n=135	-1.74 ± 0.076‡	n=146	-1.70 ± 0.073‡
Vaginal births	Vaginal birth = 0	n=26	-1.19 ± 0.171	n=22	-1.74 ± 0.189*	n=29	-1.68 ± 0.161*	n=31	-1.76 ± 0.160*
	Vaginal birth ≥ 1	n=121	-1.30 ± 0.080	n=112	-1.51 ± 0.082	n=106	-1.77 ± 0.085‡	n=115	-1.69 ± 0.082‡

*p<0.05; †p<0.01; ‡p<0.001; §p<0.0001 vs placebo.

S-7.

The Care Experience for Genitourinary Syndrome of Menopause in Primary Care and Gynecology Clinics

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Objective: Nearly 50% of postmenopausal women experience symptoms related to genitourinary syndrome of menopause (GSM) including vulvovaginal dryness and irritation, painful intercourse, and lower urinary tract symptoms. As part of a clinician-focused intervention to improve diagnosis and management of GSM at Kaiser Permanente Northwest, we conducted an on-line survey of women with a well-woman visit to primary care (PC) and gynecology (GYN) to assess patient health care experience related to vulvovaginal, urinary, and sexual symptoms. **Design:** All female health plan members ≥ 55 years old with a well-woman visit to PC or GYN between March and October, 2015 were identified using the electronic medical record. Within one week alll eligible women were emailed a survey invitation. As well as questions regarding medical and prescription history, and vulvovaginal, urinary, and sexual symptoms; the survey also assessed the clinician-patient communication on these topics. We asked whether the patient and clinician had discussed each type of symptom, and if so, who started the conversation and whether the patient was satisfied with the conversation. If women had not discussed the symptom, we asked if they wished they had discussed the topic and if so, we asked why the topic wasn't discussed. **Results:** Of the 7,625 eligible women, 78% (5,915) had a working email address; the final survey response rate was 26% (1,546/5,915). Thirteen respondents who had been seen by study clinicians were dropped from the analysis resulting in a total analytic sample of 1,533. The majority of respondents were seen by PC (83%; PC=1,273 vs. GYN=260). Approximately 22% of women reported that they discussed vulvovaginal symptoms (VV) with their clinician, but this varied significantly by clinician type (PC=15%, GYN=54%, p<.001). Most women reported that they started the conversation (51%), while the clinician started the conversation for 28% of respondents. Most women (83%) were satisfied or very satisfied with the conversation, women seen in GYN were more likely to be "very satisfied" (56%) while women seen in PC were more likely to be "satisfied" (67%; p<.001). Urinary symptoms were discussed during the visit by 21% of women, and this varied significantly by clinician type (PC=20%, GYN=27%, p=.01). Respondents reported that they and their clinician started the conversation at about the same rate (patient 43%, clinician 40%). Most women (77%) were satisfied or very satisfied with the conversation; women seen in GYN were more likely to be "very satisfied" (58%) than women seen in PC (38%, p=.0581). Approximately 14% of women reported that they discussed sexual health symptoms with their clinician, but this varied significantly by clinician type (PC=9%, GYN=38%, p<.001). Overall, the respondents reported that they started the conversation (42%) about the same percent of the time as the clinician did (39%). However, this varied significantly by clinician type with the GYN clinicians starting the conversation 51% of the time, while PC clinicians started the conversation 28% of the time (p=.006). Most women (80%) were satisfied or very satisfied with the conversation, women seen in GYN were more likely to be "very satisfied" (61%) while women seen in PC were more likely to be "satisfied" (42%; p=.002). Only 8% of women who did not discuss VV symptoms wished that they had, with a similar percentage (7%) wishing they had discussed sexual symptoms. A higher percentage (14%) of women who didn't discuss urinary symptoms wished that they had. For all symptom types, the two most commonly reported reasons were "I forgot or chose not to bring them up" (VV 48%, urinary 62%, sexual 45%) and "My provider didn't bring them up" (VV 42%, urinary 35%, sexual 49%). **Conclusion:** In our health system, postmenopausal women who attend a well woman visit with their primary care clinician are much less likely to receive attention for GSM and are less satisfied with the conversation than women who see a gynecologist. With the growing national shortage of primary care clinicians, women may be best served by ongoing periodic visits with a gynecologic clinician.

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S-8.

Significant Improvement in Vaginal Epithelium with TX-004HR in Postmenopausal Women with Moderate-to-Severe Vulvar and Vaginal Atrophy (VVA) and Dyspareunia

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Objective: TX-004HR is an investigational, applicator-free, low-dose vaginal softgel capsule containing solubilized 17β-estradiol (E2). TX-004HR was designed to rapidly and effectively treat all symptoms of VVA without increasing serum E2 levels, and to provide easy insertion and complete dissolution to minimize discharge. The REJOICE trial has demonstrated that TX-004HR significantly and clinically improved VVA and its symptoms by increasing vaginal superficial cells, decreasing parabasal cells, and vaginal pH, and reducing dyspareunia severity, vaginal dryness, and itching or irritation, with negligible to very low systemic E2 absorption. The current objective is to assess the effects of TX-004HR on the vaginal epithelium of postmenopausal women with moderate-to-severe VVA and dyspareunia in a large phase 3 study. **Design:** The REJOICE trial was a 12-week, phase 3, multi-center, randomized, double-blind, placebo-controlled study of TX-004HR (4 µg, 10 µg, and 25 µg), which enrolled healthy postmenopausal women (aged 40-75) with moderate-to-severe VVA and dyspareunia. Treatments were self-administered vaginally, once daily for 2 weeks and then twice weekly for 10 weeks. Visual evaluation of the vaginal epithelium, a secondary endpoint of the trial, was performed during gynecological examinations at baseline and weeks 2, 6, 8, and 12. A four-point score (0 = none, 1 = mild, 2 = moderate, 3 = severe) was used to assess changes in vaginal color, vaginal epithelial integrity, vaginal epithelial surface thickness, and vaginal secretions. Change from baseline to each time point was compared with placebo using the mixed effect model repeat measurement (MMRM) analysis. **Results:** At baseline, women had mean scores of 1.8 for vaginal color, 1.5 for epithelial integrity, 1.9 for epithelial surface thickness, and 1.7 for secretions. These scores were consistent with moderate VVA reflecting pallor, diminished vaginal wall integrity and thickness, and secretions. Significant improvements from baseline at weeks 2, 6, 8 and 12 (Table) were observed for all 3 doses of TX-004HR compared with placebo in vaginal color (white to pink), epithelial integrity, epithelial surface thickness and secretions (p<0.001 for all). After 12 weeks, women in the active TX-004HR treatment groups had mean scores less than 1 in all four characterized categories. **Conclusion:** Vaginal visual examination of women in the 3 TX-004HR groups had greater reported improvements from baseline in all vaginal parameters examined than placebo subjects and at all time points. These improved vaginal visual scores support the observed efficacy of TX-004HR (4 µg, 10 µg, and 25 µg) at treating moderate-to-severe VVA in postmenopausal women, with negligible to very low systemic E2 absorption.

Sources of Funding: TherapeuticsMD

Change from baseline at week 12 in vaginal parameters

Vaginal Parameters, mean (SD)		TX-004HR 4 µg (n=171)	TX-004HR 10 µg (n=173)	TX-004HR 25 µg (n=175)	Placebo (n=175)
Vaginal color	Baseline	1.8 (0.61)	1.7 (0.59)	1.8 (0.60)	1.7 (0.64)
	12 weeks	0.8 (0.67)	0.7 (0.64)	0.8 (0.68)	1.2 (0.80)
	Change	-1.0 (0.82)	-1.1 (0.80)	-1.0 (0.88)	-0.6 (0.83)
	LS Mean (SE)	-0.97 (0.05)*	-1.06 (0.05)*	-0.96 (0.05)*	-0.60 (0.05)
Vaginal epithelial integrity	Baseline	1.6 (0.84)	1.4 (0.83)	1.5 (0.77)	1.5 (0.84)
	12 weeks	0.5 (0.69)	0.4 (0.57)	0.5 (0.66)	0.9 (0.91)
	Change	-1.0 (0.93)	-1.0 (0.89)	-1.0 (0.91)	-0.6 (0.98)
	LS Mean (SE)	-0.97 (0.05)*	-1.07 (0.05)*	-1.01 (0.05)*	-0.60 (0.05)
Vaginal epithelial surface thickness	Baseline	1.9 (0.67)	1.8 (0.63)	1.9 (0.59)	1.9 (0.65)
	12 weeks	0.9 (0.66)	0.8 (0.63)	0.9 (0.69)	1.3 (0.85)
	Change	-1.0 (0.76)	-1.0 (0.79)	-0.9 (0.80)	-0.6 (0.82)
	LS Mean (SE)	-0.98 (0.05)*	-1.03 (0.05)*	-0.94 (0.05)*	-0.61 (0.05)
Vaginal secretions	Baseline	1.8 (0.68)	1.7 (0.66)	1.7 (0.63)	1.8 (0.63)
	12 weeks	0.8 (0.69)	0.6 (0.67)	0.7 (0.71)	1.1 (0.84)
	Change	-1.0 (0.82)	-1.0 (0.86)	-1.0 (0.85)	-0.7 (0.79)
	LS Mean (SE)	-1.01 (0.05)*	-1.06 (0.05)*	-1.04 (0.05)*	-0.64 (0.05)

Data is mean (SD) unless otherwise noted; *MMRM p<0.0001 vs placebo.

S-9.

Effect of daily intravaginal 0.50% prasterone on pain at sexual activity due to vulvovaginal atrophy

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Objective: Analyse the effects of intravaginal prasterone in the clinical trials performed in women suffering from vulvovaginal atrophy (VVA). **Design:** In three independent prospective, randomized, double-blind and placebo-controlled clinical trials, the effect of daily intravaginal 0.50% (6.5 mg) prasterone administered for 12 weeks was examined on four co-primary objectives according to the FDA guidance in women having moderate to severe (MS) pain at sexual activity (dyspareunia) identified as their most bothersome symptom (MBS). **Results:** In 436 women treated with 0.50% prasterone and 250 women who received placebo, a 35.1% decrease in the percentage of parabasal cells over placebo (p<0.0001), a 7.7% increase in the percentage of superficial cells over placebo (p<0.0001) and a 0.72 pH unit decrease in vaginal pH over placebo (p<0.0001) was observed. The severity score of MBS dyspareunia was decreased by 0.46 unit (49% over placebo) (p<0.0001). The severity score of MS vaginal dryness, on the other hand, decreased by 0.31 unit (p<0.0001 over placebo). A very positive evaluation was recorded of the acceptability of the technique of application of the ovule using an applicator while the male partners gave a very positive evaluation of the changes noted in their sexual relationship. **Conclusion:** The efficacy data demonstrate highly beneficial effects on all the VVA symptoms and signs evaluated in the absence of systemic exposure to the sex steroids in agreement with the physiology of menopause.

Sources of Funding: Endoceutics Inc.

S-10.

The EMPOWER Survey: Identifying Women's Perceptions on Vulvar and Vaginal Atrophy (VVA) and Treatments

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Objective: VVA, a component of genitourinary syndrome of menopause (GSM), affects up to two-thirds of postmenopausal women, but most symptomatic women do not receive prescription therapy. Moreover, a high level of dissatisfaction with current products on the market has been reported. The EMPOWER survey was conducted to evaluate postmenopausal women's perceptions of VVA and treatment options for symptoms. **Design:** The EMPOWER survey, conducted by Rose Research via the internet January – March 2016, assessed women's perceptions and awareness of VVA and their behaviors and attitudes associated with treatment of symptoms. A nationally representative

sample of female consumers in the US was provided by GMI, an institutional review board-approved panel source. Postmenopausal women ≥45 years of age who reported symptoms of VVA were recruited. Compensation was equivalent to ~US$10. **Results:** Respondents (N=1858) had a median age of 58 y (range 45-90). Most were white (88%), had some college education (71%) and were married (59%). The majority (81%) were not aware that VVA is a medical condition. Dyspareunia/painful intercourse and vaginal dryness were experienced concurrently by 89%, with 70% experiencing vaginal itching/irritation also. Only 7% used prescription hormone therapy (HT; local estrogen creams, tablets, inserts, or oral selective estrogen receptor modulator), while 18% were past HT users, 25% used over-the-counter treatments (moisturizers/lubricants), and half had never used any treatment. More HT users (34%) were aware of the term VVA than non-HT users (15%). Most (72%) of those who did not seek treatment had never discussed their symptoms with a health care professional (HCP), but the majority (65%) would consider using HT if properly educated, informed and if recommended. Women reported that their HCPs (mostly gynecologists) recommended HT ~25% of the time, and the majority (85%) of the discussions were initiated by the women themselves as part of the annual exam. Women who did not discuss their symptoms with an HCP felt that VVA was just a natural part of aging and something to live with (42%), were uncomfortable discussing their symptoms with their HCP (18%), or were unaware of potential treatment options for their symptoms (13%). Preferred sources of information were written material from HCPs' office (46%), questionnaires to fill out before talking with the HCP (41%), or mailed information from reliable sources such as the North American Menopause Society (33%); least preferred information sources were pharmaceutical companies and television commercials (both 13%). Of current and past HT users, the most negative attributes of products were perceived risk of systemic absorption, messiness of local creams, and the need to reuse an applicator. Current and former HT users were more familiar with the Food and Drug Administration (FDA) warning related to risks associated with estrogen use (82%) than untreated women (68%). Women consistently reported low satisfaction with available products. Half of current users reported intermittent use instead of continuous use as directed. **Conclusion:** The EMPOWER survey showed that VVA continues to be an under-recognized and under-treated condition, despite recent educational initiatives. Women who were not treated for their VVA symptoms were generally uninformed, but most were willing to try a product for symptom relief and would welcome information and treatment recommendations from their HCP, although HCPs generally do not initiate discussion on VVA. Women who used HT products reported low satisfaction and poor compliance. These facets may impact overall therapy efficacy. There is a disconnect in communication and information between HCPs and their menopausal patients. An unmet need remains for a VVA treatment that is easy to use and has an acceptable safety and efficacy profile that would facilitate interaction between HCPs and patients.

Sources of Funding: TherapeuticsMD

TOP SCORING ABSTRACT PRESENTATIONS

S-11.

Perimenopausal stage influences the prevalence of nighttime insomnia symptoms

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Objective: Perimenopause is the transition from reproductive to non-reproductive years in a women's life. During the early perimenopausal stage women begin to report sleep disturbances which are a conduit for additional health issues. This study addresses the importance of metabolic and cardiovascular risk among women suffering from insomnia. Empiric evidence consistently suggests a predisposition to insomnia in women; yet, there is a paucity of research that addresses insomnia in perimenopausal (PM) women as they transition to menopause. Our recent study reported that 31% to 42% of perimenopausal women (N=3302) had nighttime insomnia symptoms meeting the DSM-V nighttime criteria for insomnia disorder. The purpose of this study aimed to identify a stage of perimenopause when insomnia symptoms become more prevalent during the transition to menopause. This study examined the trajectory of insomnia symptoms in PM women through the transition to menopause while controlling for perimenopausal stage and number of years in each stage prior to menopause. Progression to menopause naturally and/or surgically was addressed. **Design:** A secondary analysis of 10 years of data, collected annually, from the Study of Women's Health across the Nation (SWAN) was completed, using the DSM-V criteria for insomnia disorder for nighttime impairment (any 1 insomnia symptom reported ≥ 3 per week). Descriptive analysis and repeated measures logistic regression between group and within group evaluation of change in nighttime insomnia symptoms over time were used to identify if perimenopausal stage (early vs. late), years per stage and surgical menopause (SM) in annually measured nighttime insomnia symptoms (sleep latency, wake after sleep onset, awakenings, sleep quality) influenced an insomnia disorder. **Results:** Participants (N=3302) were middle aged (45.9 + 2.69 years) diverse (African American 28%; Caucasian 50%; Asian 10%; Hispanic 12%) women, including 187 (6%) women who were identified as pre-perimenopausal or perimenopausal at baseline data collection. There is a significant difference among the perimenopausal stage groups with respect to the development of insomnia (p=0.003), with adjustment for baseline menopausal status, visit, and individual baseline sleep measures. Women that remained in the early stage were 0.82 times less likely to develop insomnia than those who progress from early to late to post-menopausal (95% CI 0.70, 0.96, p=0.015), 0.48 times less likely than those who progress from early to late to surgical menopause (95% CI 0.25, 0.94, p=0.034), 0.79 times less likely than those who progress from early to post-menopausal (95% CI 0.67, 0.93, p=0.005), and 0.65 times less likely than those who progress from early to surgical menopause (95% CI 0.51, 0.83, p<0.001). Those who progress from early to late perimenopause are 0.70 times less likely to develop insomnia disorder than those who progress from early to surgical menopause (95% CI 0.53, 0.94, p=0.016). Those who progress from early to late to post-menopausal are 0.769 times less likely to develop insomnia disorder than those who progress from early to surgical menopause (95% CI 0.63, 0.98, p=0.036). At the end of the 10 year data period women that progressed from early to late perimenopause were 3 times more likely to experience nighttime insomnia symptoms at the end of the follow-up period than at the beginning (95% CI 1.84, 5.06, p<0.001). **Conclusion:** Perimenopause predisposes women to develop nighttime insomnia symptoms with perimenopausal stage impacting the development of insomnia. Natural progression to menopause when compared to surgical progression also is protective against insomnia disorder development. Anticipatory guidance for PM women is needed to address an insomnia disorder. Providers need to routinely screen for an insomnia disorder in this high risk group. Interventions, including behavioral approaches, are needed.

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S-12.

Postmenopausal Women with Greater Paracardial Fat Have More Coronary Artery Calcification than Premenopausal Women: The Study of Women's Health Across the Nation (SWAN) Cardiovascular Fat Ancillary Study

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Objective: Cardiovascular disease (CVD) risk increases after menopause. Volumes of cardiovascular (CV) fat, shown to be associated with subclinical CVD and CVD events, are significantly higher in postmenopausal than premenopausal women. Paracardial adipose tissue (PAT), the fat outside the pericardium, has been shown to be associated with lower levels and declines of estradiol hormone, suggesting this CV fat depot as a potential menopause-specific CVD risk factor. Whether associations between CV fat depots and subclinical CVD are stronger in postmenopausal women and could be explained or modified by endogenous estradiol levels are not known. Our specific objective was to evaluate separately the cross-sectional associations of PAT and epicardial adipose tissue (EAT), the fat within the pericardium, and coronary artery calcification (CAC) in midlife women. Effect modifications by menopausal status and endogenous estradiol levels were also assessed. **Design:** Women from the SWAN cardiovascular fat ancillary study at the Pittsburgh and Chicago sites were evaluated. Volumes of CV fat depots and CAC Agatston scores were measured using electron beam computed tomography scans. CAC was evaluated as both dichotomous (presence of CAC: CAC ≥10) and continuous (extent of any CAC: log (CAC>0)) measures. CV fat volumes were log transformed to achieve normality and both linear and logistic regression modeling were used as appropriate. Final models were adjusted for study site, race, age, menopausal status, log triglycerides, systolic blood pressure, body mass index residuals, smoking status, endogenous estradiol, cycle day of the blood draw, use of medications and use of hormone therapy (HT). **Results:** The study included 478 women (38% Black, 62% White; 58% pre-/early peri-, 10% late peri-, and 32% post-menopausal) aged 46–59 years (mean (SD): 51(2.9) years). About half of the participants (n=226(47%)) had CAC scores >0 and 20% had CAC scores≥10. Both EAT and PAT were significantly associated with presence and extent of CAC in final models, P values <0.05. In models adjusted for all covariates but not estradiol and HT use, associations between PAT and presence and extent of CAC were significantly modified by menopausal status (Interaction P values: 0.0008, 0.002, respectively); such that postmenopausal women with greater volumes of PAT were more likely to have CAC presence (OR(95%CI), per 1SD increase in log PAT: 2.11(1.05, 4.24), P=0.04) and greater extent of calcification (β(SE), per 1SD increase in log PAT: 0.54(0.21), P=0.01) when compared with pre-/early perimenopausal women. Additional adjustment for estradiol level and HT use attenuated these differences. Moreover, estradiol levels significantly modified the associations between PAT and CAC extent in final models, interaction P value: 0.006; such that in the upper PAT tertile, CAC extent was significantly higher than in the lower PAT tertiles (geometric mean CAC scores 13.9 vs. 3.9, respectively, P=0.039) mainly in women with estradiol levels within the lowest estradiol tertile (≤18.65pg/ml). **Conclusion:** In midlife women, CV fat was significantly associated with presence and extent of coronary calcification independently of traditional CVD risk factors. Associations between PAT and CAC measures were stronger in postmenopausal women and in women with lower levels of estradiol. These findings suggest that paracardial fat could be a menopause-specific CVD risk factor, supporting the need to monitor and target this risk factor for intervention as women transition through menopause.

Sources of Funding: SWAN has grant support from NIH (Grants NR004061; AG012505, AG012535, AG012531, AG012539, AG012546, AG012553, AG012554, AG012495). The SWAN Heart is supported by NHLBI (Grants HL065581, HL065591). The SWAN Cardiovascular Fat Ancillary Study was supported by the AHA Great River Affiliation Clinical Research Program: 12CRP11900031.

S-13.

Changes in sexual function among midlife women: "I'm older… and I'm wiser."

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Objective: Quantitative studies indicate that many aspects of sexual function decline during midlife. However, quantitative studies may fail to capture individual women's lived experience of sexual function during midlife. Qualitative approaches that allow women to speak their own words regarding their experiences can capture nuances and individual variations in women's lived experiences of sexual function during midlife. We gathered 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. **Design:** 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. Codebook development by two investigators proceeded using an iterative process until a final codebook was agreed upon; the primary investigator then coded all data. A second investigator coded a randomly selected 10% of data and kappa scores were calculated for inter-coder reliability. Codes relating to changes in sexual function with aging were examined to identify key themes. **Results:** The mean age (N=39) was 58 (range 46-59); 53% were White, 36% were Black, and 10% were of another race. Thirteen percent were premenopausal, 44% were perimenopausal, and 28% were not sure. All but 2 women identified as heterosexual. Major themes emerged surrounding both negative and positive **changes** in sexual function, what women **attributed** these changes to, and how women **responded** to them. With regards to **changes** in sexual function, the most common *negative changes* were decreased frequency of sex, lower libido, vaginal dryness, and difficulty reaching orgasm. More women **attributed** these *negative changes* to psychosocial stressors, such as family and career, than biological factors such as menopause. For some women, partner issues, including partner health problems, relationship discord, and partner sexual dysfunction [including both erectile dysfunction (ED) and low libido] were a major source of negative sexual changes. In fact, there were several women who noted their libido was much higher than their male partner's. Among the women who reported *positive changes*, several women felt that while frequency of sexual activity had decreased, their satisfaction with sex had increased. They **attributed** these *positive changes* to higher self-confidence, increased self-knowledge, and better communication skills as they aged. When examining how women **responded** to negative changes, we identified 3 key themes: (1) indifference (small proportion of women); (2) distress (moderate proportion); and (3) adaptation (large proportion). Adaptations reported included use of vaginal lubricants, lengthening foreplay, incorporating other types of sex besides penetrative intercourse (oral and manual stimulation), trying other sexual positions, masturbating more, and encouraging use of ED treatments in their partners. Additionally, some women adapted by placing higher value on the emotional aspects of sex (such as emotional intimacy) than the physical aspects (such as achieving orgasm). **Conclusion:** Changes in sexual function, such as decreased responsiveness, vaginal dryness, lower libido, and difficulty reaching orgasm are common as women move through midlife. However, positive changes, such as increased satisfaction with sex, were also observed. Many women adapt to negative changes by modifying their expectations regarding sexual activity or changing sexual priorities in order to maintain or even increase overall sexual satisfaction. Providers who care for midlife women should ask about any changes in sexual function during routine visits. Providers should recognize that not all changes are attributable to biological changes and explore psychosocial and interpersonal factors, particularly partner sexual dysfunction or relationship discord. Providers should also recognize that women have a wide range of responses to changes in sexual function with aging, highlighting the importance of assessing not only physical sexual function, but also overall sexual satisfaction.

Sources of Funding: Agency on Healthcare Research and Quality (AHRQ) National Institute of Health's (NIH) National Heart, Lung, and Blood Institute (NHLBI)

S-14.

TX-004HR Provides Robust Efficacy for Symptomatic Postmenopausal Vulvar and Vaginal Atrophy (VVA) while Providing Negligible to Very Low Systemic Absorption of Estradiol: Results of Clinical Phase 2 and 3 Trials

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Objective: Approximately 30M US women with symptomatic VVA remain untreated. This has been reported to be due in part to concerns about estrogen exposure and its perceived risks. TX-004HR (TherapeuticsMD, Inc., Boca Raton, FL) is an investigational, applicator-free, low-dose, vaginal softgel capsule containing solubilized 17β-estradiol (E2), designed to rapidly and effectively treat symptoms of VVA without increasing serum E2 levels while providing easy insertion and complete dissolution to minimize discharge. The current objective is to present data from the TX-004HR studies that demonstrate negligible to very low systemic E2 absorption with robust efficacy data. **Design:** The REJOICE Trial was a randomized, double-blind, placebo-controlled, phase 3 study of TX-004HR 4 μg, 10 μg, and 25 μg in postmenopausal women with a self-identified most bothersome symptom of moderate-to-severe dyspareunia. Treatments were self-administered once daily for 2 weeks then twice weekly for 10 weeks. Co-primary endpoints were change from baseline in vaginal superficial and parabasal cells, vaginal pH, and severity of dyspareunia at week 12 compared with placebo, and safety. Pharmacokinetic (PK) parameters were compared with placebo. Additionally, 2 single-dose, 2-way crossover, relative bioavailability trials compared the PK of TX-004HR with FDA/EMA approved vaginal E2 tablets (10 μg and 25 μg). Estradiol PK parameters evaluated in the 3 studies are reported here. **Results:** In the phase 3 trial, all doses of TX-004HR compared with placebo (MITT n=747) significantly improved the 4 co-primary endpoints at week 2 through week 12, as well as the secondary endpoints of vaginal dryness by week 6 and vulvar and/or vaginal itching or irritation by week 12 (except 4 μg, p=0.0503), and was well-tolerated with no treatment-related serious AEs reported. The phase 3 PK study (n=72) showed no difference in systemic E2 levels for 4 μg and 10 μg TX-004HR vs placebo, as measured by AUC and C_{avg} (Table 1). E2 AUC and C_{avg} with 25 μg TX-004HR was higher than placebo, but average concentrations remained within the normal postmenopausal range (Table 1). E2 levels at day 84 were similar to placebo indicating no systemic drug accumulation. SHBG concentrations did not change with treatment. The two phase 2 studies (n=36 for each) of TX-004HR 10 μg and 25 μg resulted in statistically significantly lower E2 absorption than an approved E2 tablet at identical doses, with 25 μg TX-004HR demonstrating AUC less than 1/3 that of the approved product (Table 2). **Conclusion:** With robust efficacy demonstrated as early as 2 weeks and up to 12 weeks at all 3 doses, TX-004HR 4 μg and 10 μg showed negligible systemic E2 absorption, while 25 μg resulted in very low systemic absorption of E2 in the phase 3 trial. TX-004HR 10 μg and 25 μg showed lower systemic E2 exposure than equivalent doses of an approved E2 tablet. The absence of clinically meaningful increases in E2 concentrations paired with data consistent with a lack of systemic effects (eg no increase in SHBG) suggests that TX-004 HR delivers excellent efficacy with negligible to very low systemic exposure and thus may warrant an adjustment of estrogen class labeling.

Sources of Funding: TherapeuticsMD

Table 1. Phase 3 study PK parameters for E2 (unadjusted mean±SD).

		$AUC_{0\text{-}24}$ (pg*hr/mL)			C_{avg} (pg/mL)		
Day	Dose (μg)	TX-004HR	Placebo	p-value	TX-004HR	Placebo	p-value
1	4	91.7±37.9	117±77.3	NS	3.92±1.46	4.86±3.22	NS
	10	138±75.2	117±77.3	NS	5.76±3.13	4.86±3.22	NS
	25	217±99.0	117±77.3	0.0021	9.06±4.13	4.86±3.22	0.0021
14	4	87.2±42.8	104±66.4	NS	3.63±1.78	4.34±2.77	NS
	10	110±54.6	104±66.4	NS	4.59±2.27	4.34±2.77	NS
	25	172±80.1	104±66.4	0.0108	7.15±3.34	4.34±2.77	0.0108

Table 2. Phase 2 studies PK parameters for E2 (baseline adjusted geometric mean).

	$AUC_{0\text{-}24}$ (pg*hr/mL)			C_{max} (pg/mL)		
Dose (μg)	TX-004HR	Vaginal Tablet	p-value	TX-004HR	Vaginal Tablet	p-value
10	49.62	132.92	<0.0001	14.38	20.38	0.0194
25	89.21	292.06	<0.0001	23.08	42.70	<0.0001

FRIDAY CONCURRENT SESSION #1

S-15.

Associations between Actigraphic Sleep and Inflammatory Biomarkers in Peri- and Post-Menopausal Women

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Objective: Research suggests that sleep disturbance is associated with risk of inflammatory disease and all-cause mortality. Compared to men, women may be more vulnerable to the effects of sleep disturbance, as there is some evidence to show they have increased levels of inflammatory biomarkers with sleep disturbance. We tested whether poorer objectively measured sleep characteristics were related to a worse inflammatory profile in midlife women. **Design:** Participants included 295 midlife women (age range=40-60 years) with their uterus and at least one ovary. None of the women had a history of clinical CVD, were working night shift, or taking medications for hot flashes (e.g., estrogen, progesterone, selective serotonin/serotonin-norepinephrine reuptake inhibitors, gabapentin, clonidine), select medications impacting the cardiovascular system (beta blockers, calcium channel blockers, ACE inhibitors, insulin), or sleep (e.g., zolpidem, melatonin, Tylenol PM). Women underwent one 24 h period of sternal skin conductance monitoring overlapping with three consecutive 24 h periods of actigraphic sleep monitoring to assess sleep continuity as measured by sleep efficiency, sleep fragmentation, and wake after sleep onset (WASO). Women also underwent a fasting blood draw for assessment/assay of inflammatory markers including: C-reactive protein (CRP), interleukin-6 (IL-6), and von Willebrand factor antigen (VWF:Ag). Several variables (fragmentation, WASO, CRP, IL-6) were log transformed and sleep efficiency was inverse log transformed such that higher values indicated more inefficient sleep. Relations between sleep actigraphy and biomarkers were examined adjusting for age, education, race/ethnicity, Berlin score (measure of sleep apnea risk), body mass index (BMI), homeostatic model assessment (HOMA), systolic blood pressure, low-density lipoprotein (LDL) cholesterol, physical activity, and sleep hot flashes. **Results:** Women were on average 54 years old, overweight (BMI=29), and postmenopausal (83%). 29% were nonwhite and 51% reported hot flashes. In separate models adjustinging for age, education, and race/ethnicity; more inefficient sleep was associated with higher IL-6 [b(SE)=.02 (.10), p=.003] and VWF:Ag [b(SE)=.02 (.08), p=.002] levels. More sleep fragmentation was associated with higher IL-6 [b(SE)=.16 (.11), p=.01] and VWF:Ag

[b(SE)=.18 (.08), p=.003] levels. Higher WASO was associated with higher VWF:Ag levels [b(SE)=.12 (.06), p=.01]. Findings persisted after adjusting for BMI, Berlin score, HOMA, systolic blood pressure, LDL cholesterol, physical activity and sleep hot flashes. **Conclusion:** Greater sleep disturbance (fragmented sleep and lower sleep efficiency) were significantly associated with higher circulating levels of IL-6 and VWF:Ag, and time awake after sleep onset was significantly associated with higher circulating levels of VWF:Ag. These associations were not accounted for by traditional factors associated with markers of inflammation or sleep hot flashes. This study provides further support for a link between disturbed sleep and inflammation. It is one of the first to examine this relationship in menopausal women using actigraphy to objectively measure sleep. Future studies should examine the mechanisms that might explain this association (e.g., activation of the sympathetic effector pathway).
Sources of Funding: NIH R01HL195647 and K24HL123565 (PI: Thurston) and K23NR014008 (PI: Nowakowski)

S-16.

Sleep Characteristics and Carotid Atherosclerosis among Midlife Women

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Objective: The menopause transition can be a time of disrupted sleep as well as a time of worsening cardiovascular disease (CVD) risk for many women. Notably, short or poor sleep quality has been associated with elevated CVD risk. Despite the important changes in sleep and CVD risk occurring during the menopause transition, few studies have investigated relations between sleep and CVD risk in midlife women. We tested whether shorter objectively assessed sleep time or poorer subjective sleep quality was associated with elevated carotid atherosclerosis among midlife women. **Design:** Participants included 256 nonsmoking peri- and postmenopausal women aged 40-60 with their uterus and at least one ovary. None of the women had a history of clinical CVD, were working night shift, or were taking medications for sleep (e.g., melatonin, sedative/hypnotics, antihistamines), hot flashes (e.g., estrogen, progesterone, selective serotonin/serotonin-norepinephrine reuptake inhibitors, gabapentin, clonidine) or select medications impacting the cardiovascular system (beta blockers, calcium channel blockers, ACE inhibitors, insulin). They completed three days of wrist actigraphy, 24 hours of ambulatory sternal skin conductance hot flash monitoring, questionnaires [Pittsburgh Sleep Quality Index (PSQI), depressive symptoms, apnea symptoms], a blood draw [lipids, glucose, insulin, estradiol (E2)], and a carotid ultrasound [intima media thickness (IMT), plaque]. Associations of objectively assessed sleep time (actigraphy) and subjective sleep quality (PSQI) with IMT and plaque were tested in linear and logistic regression models. Covariates included age, race, education, body mass index, systolic and diastolic blood pressure, low density lipoprotein cholesterol, high density lipoprotein cholesterol, triglycerides, insulin resistance, medications (anti-hypertensive, anti-diabetic, lipid-lowering), apnea symptoms, depressive symptoms; and sleep hot flashes and E2. **Results:** Shorter objective sleep time was associated with significantly higher odds of carotid plaque [for each fewer hour: plaque score ≥2, odds ratio, OR (95% confidence interval, CI)=.1.58 (1.11-2.27), p=.01; plaque score=1, OR (95%CI)=.95 (.68-1.32), p=.75, relative to no plaque, multivariable]. Objective sleep time showed nonlinear relations with IMT, with the highest IMT observed among women sleeping 5-6 hours (IMT=.70mm) relative to women sleeping 6-7 hours (IMT=.66mm) [beta, b (standard error, SE)=.03(.01), p=.02, multivariable]; longer sleep (>7 hours) was not protective (IMT=.68mm). Poorer subjective sleep quality was also associated with significantly higher IMT [beta, b (standard error, SE): .004(.002), p=.03] as well as higher plaque [plaque score ≥2, OR(95% CI)=1.23 (1.09-1.40), p=.001; score=1, OR(95%CI)=1.06 (.93-1.21), p=.37, relative to no plaque] in multivariable models. Covariates, including E2, depressive symptoms, or sleep hot flashes, did not account for associations. **Conclusion:** Shorter objective sleep time and poorer subjective sleep quality were associated with increased carotid atherosclerosis among midlife women. Associations were not accounted for by CVD risk factors, mood, sleep hot flashes, or E2. Poor sleep during the menopause transition may have implications for women's cardiovascular health at midlife.
Sources of Funding: Supported by NIH/NHLBI Grants R01HL105647 and K24HL123565 (Thurston)

S-17.

Depression may be one of the strongest risk factors for coronary artery disease in women aged < 65 years: A 10-year prospective longitudinal study

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Objective: The data from a wide range of studies support depression as a risk factor for coronary artery disease (CAD). However, whether the risk may be affected by age is unknown. This objective of this study is to assess the difference in risk of developing CAD based on depression level among younger (<65) and older women (≥ 65). **Design:** Between June and August 2004, 2,082 consecutive women presenting for routine breast cancer screening mammography at four outpatient radiology facilities were invited to join the study, and 1,995 were enrolled. Each woman gave consent and completed a modified depression questionnaire with three questions: Do you often feel: 1. sad or depressed? 2. helpless? 3. Downhearted and blue? The demographic and CAD-relevant history included history of hypertension, diabetes, hypercholesterolemia, smoking, menopausal status, family history of CAD, exercise intensity, and hormonal therapy use. Baseline data were available for 1,919 who were then followed prospectively for 10 years. A similar questionnaire was mailed to each participant in the second, fourth, fifth and tenth years of the study to obtain follow-up data and record any change in CAD status. A logistic regression model was applied to assess the contribution of depression as well as other risk factors in the manifestation of CAD. **Results:** A total of 1,084 surveys were returned for the 10-year follow-up with a mean age (SD) of 54.8 (11.0) at baseline. Of 1,030 women with no history of CAD at baseline, 190 (18.4%) answered "yes" to at least one of depression questions. Of these, 17 (9.0%) developed one or more CAD events by year 10, significantly higher (p<0.001) than the 18 (2.1%) who reported "no" on the questionnaire. While examining the association of the total number of depression questions answered yes (1, 2, or 3) with the incidence of CAD by year 10, a significant trend was detected (Cochran–Armitage p<0.001). With aforementioned CAD risk factors included as covariates in a logistic regression model, depression was the only significant risk factor for CAD in women aged <65. The odds ratio (OR) for depression (OR=6.56, 95% CI 1.07-40.09, p=0.042) was not affected by age. However, in women aged ≥ 65, age was the only significant predictive factor for CAD. **Conclusion:** These data suggest that a history of depression or depressive symptoms increase the risk of CAD over 10 years of follow-up, and more prominently in women aged < 65 years.
Sources of Funding: None

S-18.

Prospective study on predictors of psychological well-being in Chinese mid-life women

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Objective: This study aimed to examine the predictors of perceived well-being in a 5-year follow-up study of a population-based sample of early postmenopausal Chinese women in Hong Kong. **Design:** From 2002 to 2004, 508 women aged 50-64 years, and within 10 years since menopause (defined as 12 months since the cessation of the last menses) were recruited through random telephone dialing. Eligible subjects were invited for face-to-face interviews and clinical examinations. A response rate of 62.5% was obtained. Interviews based on structured questionnaire on socio-demographic characteristics, medical history, self-reported symptoms (based on a 20-item check list) and life style factors were conducted at baseline (T_0), and at 3-year (T_1) and 5-year (T_2) follow-ups. Perceived stress was assessed using the 10-item perceived stress scale (PSS) developed by Cohen et al.[1] In the present study, the PSS was translated into Chinese and satisfactorily back-translated into English. The PSS measures the degree to which individuals perceived their daily life as being stressful during the last month with a 5-point Likert scale (0=never and 4=very often). The higher score indicated more perceived stress. The Chinese version of PSS demonstrated adequate reliability with Cronbach's α=0.81, and test-retest reliability of 0.86. Women with PSS score ≤ median (11.0) at T_0, T_1 and T_3 were considered as having sustained positive psychological well-being (SPW); while women with PSS score > 11 at all three time points as having sustained perceived stress (SPS). **Results:** Among the 508 participants, 393 (77.4%) had data through the three time points. Except more women with primary education were lost to follow-up, the baseline characteristics of those who remained and lost-to-follow-up were similar. Among the 393 women, 21.6% had SPW, while 24.4% had SPS. Stepwise multivariable logistic regression analyses were conducted with probability-of-F-to enter ≤ 0.10, and probability-F-to-remove ≥ 0.10. Predictor variables entered included baseline age, education level, marital status, work status, income, smoking, alcohol drinking, hours of sleeps, number of self-reported symptoms, number of known chronic diseases, physical activity index, and fruit and vegetable intake. Women with above secondary level of education, and those widowed/separated/divorced were less likely to have SPW, while those with fewer reported symptoms (< 4 at at T_0, T_1 and T_3 vs others) were about three time more likely to have SPW (OR 2.9, 95%CI 1.62 -5.05). Each additional increase of baseline self-reported symptom decreased the adjusted likelihood of having SPW by 19% (OR 0.81, 95%CI 0.74-0.88). A dose-response relationship was observed. Similar analyses with SPS as the outcome showed that higher level of education increased the risk of SPS (secondary vs primary OR 1.96 95%CI 1.13-1.39), more hours of sleep and fewer reported symptoms (< 4 at T_0, T_1 and T_3 vs others; OR 0.16, 95% CI 0.06-0.41) decreased the risk. Each additional baseline reported symptom increased the adjusted risk of SPS by 37% (95% CI 1.26-1.49). High intake of fruit and vegetables (≥600 g/d at T_0, T_1 and T_3 vs others) also decreased the risk of SPS by 73% (95% CI 0.06-1.15) but of marginal statistical significance. **Conclusion:** The study revealed that symptom reporting is the strongest predictor of sustained psychological well-being as well as sustained perceived stress in a 5-year follow-up study of a cohort of Chinese mid-life women. Health care providers should have close monitoring of mid-life women with high number of symptom reporting.
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S-19.

ApoE4 Genotype Modifies the Association Between Metabolic Risk Profile and Cognition in Postmenopausal Women

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Objective: It is hypothesized that a metabolic shift in perimenopause leads to a bioenergetic crisis in the brain that may contribute to late age cognitive decline and Alzheimer's Disease (AD). The presence of a positive ApoE4 genotype is the strongest genetic risk factor for AD. We hypothesized that the effect of an adverse metabolic profile on cognitive performance in postmenopausal women would be worse among ApoE4 carriers compared to non-carriers. **Design:** A total of 497 postmenopausal women from the Early versus Late Intervention Trial with Estradiol (ELITE) with available phenotype and genotype data contributed to the cross-sectional analysis. Nine metabolic biomarkers (glucose, the HOMA insulin sensitivity score, ketones, triglycerides, HDL-cholesterol, LDL-cholesterol, hemoglobin A1c, and systolic and diastolic BP) measured at baseline were used in a k-means clustering analysis to reveal three metabolic phenotypes: healthy, predominantly hypertensive, and poor metabolic with all metabolic factors worse except for BP compared to the healthy and high BP group. Three cognitive composite scores (global cognition, executive functions, and verbal memory) were generated from a 14-item test battery. ApoE genotype was classified as either ApoE4+ (homo- or heterozygous E4) or ApoE4-. General linear models were used to test whether an association of metabolic cluster with baseline cognitive performance differed by ApoE4 genotype. Analyses were adjusted for menopausal cohort and education. **Results:** Overall, the mean (SD) age of the study participants was 60.6 (7.0) years with 10.4 (7.8) years since menopause, 16 (2.2) years of education; 89% of women experienced naturally menopause. The majority of the participants were non-Hispanic White (71%). The prevalence of ApoE4+ was 31%. Age, race, years of education, type of menopause and years since menopause, and ApoE4 genotype were similar across the three metabolic clusters. The majority of the metabolic biomarkers were within the normal range, consistent with the recruitment of a healthy population of postmenopausal women in the ELITE study. The verbal memory composite significantly differed between metabolic clusters ($p = 0.04$), being lowest among the poor metabolic cluster. Although executive functions did not differ across the metabolic clusters in the total sample, executive functions were lowest in poor metabolic cluster followed by hypertension and then healthy cluster among ApoE4+ women, but not among ApoE4- women (p-value for interaction = 0.003, Table 1). Women with poor metabolic profile also had significantly lower global cognitive score compared to the other clusters among ApoE4+ women, however, the ApoE4-cluster interaction was of marginal significance for global cognition (interaction $p = 0.055$). **Conclusion:** Reduced cognitive performance associated with a poor metabolic profile is evident in ApoE4+ postmenopausal women, but not in ApoE4 - women. Preventive measures targeting ApoE4+ women with a poor metabolic profile may substantially reduce the burden of cognitive deficit and AD.

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Table 1. Assessment of Cluster x ApoE4 Genotype Interaction for Cognitive Composite Outcomes

		Clusters				Pairwise p-value			
Outcome	Genotype	Healthy [1]	High Blood Pressure [2]	Poor Metabolic [3]	P-value	[1] vs [2]	[1] vs [3]	[2] vs [3]	Interaction P-value
Executive Functions	ApoE4-	0.29(0.10)	0.034 (0.11)	0.11(0.15)	0.22	0.53	0.92	1.00	0.003
	ApoE4+				0.002	0.44	0.31	0.005	
Global Cognition	ApoE4-	0.37(0.14)	0.068(0.15)	0.086(0.21)	0.30	0.71	0.88	1.00	0.055
	ApoE4+	-0.098 (0.23)	0.17(0.22)	-0.91(0.31)	0.019	0.96	0.28	0.058	
Verbal Memory	ApoE4-	0.20(0.11)	0.098(0.12)	-0.022(0.16)	0.51	0.99	0.87	0.99	0.21
	ApoE4+	0.13(0.17)	0.019(0.17)	-0.65(0.23)	0.019	1.00	0.074	0.17	

FRIDAY CONCURRENT SESSION #2

S-20.

Comparison of Global Index Scores among Users of Oral and Transdermal Estrogen-Containing Therapy in the WHI Observational Study

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Objective: To compare the time to first global index event (coronary heart disease, breast cancer, stroke, pulmonary embolism, hip fracture, colorectal cancer, endometrial cancer, or death) associated with oral conjugated equine estrogens (CEE), oral estradiol, and transdermal estradiol, alone or with a progestogen. **Design:** We used data from 46,243 postmenopausal women aged 50-79 years participating in the Women's Health Initiative Observational Study to examine the associations of menopausal hormone therapy dose and route of delivery with time to a global index event (mean follow-up 8.2 yrs). To simulate eligibility criteria of the WHI Hormone Therapy trials and clinical practice, we excluded data from women with myocardial infarction in the past 6 months, past history of deep vein thrombosis or pulmonary embolism, past history of breast or endometrial cancer, and any invasive cancer within 10 years prior to study enrollment. Cox models were used for estimating hazard ratios for menopausal hormone therapy. **Results:** Compared with women taking oral CEE alone, women taking oral estrogen + progestogen were at 25% higher risk of a global index event (hazard ratio [HR] 1.25, 95% confidence interval [95% CI] 1.15-1.35). This greater risk was most apparent with ≥5 years of use (HR 1.24 [95% CI 1.10-1.40] for ≥5 years; HR 1.05 [95% CI 0.92-1.19] for <5 years). In contrast, the risk of a global index event with oral estradiol alone, transdermal estradiol alone, or transdermal combined estradiol + progestogen was not significantly different from that of oral CEE alone. The risk of a global index event with transdermal estradiol (with or without progestogen) was not significantly different from the risk with oral estradiol alone. Compared with oral CEE 0.625 mg/d, the risk of a global index event was not significantly different with oral CEE > 0.625 mg/day, oral CEE <0.625 mg/d, or transdermal estradiol. **Conclusion:** Compared with the use of oral CEE alone, the use of oral estrogen + progestogen, but not oral or transdermal estradiol, was associated with increased risk of a global index event. The risks of a global index event were similar for oral and transdermal estradiol. These findings may inform counseling regarding risks of menopausal hormone therapy.

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Table 1. Hazard ratio (95% CI) for global Index by HT type

	N events	
		HR (95% CI)
Oral CEE alone	1,767	1.0 (ref)
Oral E+P	1,766	1.25 (1.15-1.35)
Oral Estradiol alone	207	0.94 (0.79-1.10)
Transdermal E alone	166	0.90 (0.75-1.09)
Transdermal E+P	64	1.10 (0.84-1.46)
Oral estradiol alone	207	1.0 (ref)
Transdermal E alone	166	0.97 (0.77-1.22)
Transdermal E+P	64	1.18 (0.86-1.62)

Oral E + P – oral CEE and oral estradiol + progestin or progesterone.
CEE – conjugated equine estrogen
Cox hazard model stratified by baseline 5-year age intervals, adj. for age, ethn., educ., inc., smoking, BMI, physical activity, alcohol, diabetes, blood pressure, aspirin, statin, history of CVD, history of cancer, Gail score, family history of breast cancer, age at menopause, age at first birth.
Global Index = time to first CHD, breast cancer, stroke, pulmonary embolism, hip fractures, colorectal cancer, endometrial cancer, or death. Outcomes through end of extension 1.
History of CVD includes MI, stroke or revascularization

S-21.

Clinician Education and Electronic Medical Record Tools to Enhance Care for Genitourinary Syndrome of Menopause--a Randomized Trial

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Objective: Nearly 50% of postmenopausal women experience symptoms related to genitourinary syndrome of menopause (GSM) yet studies show few clinicians ask patients about these symptoms and few women seek treatment. We performed a cluster randomized trial of a health system-based intervention to improve diagnosis and treatment of GSM. **Design:** We randomized our primary care (PC) and gynecology clinics (GYN) to intervention (8 PC, 3 GYN) and control (8 PC, 3 GYN). Our intervention was comprised of an on-line PowerPoint (1 hour CME credit) and a 25 minute face-to-face presentation that contained information about GSM diagnosis and treatment, and electronic medical record (EMR) tools (EPIC SmartSet, SmartRx, and SmartText) designed to facilitate GSM diagnosis, treatment, and patient education. From September to November 2014, we gave our presentation at each intervention clinic and placed written materials on each clinician's desk. We sent email reminders to all intervention clinicians about the on-line CME and about updates in the EMR tools over the following year. The EMR tools were available to all clinicians, but the control group received no notice of their availability. From the electronic medical record, we identified all well visits occurring in PC or GYN clinics from 11/15/14 through 11/15/15, all GSM diagnoses (both vulvovaginal and urinary) occurring at the visits, and all prescriptions for vaginal estrogen or topical lidocaine products occurring within 4 weeks of the visit. We additionally evaluated clinician use of the electronic tools during the one-year observation period. We tested department (PC and GYN) by intervention interactions to see if the results differed for PC and GYN. **Results:** There were 407 clinicians (204 intervention, 203 control) and 15,062 well visits (7,749 intervention, 7,313 control) during the study period. The intervention and control clinics did not differ in number of well visits performed, patient age (66.4 ± 8.4 vs 66.5 ± 8.3) or BMI (29.0 ± 7.0 vs 28.5 ±6.7). Eighty percent of the clinicians were primary care providers (Table 1) and 85.8% of the well visits occurred in primary care clinics (Table 2). Table 1 shows the average number of uses of the EMR tools per clinician by department. The intervention clinicians were significantly more likely to use the Smart Set and the Smart Text for patient care. The difference between intervention and control in Smart Set use was proportionally greater for PC

than GYN (p=.06). Table 2 shows the proportion of well visits that included a GSM diagnosis or resulted in the prescription of a vaginal estrogen or topical lidocaine product. The intervention group was not more likely to diagnose GSM. However, there was a significant arm by clinic type interaction (OR=1.57, p=.01), such that there was an increase in GSM diagnoses in the GYN clinics (28.1% vs 23.1%) but not the PC clinics (5.4% vs 6.3%). The intervention group was more likely to prescribe topical lidocaine (0.6% vs 0.3% of visits, p=.02) but not vaginal estrogen (6.5% vs 5.8%, p=.70). **Conclusion:** We found that PC and GYN clinicians will use electronic charting tools for GSM related patient care, but the diagnosis of GSM at well visits was only significatly increased among gynecologists. Since PC providers perform the majority of well care visits for postmenopausal women in our health care system, different strategies should be tested for improving postmenopausal genitourinary health.

Sources of Funding: NAMS and Pfizer Independent grant for learning and change #10319

Table 1. Clinician use of electronic tools for GSM-related patient care

	Intervention			Control			
	GYN N=44	PC N=162	Overall N=206	GYN N=36	PC N=165	Overall N=201	p
SmartSet	6.80	1.74	2.79	0.26	0.01	0.06	<001
SmartText	3.23	0.61	1.09	0.22	0.04	0.07	<001
SmartRx	0.05	0.27	0.22	0.17	0.13	0.13	0.11

Table 2. Proportion of well woman visits receiving a GSM-related diagnosis or treatment

Outcome	Intervention			Control			
	GYN N=1,296	PC N=6,453	Overall N=7,749	GYN N=845	PC N=6,468	Overall N=7,313	p
Vulvovaginal atrophy diagnosis	25.9%	3.5%	7.2%	20.0%	3.6%	5.5%	0.55
GSM diagnosis*	28.1%	5.4%	9.2%	23.1%	6.3%	8.2%	0.98
Vaginal estrogen prescription	20.6%	3.6%	6.5%	21.2%	3.8%	5.8%	0.70
Topical lidocaine prescription	1.0%	0.6%	0.6%	0.95%	0.3%	0.3%	0.02

***Includes vulvovaginal and urinary diagnoses**

S-22.

Development of a Clinical Toolkit for use by Primary Care Providers regarding Genitourinary Syndrome of Menopause

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Objective: Genitourinary syndrome of menopause (GSM) has a significant negative impact on a woman's quality of life, yet issues that are commonly encountered for both providers and patients include poor communication, a deficit in recognition of GSM, and inadequate knowledge and resistance regarding treatment strategies. Research indicates that primary care providers (PCPs) feel inadequately prepared to recognize and treat this common diagnosis. **Background:** In 2010, the United States population was 308 million with 17 to 21 percent composed of menopausal women. It was estimated that 11 to 32 million of menopausal women would experience GSM, previously referred to as *atrophic vaginitis*. While vasomotor symptoms of menopause eventually resolve, GSM persists and worsens with time. Common symptoms of GSM include recurrent urinary symptoms, vaginitis, and dyspareunia. Women frequently do not recognize these symptoms as being related to menopause and are often resistant to effective treatment strategies for GSM. Many providers do not understand that GSM impact goes beyond symptoms of vaginal dryness. Because of this lack of recognition and understanding, treatments may be inappropriate. It has also been found providers do not discuss GSM in a meaningful way with patients. **Purpose of Translational Research:** There is a need for PCP education regarding the recognition and appropriate treatment strategies for care of the woman with GSM. **Objective**: Development of a comprehensive, easily accessible, clinical toolkit for PCP's regarding the recognition and comprehensive treatment of the individual with GSM. **Design:** This was a translational research project. A thorough review of the literature, consultations with expert providers and other stakeholders, as well as review and successful completion of NCMP certification was taken in order to develop this GSM specific clinical toolkit. Key information was gained while participating in the 2015 NAMS Conference as a Doctors of Nursing Practice (In Training) Reporter Scholarship awardee. **Results:** Clear evidence exists that there is a lack of information available to PCPs regarding this important and common menopausal health issue. A clinical toolkit was developed that includes a powerpoint presentation that is currently being utilized in the education of PCPs regarding GSM (both regional and national conferences). Components of the toolkit include: 1) PowerPoint slide presentation for PCP's regarding the significance of GSM, diagnosis, and treatment options, including allopathic and complementary, as well as alternative measures. 2) A list of key references for use in clinical practice. 3) A handout for PCP's summarizing the recognition and care of the woman with GSM. 4) A resource handout for PCPs to utilize. 5) A patient education brochure regarding GSM. 6) A resource handout for use by patients regarding their self care of GSM. **Conclusion:** Primary care providers lack significant knowledge and information regarding GSM. Many providers and patients express concern regarding safety of local estrogen therapy although there is significant evidence that it is a safe and effective treatment. There is a need to educate providers about this issue as well as appropriate history, recognition, and treatment strategies to improve quality of life of their patients. While local estrogen therapy is a safe and effective treatment strategy, there are other treatments under evaluation and available for utilization in clinical practice. The purpose of this project has been to develop a clinical toolkit in order to meet this important educational need for primary care providers.

Sources of Funding: None

S-23.

Functional change in rat tail artery by Gamma-Oryzanol

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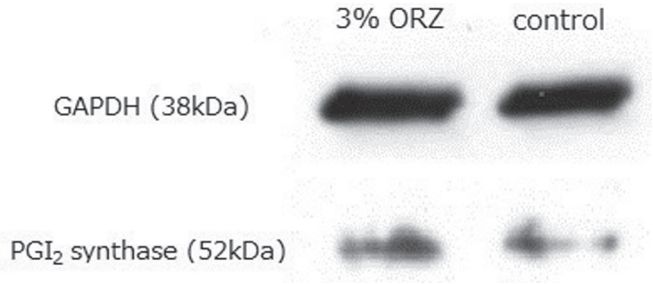
Objective: Loss of estrogen in middle age women causes various menopausal symptoms; hot flash, hyperlipidemia, atherosclerosis, etc. Although Gamma-Oryzanol (ORZ) extracted from rice bran oil was recognized to have several functions for improving these symptoms, there were no report about regulating vascular function. The aim of this study is to investigate if ORZ affects to the vascular endothelial function in rat tail artery (TA). **Design:** All female Sprague-Dawley rats were ovariectomized at 12th week. After giving soy been free diet, AIN-93G to eliminate the effect of phytoestrogen for 4 weeks, they were classified into 3 groups according to the containing ratio in their food; 3% ORZ (n=6), 5% ORZ (n=8), and 0% as control (n=7). At 18th week, we made denudation to induce intimal hyperplasia using a 2Fr Forgarty balloon catheter on left carotid arteries (CA) with microscopic procedure. All rats were sacrificed at 20th week, and TA was picked up as a representative of peripheral vessels. The magnitude of intimal hyperplasia in CA was evaluated as intima media area ratio (I/M) with light microscopy under HE staining. The isometric tension change in TA was measured with using myograph in order to evaluate either nitric oxide (NO) or prostaglandin (PG) was involved in TA relaxation response. Acetylcholine (ACH: 10(-9) to 3 x 10(-5) M) was used as a receptor-mediated, endothelium-dependent agonist and induced relaxation with or without NO synthase inhibitor (N^G nitro L-arginine: LNA: 10(-4) M) under U46619 (10(-7) M) evoked contraction. U46619 (10(-9) to 3 x 10(-5) M) as a thromboxane A_2 (TXA_2) analogue induced dose-dependent contraction with or without non-specific COX inhibitor indomethacin (IM: 10(-5) M). TA sample was utilized to measure the protein expression of PGI_2 synthase compared with glyceraldehyde-3-phosphate dehydrogenase (GAPDH) in western blottng. All results were expressed as mean ± S.E.M. Statistical analysis was performed with t-test with Stat View J 5.0 program and $p<0.05$ was considered as statistically significant. All studies complied with the Animal Welfare Regulations of the Tokyo Medical and Dental University. **Results:** There were no significant differences in body weight increases among 3 groups. On the other hand, I/M ratio after denudation in ORZ treated groups were reduced than control group (3% group: 59.2±4.9(%), 5% group: 50.4±3.3, control: 88.2±8.6, respectively). Significant differences were not observed among 3 groups in both ACH induced endothelium dependent relaxation with or without LNA in TA (without LNA: 3% group: 69.8±6.3 (%), 5% group: 77.0±2.9, control: 71.0±2.9, with LNA: 3% group: 46.0±9.0, 5% group: 68.8±9.6, control: 88.2±8.6, respectively). Additionally, U46619 induced contractions were not also changed among 3 groups (3% group: 29.2±4.9 (%), 5% group: 27.5±6.68, control: 38.5±9.00, respectively), but IM pretreatment enhanced these contractions only in TA in ORZ groups (3% group: 55.7±9.27 (%), 5% group: 56.0±6.71, control: 4.8±6.80), which suggested that ORZ might enhance some relaxing factors within PG cascade. Increased protein expression of PGI_2 synthase in the 3% ORZ group provided further evidence for PG cascade involvement. **Conclusion:** Functional change with ORZ on TA seemed to exist in PG cascade, like PGI_2 apart from NO modification, resulted in inhibiting contraction and formation of hyperlipidemia.

Sources of Funding: None



S-24.

Cardiovascular Symptoms Experienced During Menopausal Transition By Immigration Status

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Objective: Menopausal transition brings about multiple changes that could make women at risk of cardiovascular diseases. Especially when immigration is added to the women's menopausal transition, the picture of their cardiovascular diseases and/or symptom experience gets more complicated. Moreover, the directions of the associations between immigration and cardiovascular symptoms are inconsistent in the literature. The purpose of the study was to explore the differences in cardiovascular symptoms experienced during menopausal transition by immigration status. **Design:** This secondary analysis included the data from two national Internet surveys on menopausal symptoms and physical activities of midlife women. A total of 1,054 midlife women from four major ethnic groups (non-Hispanic White, non-Hispanic African American, Hispanic, and non-Hispanic Asian) were included in this analysis. The instruments were: multiple questions on background characteristics and immigration-related variables, and the Cardiovascular Symptom Index for Midlife Women (CSIMW). Cronbach's alpha of the CSIMW was .87 for the frequency subscale, and .89 for the severity subscale. The data were analyzed using inferential statistics including hierarchical multiple regressions. **Results:** There

existed significant differences in the total numbers (t=5.268, p<.01) and total severity scores (t=5.493, p<.01) of cardiovascular symptoms by immigration status (see Table 1). However, when the analyses were limited to each ethnic group, there existed no significant differences in the total numbers and total severity scores of cardiovascular symptom by immigration status. In multiple regression analyses, after controlling for background characteristics and self-reported ethnic identify, the associations of immigration status, length of stay in the U.S., and level of acculturation to cardiovascular symptoms became non-significant. However, the associations of self-reported ethnic identify to the total numbers (partial R^2=.022, Fch=9.100, p<.01) and total severity scores (partial R^2=.020, Fch=8.564, p<.01) of cardiovascular symptoms were significant after controlling for background characteristics and other immigration-related variables (immigration status, length of stay in the U.S., and level of acculturation). **Conclusion:** Immigration status and self-reported ethnic identity need to be considered in future intervention development for cardiovascular health of midlife women in menopausal transition.

Sources of Funding: The original two studies that provided the data for this secondary analysis were funded by the National Institutes of Health (NIH/NINR/NIA and NIH/NINR/ NHLBI) (R01NR008926 and R01NR010568).

Table 1. Cardiovascluar symptoms experienced during menopausal transition by immigration status (N=1,054).

M±SD	Total number of symptoms	Total severity scores of symptoms
Non-immigrants (n=811)	6.99±5.50	21.01±19.06
Immigrants (n=243)	5.12±4.66	14.44±15.43
t (p)	5.268 (<0.01)	5.493 (<0.01)

FEATURED POSTER PRESENTATIONS

P-1.

Reported sexual activity and orgasm frequency in a comparative study of the SERMs Lasofoxifene and Raloxifene in an osteoporosis prevention study

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Objective: As part of a Phase 2 osteoporosis clinical trial, 2 doses of lasofoxifene were assessed versus raloxifene (60 mg) or placebo on exploratory endpoints of sexual function. **Design:** A 2-year randomized, double-blind, placebo- and active treatment- controlled in which subjects were randomized to receive one of the four treatments: 0.25 mg/day or 1.0 mg/day lasofoxifene, 60 mg/day raloxifene, or placebo. Inclusion criteria included: postmenopausal women 50 - 74 years of age, inclusive (at least one year since last menstrual period or estradiol level < 110 pmol/L (30 pg/ml) and FSH greater than 30 IU/L, body mass index (BMI) less than 32, able to provide written informed consent, non-osteoporotic based on lumbar spine BMD, have a normal gynecological exam, mammogram, and endometrial thickness < 5mm based on transvaginal ultrasound. Women were ineligible if they were on estrogen therapy, had a history of any metabolic bone disease, history of other significant medical disorders, use of any estrogenic compounds within 3 months prior to screening, utilization of calcitonin or related products within the 3 months prior to screening, or sodium fluoride (at doses > 2 mg/day) or any bisphosphonates within the 12 months prior to screening visit. Detailed exclusion criteria are further elaborated in the protocol. Sexual function was assessed by means of the Women's Health Questionnaire administered at Baseline, Week 12, Month 6, and Month 12. At each time point subjects provided a rating of their vaginal health based on dyspareunia, dryness, irritation or dysuria. Subjects provided an estimate of occurrence and frequency of any sexual activity and orgasm. Subjects also indicated whether health status or relationship had changed in their personal life that might influence their sexual activity. Only women who did not have a change in their personal life were included in the analyses. Sexual frequency and orgasm were an exploratory outcome without statistical modeling. At each time point, change from baseline for sexual frequency and orgasm was assessed by means of the Cochran-Mantel-Haenszl test. **Results:** A total of 410 postmenopausal women were enrolled into the study: 82 women randomized to lasofoxifene 0.25 mg and 1.0 mg groups, 83 to placebo and 164 women randomized to the raloxifene 60 mg. At 6 months of treatment there were numerically higher percentages of women on either dose of lasofoxifene that reported an increase in sexual activity and orgasm, however this did not reach statistical significance. At month 12 there was a larger increase for sexual activity in the lasofoxifene doses compared to raloxifene or placebo that approached significance (p = 0.077). At Month 12, there was a significant difference in subjects reporting an increase in orgasm between the lasofoxifene doses and raloxifene and placebo (p=0.006). The percentage of subjects with AEs was similar for both the lasofoxifene and raloxifene groups. There was no significant difference between treatment groups for vaginal bleeding. Subjects treated with lasofoxifene experienced increased hot flushes at month 3. This difference decreased with time and disappeared by month 24. Mean endometrial thickness at month 24 was higher in the 0.25 and 1 mg lasofoxifene groups compared to placebo (p< 0.001). The mean increase compared to placebo in the 0.25 mg and 1 mg lasofoxifene groups was 1.65 and 1.75 mm, respectively. No endometrial hyperplasia, atypia or cancer was seen. **Conclusion:** Lasofoxifene increased sexual activity and orgasm in postmenopausal women that were participating in an osteoporosis prevention trial. The results are suggestive that lasofoxifene at the doses administered in this trial appear to be safe and comparable to raloxifene and that lasofoxifene may have beneficial sexual effects. The increase in endometrial thickness reported with lasofoxifene did not increase the incidence of vaginal bleeding. While some change in sexual function may be attributed to improved symptoms of vaginal dryness and dyspareunia, additional research is necessary to further characterize the impact of lasofoxifene on sexual function

Sources of Funding: This research was funded by Sermonix Pharmaceuticals

P-2.

Efficacy of Conjugated Estrogens/Bazedoxifene (CE/BZA): Analysis of the Influence of Years Since Menopause (YSM) on the Time Course of Treatment Effects

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Objective: In phase 3 clinical trials, CE/BZA reduced the frequency/severity of hot flushes (HFs), increased bone mineral density (BMD), reduced bone turnover marker (BTMs) levels, alleviated vulvar-vaginal atrophy (VVA), improved some measures of sleep, and improved scores on the menopause-specific quality of life (MENQOL) questionnaire. Clinicians would like to know if these treatment effects for CE/BZA were similar for women close to menopause compared with those farther from menopause. This post hoc analysis evaluated whether YSM at start of treatment influenced any of these treatment effects. **Design:** Data were analyzed from five phase 3 trials: SMART-1 (NCT00675688; 2 yrs), SMART-2 (NCT00234819; 12 wks), SMART-3 (NCT00238732; 12 wks), SMART-4 (NCT00242710; 2 yrs), and SMART-5 (NCT00808132; 1 yr). This analysis focused on the effects of treatment with CE 0.45 mg/BZA 20 mg, CE 0.625 mg/BZA 20 mg, and placebo on HF frequency/severity collected in daily diaries (calculated weekly through wk 12 in SMART-1 and -2, then monthly in SMART-1); BMD at the lumbar spine, total hip, femoral neck, and femoral trochanter (mo 6, 12, 18, and 24 in SMART-1; mo 12 and 24 in SMART-4; mo 6 and 12 in SMART-5); BTMs (osteocalcin, C-telopeptide at mo 6, 12, 18, and 24 in SMART-1; mo 3, 6, and 12 in SMART-5); VVA (% superficial and % parabasal cells at mo 6, 12, 18, and 24 in SMART-1; wk 4 and 12 in SMART-3); MENQOL total and individual domain scores (mo 3, 6, 12, 18, and 24 in SMART-1; mo 3 and 12 in SMART-5); and sleep outcomes assessed by daily diary (wk 1-13 then mo 6, 12, 18, and 24 in SMART-1) or MOS sleep scale (mo 3 and 12 in SMART-5). Analysis of covariance was used, adjusting for treatment, study site or region, baseline values, YSM, and the interaction of treatment and YSM. An interaction *P* value of <0.05 was considered statistically significant, without a multiplicity adjustment. **Results:** Participants were generally healthy, mostly Caucasian, postmenopausal women aged 40–65 yrs (40–75 yrs in SMART-1), ranging from 1–35 YSM (mean ~4–8 yrs). For most outcomes and time points, treatment effect was not significantly modified by YSM (ie, CE/BZA worked equally well when initiated close to menopause or further away). No significant treatment and YSM interaction was found at any time point for frequency of moderate/severe HFs or severity of HFs in SMART-1; BMD at any site in SMART-1, -4, or -5; BTMs in SMART-1 or -5; % vaginal parabasal cells in SMART-1 and -3; % vaginal superficial cells in SMART-1; MENQOL total score in SMART-1 and-5; daily minutes slept and mean sleep quality score in SMART-1; and minutes to fall asleep, hours slept, snoring, and somnolence in SMART-5. The timing of menopause significantly influenced the treatment effect at some time points for some outcomes: significant treatment and YSM interactions were identified for HF frequency only at wk 8 and HF severity at wks 4, 6, 8, and 9 in SMART-2; for % vaginal superficial cells at both assessments (wks 4 and 12) in SMART-3; MENQOL vasomotor function domain at mo 12 and 24 in SMART-1; MENQOL psychosocial function domain at mo 12 in SMART-5; daily minutes to fall asleep at wk 2 in SMART-1; sleep disturbance, sleep adequacy, and sleep problem index I and II at mo 3 in SMART-5; and sleep short of breath/headache at both mo 3 and 12 in SMART-5. **Conclusion:** Postmenopausal women can largely expect a similar time course of improvement in bothersome HFs, prevention of bone loss, and improvement in sleep, quality of life, and VVA regardless of how far from menopause they are when starting therapy with CE/BZA.

Sources of Funding: This study was sponsored by Pfizer Inc.

P-3.

Improvement in Female Sexual Function using CO_2 Laser Therapy

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Objective: Female Sexual Dysfunction (FSD) affects millions of women worldwide and has been largely underdiagnosed. Dyspareunia resulting from the hypoestrogenic effects of Genitourinary Syndrome of Menopause (GSM), is a common presenting symptom seen with FSD. Microablative Laser Therapy is a novel treatment that uses CO_2 laser to create small penetrative injuries to the vaginal wall which stimulate the production of new collagen and neovascularization. This study examined the clinical efficacy of a specific laser treatment algorithm in improving the sexual function of postmenopausal women suffering from dyspareunia due to GSM, using a validated Female Sexual Function Index (FSFI) questionnaire. **Design:** 62 postmenopausal women aged 46-75 were given three treatments six weeks apart of vaginal microablative laser therapy using the SmartXide CO_2 laser (DEKA, Florence, Italy). Each treatment lasted approximately three-and-a-half minutes. The laser settings were identical for all parameters at each visit except we increased the depth of penetration to 600 microns for the second and third treatments. The power (30W), dwell time (1,000 μs) and spacing distance between dots (1,000 μm) remained the same. Patients completed FSFI questionnaires prior to initial treatment. They completed their post treatment cycle questionnaire either in person or through follow up calls. The post procedure FSFI was obtained within three months of treatment completion. **Results:** 82.3% of patients reported improvement in sexual function, specifically an increase in moisture and decrease in discomfort with coitus. A primary analysis was conducted in which the overall FSFI scores and each of the six domains -- desire, arousal, lubrication, orgasm, satisfaction, and pain -- were separately tested for statistical significance between the pre- and post MLT treatment scores using a matched pairs t-test. Each of the seven studies conducted resulted in a p-value that was less than the threshold of a 0.05 or even a 0.01 significance level thus deeming them statistically significant (Table 1). A secondary analysis was conducted in which the difference in FSFI scores for those who only received the MLT treatment and those

who received the MLT treatment coupled with estrogen and/or ospemifene was tested. Group 1 contained 31 patients who only received the MLT treatment. Group 2 contained 31 patients who received the MLT treatment along with estrogen and/or ospemifene. The mean difference between the two groups was calculated using a 95% confidence interval and was found to be 2.09 ± 4.23. A two-sample t-test was conducted, resulting in a t-statistic of 1.009 with a degrees of freedom of 30. A p-value greater than 0.20 but less than 0.15 was obtained. We had presumed an additive or possibly synergistic effect that would yield statistical significance in favor of those taking estrogen and/or ospemifene, but because the p-value was greater than the usual threshold of a 0.05 significance level, we concluded that there is no statistical significance between the difference in FSFI scores for those who only completed the MLT series and those who completed the MLT series and took estrogen and/or ospemifene as well. **Conclusion:** CO_2 microablative laser therapy is a promising tool in our limited selection of treatments for GSM. There was no statistical difference between those who had MLT therapy alone versus those who had MTL therapy in conjunction with SERM/estrogen therapy. 82.3% of the women we treated showed statistically significant improvement in all parameters of the FSFI. Higher powered studies including sham studies and head-to-head-comparison studies with vaginal estrogens and ospemifene are needed. Cost and availability remain barriers to widespread use. Nonetheless, the procedure is easy to learn, quick to perform, well tolerated, and has an excellent safety and side effect profile. For women without access to or tolerance of medical therapy, it may present an excellent alternative.

Sources of Funding: None

FSFI prior and post MLT treatment study results and individual domain results

	FSFI Scores	Desire Scores	Arousal Scores	Lubrication Scores	Orgasm Scores	Satisfaction Scores	Pain Scores
Raw Percentages of Improvement	(51/62) 82.3% showed an increased FSFI score.	(34/62) 54.8% showed increased sexual desire.	(39/62) 62.9% showed increased sexual arousal.	(46/62) 74.2% showed increased lubrication.	(32/62) 51.6% showed enhanced orgasms.	(38/62) 61.3% showed increased sexual satisfaction.	(43/62) 69.4% showed less pain with vaginal penetration.
Mean of Difference between Pre and Post Scores with 99% Confidence	6.49 ± 2.79	0.72 ± 0.36	0.73 ± 0.57	1.58 ± 0.64	2.8 ± 0.58	0.74 ± 0.52	1.78 ± 0.68
Number of Participants (n)	62	62	62	62	62	62	62
t-statistic and degrees of freedom (df)	6.19 with 61 df	5.27 with 61 df	3.37 with 61 df	6.57 with 61 df	12.87 with 61 df	3.78 with 61 df	6.95 with 61 df
p-value	< 0.001	< 0.001	< 0.002	< 0.001	< 0.001	< 0.001	< 0.001
Statistical Significance	Yes, at α = 0.01	Yes, at α = 0.01	Yes, at α = 0.01	Yes, at α = 0.01	Yes, at α = 0.01	Yes, at α = 0.01	Yes, at α = 0.01

BONE POSTER PRESENTATIONS

P-4.

Up-regulation of inhibitors of DNA binding/differentiation gene during alendronate-induced osteoblast differentiation

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Objective: Alendronate enhances bone morphogenetic proteins (BMP)-mediated osteoblast differentiation. A balanced regulation of inhibitors of DNA binding/differentiation (Ids) plays an important role in BMP-induced osteoblast differentiation. However, there are no studies on the possible roles of *Id* genes in alendronate-induced osteoblast differentiation. This study investigated the effect of alendronate on the expression of*I d* genes in osteoblast differentiation. **Design:** C2C12 cells were treated with alendronate for various concentrations and time periods. For evaluation of alendronate-induced osteoblast differentiation in C2C12 cells, alkaline phosphatase (ALP) activity was measured. The expression of osteoblast differentiation markers such as ALP, type-1 collagen (Col 1), and osteocalcin (OCN), and the expression of Id-1 and Id-2 were measured by RT-PCR. In order to understand the mechanism underlying the regulation of *Id* genes, the promoter region of the *Id-1* gene was identified. Database analysis of the promoter region for *Id-1* using known consensus sequences identified several putative response elements, including CCAAT/enhancer-binding protein beta (C/EBPβ). **Results:** : Alendronate treatment significantly increased not only ALP activity but also expression of ALP, Col 1, and OCN, Id-1 and Id-2. C/EBPβ and alendronate cooperatively increased the promoter activity and expression of Id-1. **Conclusion:** These results suggest that C/EBP β-mediated *Id-1* transcriptional activation may regulate alendronate-induced osteoblast differentiation of C2 C12 cells.

Sources of Funding: None

P-5.

A Retrospective Study of Bone Mineral Density in Patients with Endometrial Cancer without Bone Metastases

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Objective: A Retrospective Study of Bone Mineral Density in Patients with Endometrial Cancer without Bone Metastases **Design:** We retrospectively analyzed the BMD of spinal bone and the femur in 26 endometrial cancer patients and 32 control women. All of the patients and control women had reached their menopause. The control group was treated with benign uterine myoma whose age and body mass index are consistent with the case group. All BMD was measured by dual-energy X-ray absorptiometry. **Results:** Among the serum calcium concentrations and bone markers, alkaline phosphatase level was higher in endometrial cancer group than in controls. BMD of 4th lumbar vertebra was significantly lower in endometrial cancer patients (T-score: -0.63±0.77) than in controls (T-score: 0.88±1.83). Serum calcium concentration was higher in stage I patients (9.63±0.31 mg/dL) than that in stage II-III patients (9.26±0.31mg/dL). BMD of 1st vertebra was lower in stage I patients (T-score: -1.80±0.97) than that in stage II-III patients (T-score: -0.60±0.95). **Conclusion:** We observed the increase of bone turnover along with the decrease of BMD in endometrial cancer which is estrogen dependent malignancy. Bone turnover increase and BMD decrease was even more distinct in early stage of endometrial cancer than later stages. A prospective randomized trial in large scale is warranted to elucidate the relation between the factors affecting bone density in endometrial cancer.

Sources of Funding: None

P-6.

Effect of Isolated Vitamin D Supplementation on the Bone Turnover Markers in Postmenopausal Women: randomized, double-blind, placebo controlled trial.

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Objective: Vitamin D plays an important role in bone mineralization. However, vitamin D deficiency is a common medical condition worldwide. We aimed to evaluate the effect of supplementation of vitamin D (VITD) alone on the bone turnover markers in postmenopausal women. **Design:** In this double-blind, placebo-controlled trial, 160 Brazilian postmenopausal women were randomized into two groups: VITD group, vitamin D3 supplementation 1,000IU/day orally (n=80) or placebo group (n=80). Women with amenorrhea ≥12months and age 50-65years, with normal bone mineral density (BMD) were included. Those with previous use of pharmacological doses of vitamin D; use of drugs that could interfere with bone metabolism (bisphosphonate, estrogen, testosterone, corticosteroids, tamoxifen, calcitonin); primary hyperparathyroidism or hypercalciuria; renal failure (or creatinine >1.4 mg/dL); liver disorders and thyroid disease were excluded. The intervention time was 10 months, with assessments at the start and end of treatment. Serum levels of total calcium, parathormone (PTH), alkaline phosphatase (AP) and calciuria in 24h-urine were determined. The s-CTX (serum C-terminal telopeptide of type I collagen) as a marker of bone resorption and P1NP (of procollagen type I amino-terminal fragments) of bone formation were measured by immunoassay (Kit Elecsys, Roche™). The plasma concentrations of 25-hydroxyvitamin D [25(OH)D] were measured by HPLC (high-performance liquid chromatography). The study was registered at and approved by the Brazilian Clinical Trials Registry under the registration number RBR-222wfk. Statistical analysis was by intention-to-treat (ITT), using ANOVA, Student's t-test, Tukey test and Gamma distribution. **Results:** The mean age of the patients included was 58.8 ± 6.6 years in the VITD group and 59.3 ± 6.7 years in the placebo group, with time since menopause of 12.0 ± 8.8 years and 12.3 ± 8.4 years, respectively (p>0.05). The patients showed on average normal BMD (T-score > –1.0 DP) at the two sites (the lumbar spine and femoral neck) evaluated. After 10 months, there was increase in the 25(OH)D concentrations from 15.0 ± 7.5 ng/ml to 27.5 ± 10.4 ng/ml (+45.4%) in VITD group, and decrease from 16.9 ± 6.7 ng/ml to 13.8 ± 6.0 ng/ml (-18.5%) in placebo group (p <.001). In VITD group, there was significant decreased (-21.3%) in PTH values (p <.001). No significant differences were observed in the other laboratory parameters (total calcium, AP and calciuria) in both groups (p> 0.05). In comparison of bone turnover markers, there was significant reduction in s-CTX values (-24.2%, p <.0001) and P1NP (-13.4%, p=0.003) in VITD group. In the placebo group was not observed significant variations on bone turnover markers. For the participants who completed the study, adherence was 92% for the study intervention (vitamin D3 or placebo). **Conclusion:** In postmenopausal women with vitamin D deficiency, the isolated supplementation of 1,000 IU of vitamin D3 for 10 months may be associated with a reduction in the bone turnover markers.

Sources of Funding: Financial support from FAPESP (Sao Paulo Research Foundation) process number 2014/00001-0.

CARDIOVASCULAR HEALTH POSTER PRESENTATIONS

P-7.

Age At Natural Menopause and Blood Pressure: Bi-Directional Mendelian Randomization Analysis

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Objective: Age at natural menopause (ANM) varies considerably and has been associated with hypertension and cardiovascular health. We aimed to study a potential causal effect between ANM and blood pressure by using genetic variants in a bi-directional Mendelian randomization analysis. **Design:** We studied 3,994 postmenopausal women, participants of the Rotterdam Study; an observational, prospective population-based cohort study. Multivariable linear and logistic regression models were used to assess the association between ANM (continuous), systolic blood pressure (SBP), diastolic blood pressure (DBP) and the presence of hypertension (HTA). We also compared levels of blood pressure and prevalence of HTA by categories of ANM (early; 40-44 years, intermediate; 45-49 years, normal: 50 to 54 years (reference) and late menopause 55-60 years).

We used genetic variants related to SBP, DBP and ANM to compute genetic risk scores and performed bi-directional Mendelian randomization analysis. **Results:** There was a non-linear association between ANM and SBP (p for non-linearity = 0.026). Early menopause, compared to menopause age 50-54 years, was associated with lower SBP (β = -3.40, 95%CI: -5.8; -1.01) after adjustment for age, cardiovascular risk factors and medication, presence of comorbidity, hormone replacement therapy and estradiol levels. No association was found between ANM and DBP. Early menopause was associated with lower prevalence of HTA (early menopause vs. menopause age 50-54: odds ratio (OR) = 0.72, 95%CI: 0.54-0.95). Also, younger age at menopause was associated with lower prevalence of HTA (per 1 year younger age at menopause, OR= 0.97, 95%CI: 0.95-0.99). Bi-directional Mendelian randomization analysis showed no association between ANM genetic risk score, SBP, DBP or HTA. Genetic risk scores of SBP and DBP were associated with higher ANM (SBP: β=0.025; 95%CI: 0.002-0.04; DBP: β=0.028; 95%CI: 0.01-0.05). Genetic risk score of SBP (p<0.0001) and DBP (p<0.0001) were also associated with a higher probability of taking antihypertensive medication. **Conclusion:** These results suggest that higher blood pressure, or some environmental exposure related with higher blood pressure, such as use of antihypertensive medications, are causally associated with a later onset of natural menopause.

Sources of Funding: None

P-8.

The Association of Breast Arterial Calcifications (BACs) and Cardiovascular Disease (CVD): Results of a 10-Year Prospective Study

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Objective: Breast Arterial Calcifications (BACs) are calcifications of the medial layer of breast arteries/arterioles that are not consistently reported on mammography reports. It is postulated that the underlying pathophysiology of these calcifications differ from that of intimal calcifications. Whereas a benign nature of BACs have been suggested, intimal calcifications are strongly associated with Cardiovascular Disease (CVD)-related morbidity and mortality. The true clinical significance of BAC presence is not yet known. Thus, the primary objective of this 10-yr follow up prospective study is to assess whether the presence of BACs on routine mammography can be an early marker for predicting the development of CVD in women without CVD at baseline. **Design:** Women presenting for routine mammography between June and August 2004 were recruited for this prospective study. Baseline data collection included risk factors for CVD, as well as any CVD events, including Coronary Artery Disease (CAD) (eg, angina, MI, abnormal coronary angiogram, or CABG) and stroke, experienced by the patient over the 10 years of follow-up. Ten-year follow-up data were correlated with the baseline mammograms, which were screened for BACs along with baseline demographics, CVD presence, and CVD risk factors. **Results:** Of 1,995 subjects who had BAC data at baseline, 1,029 answered questions regarding CAD events at the 10-year follow-up without having a history of CAD or CAD risk factors at baseline. Of 1029, 112 (10.9%) were BAC positive and 917 (89.1%) were BAC negative at baseline, of which 11 (9.8%) and 30 (3.3%) developed CAD by year 10, respectively (p=.001). After controlling for age, BAC positive women were 2.3 times more likely to have CAD, with a confidence interval (CI) of 1.07-5.07 (p=0.034). Of the 1,995, 1,039 had neither history of stroke nor stroke risk factors, and answered questions regarding stroke event at the 10-year follow-up. Of these, 114 (11%) were BAC positive and 925 (89%) were BAC negative at baseline, of which 10 (8.8%) and 19 (2.1%) had at least 1 Stroke event by year 10, respectively (p <.001). After controlling for age, BAC positive women were 3.2 times more likely to have a stroke, with a CI of 1.22-8.41 (p=0.018). **Conclusion:** The presence of BACs on routine mammography may be associated with a significantly increased 10-year risk of developing CAD and stroke. Additional large prospective, population-based studies are needed to confirm BAC as a predictor of future development of CVD.

Sources of Funding: None.

P-9.

Telmisartan have a beneficial effect for intimal atherosclerosis in ovariectomized rats

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Objective: Loss of ovarian hormone has impairment on endothelial function and cardiovascular disease. In recent years, Angiotensin receptor blockers (ARB) has been used to improve hypertension and to prevent cardiovascular diseases, but its precise mechanism was not clarified. We examined whether ARB represents some beneficial effects on the endothelial dysfunction and vascular smooth muscle including neointimal hyperplasia. The aim of this study was to determine the bioavailability of ARB and possible involvements in arterial function. **Design:** Twelve weeks female Sprague-Dawley rats underwent abdominal overiectomy and fed by soy-bean free diet, AIN-93G for 2 months in order to eliminate the effect of endogenous estrogen and phytoestrogens. After 16th week, rat were divided into 2 groups and given the following administration: Group1 (n=6), control; Group2 (n=8), subcutaneous administration of telmisartan (35-70 mg/day) with an osomotic pump ; At 18th weeks, the left carotid arteries were denuded with 2 Fr forgaty balloon catheter to induce intimal hyperplasia and all rats were sacrificed at 20th week. The effect of telmisartan (35-70 mg/day) on the value of blood pressure was evaluated when rats was sacrificed. And intimal hyperplasia was evaluated with pathological findings. Statistical analyses were performed with t-test with Statview J 5.0 program and values of p<0.05 were considered as statistically significant. All studies complied with the Animal Welfare Regulations of the Tokyo Medical and Dental University. **Results:** There were no significant differences in systolic blood pressure between control group and ARB group (control vs. ARB: 118.3 ± 2.38 vs. 119.3 ± 2.38 (mmHg)). Additionally, there were no significant differences in diastolic blood pressure between the 2 groups (control vs. ARB: 77.7 ± 1.41 vs. 80.1 ± 1.62 (mmHg)). The ARB group indicated to reduce intimal hyperplasia (ARB group: 62.7±8.22 (%)) more than control group (control: 90.44±7.30 (%)). **Conclusion:** The endothelial cells are active organization. Therefore, both reendothelialization and improving endothelial function are essential to inhibit intimal hyperplasia after denudation. The lower I/M in ARB group in this paper might suggest the effect to accelerate that repairing function in endothelial cell numbers and function by ARB. ARB may have a beneficial effect not only to reduce blood pressure, but also to reduce intimal hyperplasia and cardiovascular disease with modulating endothelial function through blocking angiotensin receptors.

Sources of Funding: None

P-10.

The Role of Vitamin D Receptor (VDR) Expression on the Development of Iliac Artery Atherosclerosis in Post-menopausal Nonhuman Primates

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Objective: The aim of this study was to analyze the relationship between the abundance of iliac artery vitamin D receptor (VDR) expression and the degree of iliac artery atherosclerosis in postmenopausal monkeys. **Design:** 37 adult female, pre-menopausal, cynomolgus monkeys (*Macacca fascicularis*) were fed atherogenic diets which contained a women's equivalent of 1,000 IU 25-OHD3 and 1,200 mg calcium daily for 32 months. The monkeys then underwent bilateral oophorectomy (surgical menopause) and extraction of the left common iliac artery (LCI). After an additional 32 months (in the post-menopausal state) the monkeys underwent necropsy and the right common iliac arteries (RCI) were extracted. Atherosclerosis severity and degree of VDR expression (VDR H-score) were quantified at baseline (oophorectomy) and necropsy (end of menopausal phase). **Results:** Over the 32 month postmenopausal phase, the intimal area (IA) of the right common iliac artery was significantly greater than the IA of the left common iliac artery (pre-menopause) with a mean (SD) change of 0.34 (0.44) mm^2, p< 0.0001. However, the VDR H score also increased with a mean (SD) change of 26.47 (25.64), p<0.0001. The change in VDR abundance positively correlated with the American Heart Association (AHA) severity scores increase from premenopausal to postmenopausal state (Spearman r=0.43, p=0.0076*)*. There was an inverse correlation between pre-menopausal VDR in LCI and post-menopausal VDR increase in the RCI (r= -0.67, p< 0.0001). The VDR baseline in LCI was found to be inversely correlated with maximum intimal thickness changes (r=-0.27), iliac intimal area changes (r=-0.22), and AHA severity score changes (r=-0.26), although these correlations were statistically insignificant. Having high baseline serum vitamin D concentration and low baseline VDR was associated with the higher changes in maximum intimal thickness (p=0.075), iliac intimal area (p=0.044), and AHA severity score (p=0.014), when compared to all other combinations of dichotic (high or low) baseline vitamin D and VDR levels. **Conclusion:** Surgical menopause increased VDR expression in iliac arteries of nonhuman primates. The extent of VDR up-regulation was significantly associated with worsening atherosclerosis at the same arterial site. A low baseline VDR expression may be correlated with increased VDR expression from pre-to post-menopause along with worsening vascular atherosclerotic change. The worst vascular atherosclerotic changes after surgical menopause were seen in monkeys with low VDR expression along with high vitamin D concentration at baseline.

Sources of Funding: None

P-11.

Bone Mineral Density is Associated with Progression of Subclinical Atherosclerosis in Healthy Postmenopausal Women : A Longitudinal Analysis of Randomized Clinical Trial Data

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Objective: Atherosclerosis and osteoporosis are major causes of morbidity and mortality in postmenopausal women. These two age-related chronic diseases share several vascular and metabolic risk factors; hence it is of interest to understand the coexistence of these diseases. Several cross-sectional studies reported a positive association of subclinical with osteoporosis among elderly women. However, no longitudinal studies of sufficiently large sample size have been conducted to evaluate the impact of bone mineral density (BMD) on atherosclerosis progression in postmenopausal women. In the present community-based longitudinal study, we examined the association between BMD and progression of carotid artery intima-media thickness (CIMT), providing more evidence for the relation between osteoporosis and subclinical atherosclerosis in postmenopausal women. **Design:** This is a posthoc analysis of BMD and CIMT measures collected from 349 postmenopausal women over 3 years as part of the Women's Isoflavone Soy Health (WISH) trial. On average, each woman had 6 CIMT assessments, completed at baseline and every 6 months using high resolution B-mode carotid ultrasound. Total hip and lumbar spine BMD were measured at baseline using DXA scan. A linear mixed-effects model was used to analyze the association between baseline BMD and CIMT progression

controlling for confounding variables. **Results:** The mean (SD) age of participants was 61(7) years. The majority (64%) of the study population was White (non-Hispanic). Of the 349 participants, 60% had a bachelor's degree or above education level, 59% were never smokers and 70% had hormone therapy before the trial. The mean (SD) BMI was 26.6 (5.2) kg/m^2. The majority (57%) of the study population were overweight or obese. The mean baseline CIMT was 0.811 (0.100) mm. The mean baseline total hip BMD was 0.937 (0.137) g/cm^2 and the mean baseline lumbar spine BMD was 0.898 (0.122) g/cm^2. Mean lumbar spine BMD was positively significantly associated with CIMT ($P<0.01$); total hip BMD was not associated with baseline CIMT. Longitudinally, both total hip ($P = 0.01$) and lumbar spine ($P = 0.03$) BMD were significantly inversely associated with CIMT progression. The mean CIMT rate was 0.002 mm/year (95% CI: -0.020, -0.003) lower per 0.137g/cm^2 total hip BMD. The mean CIMT rate was 0.001 mm/year (95% CI: -0.016, -0.001) lower per 0.122g/cm^2 mean lumbar spine BMD. The longitudinal association between total hip BMD and CIMT was not altered with adjustment for age. **Conclusion:** Low BMD in the total hip and lumbar spine may represent a marker of both osteoporosis and atherosclerosis progression for healthy postmenopausal women. Postmenopausal women at higher risk for osteoporosis should also have concern about the risk of atherosclerosis. These results have clinical and public health implications with regard to co-occurrence of osteoporosis and atherosclerosis for postmenopausal women.
Sources of Funding: National Center for Complementary and Alternative Medicine, Office of the Dietary Supplement, and the Office of the Research on Women's Health (NIH grant U01_AT001653) and P01AG026572

P-12.

Telmirsartan increases NO production of carotid endothelium in ovariectomized rats.

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Objective: Angiotensin receptor blockers (ARBs) are angiotensin 1 (AT1)-receptor antagonists used in the treatment of hypertension, diabetic nephropathy and congestive heart failure. Because of reducing atherosclerosis, it is also expected that ARBs have some effects on endothelial cells through modulating activity of endothelium derived relaxing factor (EDRF). We assessed about the role of telmisartan for the function of nitric oxide (NO) production of carotid endothelial cells in an ovariectomized rat model. **Design:** Twelve-week-old female Sprague-Dawley rats were randomly assigned to one of two ovariectomized groups: control (n=6), ARB (35-70 mg/day, telmisartan, n=8). Rats were fed the AIN-93G diet, which contained no soy oil or soy protein three days after ovariectomy. At sixteen weeks, administration of telmisartan to ARB group with subcutaneous osmotic pumps was started. At twenty weeks, all rats were sacrificed, and we measured cyclic GMP levels within the vessel walls and changes in isometric tension of common carotid arteries. As the experiments of isometric tension changes, specimens of common carotid arteries were cut into 5mm length, which was stretched to an optimal resting tension of 350mg for one hour in organ chamber in modified Krebs solution. During contraction caused by U46619 10-^{7}M, acetylcholine(ACh; 10^{-9} to 3×10^{-5} M)was given in order to measure the endothelial dependent relaxation. Sodium nitroprusside (SNP;10^{-9} to 3×10^{-5} M) as an NO donor and N^G-nitro-L-arginine (LNA; 10^{-4} M) as an endothelial NO synthase inhibitor were also used. ACh and SNP were applied into organ chamber in a cumulative fashion at increasing concentrations of 0.5 log unit. The levels of cyclic GMP as 2nd messenger of NO were determined by radioimmunoassay kit. All results are expressed as mean ± SEM. Statistical analyses were performed with t-test or two-way ANOVA of Stat View J 5.0 program. Values of $p<0.05$ were considered as statistically significant. All studies were complied with the Animal Welfare Regulations of the Tokyo Medical and Dental University. **Results:** There was no change of blood pressure between the two groups. The relaxation in response to ACh was abolished by the endothelial removal and preincubation with LNA, suggesting that the relaxation is endothelium-dependent and mediated through activation of endothelial NOS. ACh induced relaxations in the group of ARB were increased than control group. On the other hand, SNP induced relaxations in all groups showed no difference, suggesting there was no change in NO sensitivity of smooth muscle cells. The levels of cyclic GMP in the group of ARB was significantly increased than control group. **Conclusion:** It was suggested that telmisartan increases endothelial NO production in common carotid arteries in ovariectomized and isoflavone free rats. Telmisartan may have a beneficial role for increased release of endothelial nitric oxide and for prevention of arteriosclerosis.
Sources of Funding: none

P-13.

Association Between Testosterone and Cardiovascular Risk Across the Menopausal Transition

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Objective: To examine the association between serum testosterone levels and cardiovascular risk in women across the menopausal transition. **Design:** Participants were from the epidemiologically sourced, longitudinal prospective Women's Healthy Aging Project, a cohort of Australian-born women initially recruited between 45 to 55 years old. Participants were seen in baseline year 1992 when they were premenopausal and in 2012 when they had been menopausal for at least 10 years. Fasting blood tests, physical and clinical measurements, and a battery of questionnaires assessing lifestyle and socio-demographics were performed at each interview stage. Cardiovascular disease risk was calculated using the PROCAM scoring system, which considers age, smoking status, diabetes diagnosis, low-density lipoproteins (LDL), high-density lipoproteins (HDL), triglycerides, systolic blood pressure and family history of myocardial infraction. **Results:** 181 participants had complete measures at both time-points. They had an average PROCAM score of 29.9 (2.4% risk of a cardiovascular incident in 10 years) in 1992 and this rose to 44.5 (9.5% risk of a cardiovascular incident in 10 years) in 2012. Serum testosterone levels decreased from 1992 (1.48nmol/L) to 2012 (0.88nmol/L), within normal ranges (0.4nmol/L – 2.0nmol/L). In pre-menopausal women at baseline year 1992, there was no significant difference between testosterone and cardiovascular risk score. However in postmenopause a decade later, higher testosterone levels were significantly correlated with an increased cardiovascular risk score ($p<0.05$). **Conclusion:** There is conflicting evidence on the risk of testosterone for heart disease in women. In the setting of available testosterone therapies for postmenopausal women, prospective studies are needed to examine the relation between the physiological level of circulating androgens and cardiovascular disease risk. In our cohort higher testosterone levels were associated with an increase in cardiovascular risk after menopause but not before. The contrast between premenopausal and postmenopausal women suggests that menopausal status affects the interaction of testosterone levels with cardiovascular risk which may explain some of the conflicting results in previous literature. It is important to consider the cardiovascular impact of exogenous testosterone.
Sources of Funding: Funding has been provided by the National Health and Medical Research Council (Grants 547500, 1032350 & 1062133), Alzheimer's Association (NIA320312), Australian Healthy Ageing Organisation, and the Alzheimer's Association of Australia.

P-14.

A Cluster Analysis of Cardiovascular Symptoms Experienced During Menopausal Transition

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Objective: The differences in hormone levels by race/ethnicity could result in racial/ethnic differences in the cardiovascular symptoms experienced during menopausal transition. However, the findings reported in the literature are inconsistent, which makes it imperative to clarify the association of race/ethnicity to the cardiovascular symptoms experienced during the menopausal transition through various methods. In this study, a cluster analysis was used to select the clusters of midlife women by cardiovascular symptoms and to determine racial/ethnic differences in the clusters to identify groups at risk of cardiovascular diseases. **Design:** This was a secondary analysis of the data from two national Internet surveys among midlife women from four major racial/ethnic groups in the U.S. The analysis included 966 midlife women (298 Non-Hispanic [N-H] Whites, 238 N-H African Americans, 234 Hispanics, 196 N-H Asians). The instruments in the original studies included the Cardiovascular Symptom Index for Midlife Women (CSIMW) and various questions on background characteristics and health and menopausal status. The CSIMW includes 25 items on midlife women's symptoms associated with cardiovascular symptoms. Individual items had a dichotomous frequency sub-scale (1 = yes; 0 = no) and a 6-point Likert scale severity sub-scale (0 = no symptom; 5 = extremely). Cronbach's alpha of the CSIMW was .87 for the frequency subscale, and .89 for the severity subscale. To analyze the data, multiple statistical methods including factor analysis, hierarchical cluster analysis, and multinominal logistic analysis were used. **Results:** Based on the ANOVA and Dendrogram, a 3-cluster solution was taken, and the clusters included Cluster 1 (45%; high vasomotor and low cardiorespiratory symptoms), Cluster 2 (38%; low vasomotor and high cardiorespiratory symptoms and high discomfort/pain), and Cluster 3 (16%; high discomfort/pain and high indigestion symptoms). There existed statistically significant differences in the characteristics of midlife women (age, family income, race/ethnicity, self-reported health, and menopausal status) among the clusters ($p<.05$). There existed significant racial/ethnic differences in the frequencies and severity scores of cardiovascular symptoms in each of the three Clusters ($p<.01$). Across the clusters, Asian women were less likelty to report cardiovascular symptoms than other racial/ethnic groups ($p<.01$). Among the clusters, Cluster 1 (with high vasomotor and low cardiorespiratory symptoms) might be the unique group at risk of cardiovascular diseases during menopausal transition. **Conclusion:** In future health care or research with midlife women in menopausal transition, racial/ethnic differences in the cardiovascular symptom experience need to be considered. Also, some characteristics of midlife women (age, family income, race/ethnicity, self-reported health, and menopausal status) need to be considered in future preventive and/or treatment interventions for cardiovascular diseases.
Sources of Funding: This is a secondary analysis of the quantitative data from two lager studies that were funded by the National Institutes of Health (NIH/NINR/NIA, 1R01NR008926 and NIH/NINR/ NHLBI, R01NR010568).

P-15.

The effect of high-density lipoprotein cholesterol and cardiovascular in women at difference menopausal stages.

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Objective: Numerous studies have examined the effect of high-density lipoprotein cholesterol (HDL-C) on cardiovascular risk (CVR) but the results were controversial. Women are known for lower prevalence in cardiovascular disease than men but their risk increases post-menopause. Insufficient studies have focused on women across menopausal transition and the effect of HDL-C on CVR. **Design:** Women's Healthy Aging Project followed 438 Australian women aged 45-57 at baseline for twenty

years. Measurements including, HDL-C, menopausal factors, and other CVR factors were recorded throughout the study. CVR were calculated according to Framingham 10-year CVR scores. STRAW+10 was used to categorize participant's menopausal status. The correlation between HDL-C and CVR was determined with Spearman's Correlation. **Results:** In all years, weak negative associations were found between HDL-C and Framingham Risk Score (FRS) [1991: rs (473)= -0.272, p<0.0005; 2002: rs (246)= -0.277, p<0.0005; 2012: rs (172)= -0.217, p<0.005]. After adjusting by confounders, the correlation remained significant. On average, each 0.18mmol/L decrease in HDL-C level was associated with 1% increase in cardiovascular risk. Across menopausal transition in all cohorts, weak negative correlations were found between HDL-C and FRS. The significance maintained after adjustment with confounders. The cardioprotective effect of HDL-C increased transiting from premenopausal to postmenopausal status (with each 0.211 and 0.262mmol/L increase in HDL-C respectively, FRS decreased by 1%). **Conclusion:** In our cohort, HDL-C was weak negatively associated with CVR across all menopausal stages. Greater effect was observed in postmenopausal women. Therefore, the cardioprotective effect of HDL-C was seen from this study.

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GENERAL MENOPAUSE POSTER PRESENTATIONS

P-16.

Association Between Obesity and Menopausal Symptoms Evaluated by Menopause Rating Scale: A Populational Study

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Objective: Evaluate the association between menopausal symptoms and obesity in climacterical women **Design:** A cross-sectional, populational-based study was conducted with 749 women between 45 and 60 who underwent a household interview. Households were selected through census tracts according to demographic cense. The dependent variable was the intensity of menopausal symptoms assessed by the Menopause Rating Scale (MRS) questionnaire. The independent variables were characteristic sociodemographic and clinics. The obesity was measured by the body mass index (BMI) classified into three criteria: BMI <25 kg / m2; BMI between 25 and 29.9 kg / m2; and BMI> 30 kg / m2. The statistics analysis was performed using the $\chi 2$ test and Poisson regression **Results:** The mean age of the study population was 52.5 (± 4.4 SD) years. Regarding the menopausal status 16% were premenopausal, 16% perimenopausal and 68% postmenopausal women. There was no significant difference in most clinical and sociodemographic characteristics among the BMI groups. Obese women had lower frequency of physical activity (p - 0.019), higher prevalence of hypertension (p <0.001), diabetes (p = 0.002) urinary incontinence (p <0.001) and urgency (p = 0.0006). The mean total score of the MRS was 9.7. Of the 11 symptoms of MRS, only three were associated with BMI. The hot flashes score increased progressively being higher for the group with a BMI of 30 kg / m2 or more (p = 0.027). The muscle and joint pain score also increased with increasing BMI (p <0.001). Among the urogenital symptoms, there was a significant difference only in urinary problems, which were most intense in obese women, BMI> 30 kg / m2 (p <0.0001). There was no significant difference in any of the psychological symptoms of MRS. **Conclusion:** The menopausal symptoms such as vasomotor, joint and urinary symptoms are related to obesity. Understanding this relationship can contribute to the development of health strategies to minimize the impact of obesity on various aspects of women's health in middle age.

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P-17.

Moderate to severe vasomotor symptoms in women aged 60 years and older: Results from the Data Registry on Experiences of Aging, Menopause and Sexuality (DREAMS)

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Objective: Vasomotor symptoms (VMS) of menopause adversely affect quality of life. Symptoms can last for several years after the onset of menopause, and for some, can continue into the seventh and eighth decades. Factors contributing to VMS in older women have not been fully explored. Our objective was to examine the frequency of moderate to severe vasomotor symptom (msVMS) bother in older women (>60 years of age) presenting to a menopause clinic, and compare the associated characteristics and lifestyle factors in those with and without msVMS bother. **Design:** All women presenting for a menopause consultation in the Women's Health Clinic (WHC) (Rochester, MN) complete the Menopause Health Questionnaire (MHQ). The present study is restricted to women 60 years of age and older who completed the MHQ between January 1, 2006 and October 7, 2014. Menopausal symptom presence and severity were assessed in the MHQ with questions about hot flashes and night sweats, and rated with a score of 1 to 4 for degree of bother (1=not at all; 2= a little bit, 3=quite a bit; 4=extremely). Women were classified as having msVMS bother if they reported "quite a bit" or "extremely" for either of these questions and comparison made to women reporting "not at all" or "a little bit" of bother related to VMS. The type of menopause was self-reported as spontaneous, surgical, due to chemotherapy/radiation or other; self-rated health was reported as poor, fair, good and excellent; current tobacco, caffeine and alcohol use was assessed as present/absent (yes/no). Demographic data (age, BMI, education, employment status, marital status and race/ethnicity) were obtained from the electronic medical record. Logistic regression was used to assess the association of each characteristic with msVMS bother. In addition to univariate analyses, each characteristic was also assessed using a multivariable model with age included as a covariate. In all cases, p-values<0.05 were considered statistically significant. **Results:** Of 921 women over age 60 years evaluated in the WHC for menopause concerns, 379 (41.2%) reported msVMS bother. The frequency of msVMS bother was 40.0%, 40.9%, and 44.1% for those aged 60-64 years, 65-69 years, and 70+ years respectively, p=0.625. From univariate analyses, the percentage of women reporting msVMS bother differed significantly according to race (40.4% vs 55.6% for white vs non-white, p=0.044), marital status (43.0% vs 30.1% for those who were married or in a committed relationship versus not, p=0.009), cause of menopause (37.9% vs 48.4% vs 40.8% for spontaneous vs surgical vs other, p=0.027) and self-reported health status (51.5% vs 40.5% vs 29.2% for fair, good and excellent, p=0.002). In all cases, these characteristics remained significant in analyses which adjusted for age. In addition, when assessing potential interactions with age, the age-by-caffeine use interaction was found to be statistically significant (p=0.049), indicating that the effect of caffeine on the frequency of msVMS bother increased with older age. The frequency of msVMS bother in those using caffeine versus not was 39.2% vs 40.3%, p=0.861 in those aged 60-64 years; 42.7% vs 34.1%, p=0.293 in those aged 65-69 years; and 48.0% vs 24.0%, p=0.026 in those aged 70+ years. **Conclusion:** In the present study from the Data Registry on Experiences of Aging, Menopause and Sexuality (DREAMS), women aged 60 years and older presenting for menopause consultation report significant VMS bother. Older women with moderate to severe VMS bother were more likely to be non-white, more likely to be married or in a committed relationship, less likely to have some college or a higher degree, and less likely to report their health as good or excellent. Caffeine use was associated with greater VMS symptom bother in those aged 70 years and older. Additional study regarding the factors associated with msVMS bother in older women could allow for targeted interventions specific to this group.

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P-18.

Prevalence and associated factor to self-perception of health in climacteric women

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Objective: To investigate the prevalence of negative self-perception of health and identify associated factors in climacteric women. **Design:** Cross-sectional and analytical study conducted with menopausal women enrolled in the units of the Family Health Strategy (FHS) in the city of Montes Claros, Minas Gerais, Brazil. Sampling of probabilistic type consisting of a sample of 761 women aged 40 to 65 years. Data collection was made through a questionnaire about demographic, behavioral and health status characteristics factors. The dependent variable was the negative self-perception of health. The questionnaires were applied in August 2014 to January 2015. Descriptive analyzes were conducted bivariate and multivariate analysis by hierarchical regression of Poisson being considered as a distal block of demographic variables, intermediate block for behavioral variables and the most proximal level the variables related to health status characteristics. The adopted measure of association was the prevalence ratio (PR). **Results:** The prevalence of negative self-rated health was 41.6%. The prevalence ratio for negative self-rated health was presented in women with more than 52 years old anos (PR=1,43, 95% IC: 1,36-1,52), schooling until 8 years of study (PR=2,14, 95% IC: 2,02-2,27), with partner (PR =1,15, 95% IC: 1,09-1,22) and with no formal work (PR =1,25, 95% IC: 1,19-1,33). After adjustment of distal block, it was observed a prevalence of negative self-perception in women smokers (PR=1,77, 95% IC: 1,64-1,93) and sedentarism (PR=1,36, 95% IC: 1,29-1,44). For the adjustment to proximal level were presented associations to the negative self-perception of women who used medications (PR =1,11, 95% IC: 1,03-1,20), has high blood pressure (PR =1,55, 95% IC: 1,44-1,66), elevated cholesterol (PR =1,39, 95% IC: 1,31-1,48), heart diseases (PR =1,83, 95% IC: 1,68-1,99), diabetes (PR =1,68, 95% IC: 1,55-1,83), spine problems (RP PR=2,38, 95% IC: 2,24-2,52), depression (PR=1,40, 95% IC: 1,30-1,50), has overweight/obesity (PR=1,41, 95% IC: 1,31-1,51) and has syntoms of climacteric (PR=2,41, 95% IC: 2,28-2,56). **Conclusion:** There is a high proportion of women in climacteric period with negative perception of their health. And that perception is influenced by modifiable and non-modifiable factors, such as women over 52 years, schooling up to eight years of study, with a partner, without formal work, smoking, sedentary lifestyle, medication use, high blood pressure, high cholesterol problem heart, diabetes, spinal problems, depression, overweight/obesity and has symptoms during menopause.

Sources of Funding: None

Prevalence ratio adjusted according to demographic, behavioral and health status characteristics for negative self-perception of health in climacteric women, 2014.

Variables	p-value	RP*	IC 95%**
Distal Component			
Age > 52 years	< 0,001	1,43	1,36-1,52
Schooling < 8 years of study	< 0,001	2,14	2,02-2,27
With partner	< 0,001	1,15	1,09-1,22
No formal work	< 0,001	1,25	1,19-1,33
Intermediate Component			
Current smoking	< 0,001	1,77	1,64-1,93
Sedentarism	< 0,001	1,36	1,29-1,44
Proximal Component			
Current use of medication	0,008	1,11	1,03-1,20
High blood pressure	< 0,001	1,55	1,44-1,66
High cholesteral	< 0,001	1,39	1,31-1,48
Heart diseases	< 0,001	1,83	1,68-1,99
Diabetes	< 0,001	1,68	1,55-1,83
Spine problems	< 0,001	2,38	2,24-2,52
Depression	< 0,001	1,40	1,30-1,50
Overweight/Obesity	< 0,001	1,41	1,31-1,51
Climateric Symptoms	< 0,001	2,41	2,28-2,56

(*) RP: Prevalence Ratio; (**) IC95%: Confidence Interval of 95%.

P-19.

Demographics Of Untreated Menopausal Women In The US: Results From A Claims Database

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Objective: To explore the real world demographics of untreated menopausal women in the United States. **Design:** A retrospective analysis was performed using MarketScan® data with the observation period focus from October 01, 2008 to September 30, 2012. The untreated menopausal cohort was defined by (a) presence of a menopause diagnosis (ICD-9-CM: 627.x) with no evidence of a menopause diagnosis in the year prior (index date = date of menopause diagnosis) ; (b) female gender and > 45 years of age at index date; (c) no evidence of pregnancy (ICD-9-CM diagnosis codes 630-679, V22, V23, V24, V27, V28, V61.6, V61.7, 792.3, 796.5 or ICD-9-CM procedure codes 72-75.99) during the full study period; and (d) no prescription for any type of hormone therapy, or for venlafaxine or paroxetine during the study period. For women with multiple diagnoses during the study period, the first menopause diagnosis was selected. Descriptive review captured the proportion of menopausal women that did not take hormone therapy during this period, the associated age groups, and US geographic variation. All-cause healthcare utilization and other outcomes were reviewed in a difference-of-difference analysis in a larger pharmacoeconomic study. **Results:** Among 209,548 women 45+ years of age, 20.6% (n=43,237) had a diagnosis of menopause within the observation period. Of those with menopausal diagnosis, 52.4% (n=22,639) were not treated with hormone therapy, venlafaxine or paroxetine. Women in the Northeast had a higher proportion of untreated menopausal women during this period (n=4,028/6,571, 61.3%) compared to the western US which had the lowest proportion of untreated women (n=4,343/8,964, 48.4%). Variability was also seen by age, with older cohorts (65+: 248/436, 56.9%) showing higher proportions of untreated menopausal women than younger cohorts (45-49: 5,302/10,560, 50.2%) during the observation period. Lack of studied treatments also showed directional increase by year, with the later years from the study period (2011/2012) showing a higher proportion of menopausal women untreated. **Conclusion:** Differences exist among menopausal women in the United States by age, geography, and across time. Further exploration is needed to better understand drivers of lack of therapy, particularly in cohorts with high rates of non-adoption. In identifying women who have ostensibly presented for an evaluation of symptoms and have also received a formal diagnosis, this study suggests that opportunities remain for enhanced dialogue on the role of menopause therapies. Such dialogue may be needed in both health care and consumer settings.

Sources of Funding: Pfizer Inc.

P-20.

The Covariates of Menopausal Symptoms in Four Major Racial/Ethnic Groups in the U.S.

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Objective: Structural equation modeling (SEM) helps examine and estimate causal relationships among multiple variables by integrating statistical data and qualitative causal propositions. Subsequently, SEM is helpful in deciding whether a model is valid and in delineating the associations among multiple variables. The purpose of the study was to examine differences in the covariates of menopausal symptoms in four major racial/ethnic groups of midlife women in the U.S. **Design:** This secondary analysis used the combined data from two national Internet surveys on menopausal symptoms and physical activities of four major racial/ethnic groups of midlife women in the U.S. This analysis included the data from 980 midlife women that were collected using the questions on demographic and acculturation factors and health and menopausal status and the Midlife Women's Symptom Index. KR-20 of the MSI in this analysis was 0.94 for the prevalence sub-scale. Cronbach's alpha of the MSI in this analysis was 0.96 for the severity sub-scale. The data were analyzed using inferential statistics including SEM. The overall fit of the models was evaluated using a set of fit indices including the goodness of fit index (GFI), adjusted goodness of fit index (AGFI), normed fit index (NFI), comparative fit index (CFI), and the root mean square error of approximation (RMSEA). **Results:** There were significant racial/ethnic differences in the associations of multiple covariates to menopausal symptoms. In White and African American women, demographical factors (β=-.341 for White; β =-.344 for African American) and perceived general health (β=-.170 for White; β=-.149 for African American) significantly affected their menopausal symptoms. In Hispanic women, demographical factors (β=-234; having higher level of education and higher perceived family income, being employed, and having a smaller number of children) had negative effects on menopausal symptoms. Also, Hispanic women with greater BMI (β=.210) had significantly more and severe menopausal symptoms. In Asian women, greater BMI (β=.118) and poorer perceived general health (β=-.207) had positive effects on menopausal symptoms. The squared multiple correlations for the models were 24% for total participants, 41% for Whites, 20% for African Americans, 7% for Asians, and 16% for Hispanics. Fit indices for all five models were satisfactory based on the standard guidelines that were recommended by Bae. **Conclusion:** The racial/ethnic differences in the covariates of menopausal symptoms could come from different cultural contexts circumscribing the women's menopausal transition. More studies on the associations of racial/ethnic-specific covariates of menopausal symptoms could provide essential information to approach different racial/ethnic groups in menopausal transition.

Sources of Funding: The original two studies that provided the data for this secondary analysis were funded by the National Institutes of Health (NIH/NINR/NIA and NIH/NINR/ NHLBI) (R01NR008926 and R01NR010568).

Path coefficients among the variables by race/ethnicity (N=980)

Variables	Endogenous variables	African Americans	Asian	Hispanic	White	Total
Demographic factors	Menopausal symptoms	-.344**	-.013	-.234*	-.534**	-.335**
Racial/ethnic group		-	-	-	-	.010
Body-mass index		.080	.118*	.210**	.049	.117**
Usage of hormone		-.022	.020	-.094	-.060	-.055
Perceived general health		-.149*	-.207*	-.118	-.162*	-.172**
Menopausal status		-.059	.091	.015	.049	.007
Acculturation factors		-	-.011	.049	-	.084*
Squared multiple correlations (R2) for menopausal symptoms		20%	7%	16%	41%	24%

Note. Path coefficients were presented as standard regression weights.

GENITOURINARY POSTER PRESENTATIONS

P-21.

Genitourinary Syndrome of Menopause: Physical Characteristics and Prevalence

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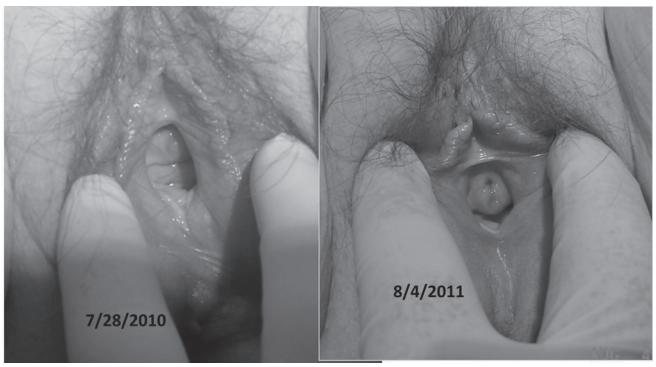
Objective: OBJECTIVE: The primary objective of this study was to determine the recognizable physical characteristics of vulvovaginal atrophy. A secondary objective was to determine the incidence of the Genitourinary Syndrome of Menopause (GSM) in asymptomatic postmenopausal women and to evaluate the correlation between vulvovaginal atrophy, vaginal pH, and serum estradiol. **Design:** DESIGN: 1500 healthy, asymptomatic postmenopausal women were examined by a single investigator in a private practice setting during routine office encounters. The women were seen for 'well-woman' visits, and none was seen for specific complaints referable to GSM: "dryness", "dyspareunia" or "irritation/pruritis". Physical examination of the vulvovaginal tissues was performed with particular attention being paid to the morphology of the vestibule (contour), the labia minora, the urethra, the hymeneal carunclae, and the introitus (elasticity). The degree of normalcy versus atrophy ("mild, moderate or severe") was recorded and vaginal pH was measured using Hydrion 3.0-5.5 pH paper strips. Serum estradiol was measured in cases of "mild" atrophy. Several women were followed photographically to illustrate the characteristic progressive atrophic change over time (*Figures) **Results:** RESULTS: Women were divided into two groups: 992 women receiving estrogen therapy (ET) versus 508 receiving no estrogen (No ET). Eighty-six percent (862/992) in the ET group had no physical signs of atrophy; 69.5 % (353/508) in the NoET group had demonstrable atrophic change. Vaginal pH was very predictive of atrophic change: NoET with a vaginal pH > 5, 85.1% (434/508) exhibited at least "mild" atrophy. A serum estradiol < 20 pg/ml was associated with a pH > 5 and atrophy in over 90% of women. Characteristic atrophic morphologic changes (*Figures) could be identified in the vestibule, labia minora, urethra, hymeneal carunclae and introitus. Atrophic change ***in*** the vagina (ie dryness, color, petechiae) was consistent only in women with "severe" atrophy. **Conclusion:** CONCLUSION: The incidence of *recognizable* atrophic change in asymptomatic hypoestrogenic postmenopausal women is approximately 70%. If the vaginal pH is >/=5, 85% of women will have demonstrable, distinct vulvovaginal atrophy at the introitus and this correlates with a serum estradiol of < 20 pg/ml.

Sources of Funding: None



P-22.

Complications of Post-Menopausal Vaginal Pessary Use for Pelvic Organ Prolapse: A Literature Review of Case Reports and Case Series

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Objective: It is estimated that 11-19% of women will develop pelvic organ prolapse (POP) during their life. Medicare estimates that 11-13% of American women will be treated with pessaries. The percent of women using pessaries will be higher in low resource countries. Caring for POP patients is multidisciplinary and includes nurses, physician assistants, gynecologists, uro-gynecologists, urologists, primary care physicians, general practitioners, internists, geriatricians, general surgeons, gastrointestinal specialists, and radiologists. A comprehensive, easily accessed centralized catalog of uncommon vaginal pessary complications based on case report and case series is being created. **Design:** A systematic search of databases including BMJ Case Report, EBSCOhost, MEDLINE, Nursing Reference Center Plus, OVID, PUBMED, and Google Scholar was conducted. Search terms included "pessary", "vaginal device", "continence device" AND "complication", "adverse effect", "infection", "injury", "bleeding", "incarceration", "evisceration", "and "cancer". Articles were examined to include only pessary use for POP in postmenopausal women. Pessary use for obstetrics, contraception, and medication administration were excluded. Additional articles were identified through reference review. **Results:** There were 955 journal articles identified from search parameters. Based on title and précis, 325 articles were examined in more detail for content. Review showed 144 case reports and case series with descriptions of 167 patients that reported a complication in a post-menopausal woman using a pessary for POP. The complications were distributed as follows: cancer 39 (23%), entrapped or embedded 38 (23%), urinary complications 28 (17%), gastrointestinal complication 21 (13%), sepsis 4 (2%), incarceration of uterus, bowel or bladder 4 (2%), evisceration 7 (4%), vaginitis 8 (5%) and other 18 (11%). **Conclusion:** The ultimate goal is to create a searchable online database containing all the pessary articles from the world literature. All articles will be available in a single web site to provide easy access to information for clinicians, practitioners, developers and industry. Case report information will be available on patient demographics, type of vaginal pessary, length of use, complication details, hormone use, treatments, and outcome. Although pessaries are safe, there can be rare devastating complications. A comprehensive database will provide timely and easier access to detailed information for best practice decision-making.

Sources of Funding: None

P-23.

A Review of 38 Case Reports of Embedded Vaginal Pessaries Used by Post-Menopausal for Pelvic Organ Prolapse

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Objective: It is estimated that 11-19% of women will develop pelvic organ prolapse (POP) during their life. Medicare estimates that 11-13% of American women will be treated with pessaries. The percent will be higher in low resource countries. Retained pessary is one of the more common complications. A pessary can become fixed in the vagina by granulation tissue, bands and scar tissue, through fistula tracts involving the cervix, vaginal mucosa or skin, or by cancer. Nurses, physician assistants, gynecologists, uro-gynecologists, urologists, primary care physicians, general practitioners, internists, geriatricians, general surgeons, gastrointestinal specialists, and radiologists who care for elderly women should be aware of this complication. **Design:** A systematic search of databases including BMJ Case Report, EBSCOhost, MEDLINE, Nursing Reference Center Plus, OVID, PUBMED, and Google Scholar was conducted. Articles were examined to include only pessary use for POP in postmenopausal women. Pessary use for obstetrics, contraception, and medication administration were excluded. Additional articles were identified through reference review. Case reports related to embedded, retained, and impacted pessary use were analyzed for content. Cases where fistulas had already formed were excluded from this analysis. **Results:** There were 955 journal articles identified from search parameters. Based on title and précis, 325 articles were examined in more detail for content. Content review showed 32 case reports and case series with descriptions of 38 patients with a retained pessary as a complication in a post-menopausal woman using a pessary for POP. The earliest description was reported in 1847. The most recent was in 2016. Reports were collected from 12 countries. The average age of patients was 73.8 with a median of 76 (range 51-99). The median parity in the case reports which included this information was 6. The following pessaries were identified; ring 19 (50%), Gelhorn 5 (3%), Watch-spring 3 (8%), metal 3 (8%), Smith-Hodge 2 (5%), and 1 each for donut, shelf, plastic balls, jade bangle, Napier-Stem, and unidentified. Seven (18%) were patient placed. Duration of use ranged from 4 weeks to 57 years with a median of 17 years. Twenty two case reports mentioned pessary care, 11 (50%) had regular care and 11 (50%) were neglected for > 1 year. Four case reports mentioned estrogen use. Presenting symptoms were divided into 8 common categories. Total exceeds 38 because some women had multiple complaints: discharge 21, bleeding 9, pain or discomfort 5, asymptomatic 5, urinary symptoms 4, fever/malaise 3, mass 2, and gastrointestinal symptoms 2. Thirty (75%) patients required an exam under anesthesia. In 13 (43%) of the cases, the pessary was cut using orthopedic instruments. In the other 25 reports, the bands of vaginal tissue or other restricting structures were resected. A buttonhole fistula to the rectum complicated one case and another case required a two-unit blood transfusion. One patient had vaginal cancer identified from a biopsy done at the time the pessary was removed. No patient died from this complication or from treatment. **Conclusion:** Ring pessaries are the most likely to become embedded. The common perception that embedded pessaries result from neglect is untrue. It is not clear if estrogen use would prevent this complication. Vaginal discharge and bleeding are the most common presenting symptoms. Most embedded pessaries will need to be handled in an operating room. In many cases, the pessary can be cut allowing it to be manipulated out of the epithelialized or granulation tissue that is restricting its extraction. Retained pessary is not a grave complication.

Sources of Funding: None

P-24.

Urinary Incontinence And Associated Factor In Climacteric Women

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Objective: To estimate the prevalence of urinary incontinence (UI) and identify associated factors in climacteric women of the Family Health Strategy (FHS) units of Montes Claros, Minas Gerais, Brazil. **Design:** A cross-sectional study which included 874 women 40-65 years with probabilistic sampling in the period 2014 to 2015. Self-reported questionnaires were applied and pre-tested, including socio-demographic, lifestyle, clinical and obstetrical factors. The dependent variable was IU characterized by International Consultation on Incontinence Questionnaire - Short Form (ICIQ-SF ™) self-reported questionnaire. It was used descriptive analysis and gross associations using the chi-square test ($p < 0.25$) and binary logistic regression analysis ($p < 0.05$). **Results:** The prevalence of UI was 22.5%. The chances of having UI in women without a partner (OR1,38, 95% CI 0.97 to 1.99), sedentary/active irregularly (OR2,14, 95% CI 1.17 to 3.93), smokers (OR1,79 ; 95% CI 1.05 to 3.03), being obese (OR1,92, 95% CI 1.21 to 3.09), presenting intense climacteric symptoms (OR2,52, 95% CI 1.48 to 4.29), have made episiotomy (OR1,47, 95% CI 1.03 to 2.12) and have ovarian cyst (OR1,71, 95% CI 1.11 to 2.64). **Conclusion:** Modifiable factors such as not having a partner, being sedentary, smoking, overweight, presenting severe symptoms of menopause, have made episiotomy and the presence of ovarian cyst was associated with UI and can be a tool for improvement of primary care health services.

Sources of Funding: none

Prevalence of UI, odds ratio (OR) crude and adjusted according to sociodemographic factors, lifestyle, anthropometric measures and clinical and obstetrical factors in climacteric women.

Variables		UI Presence %	OR (IC95%) Crude	p	OR (IC95%) Adjusted	p
Sociodemographic factors						
Age	40 to 45 years	18,6	1	0,077	-----	-----
	46 to 51 years	20,4	1,12 (0,71-1,76)		-----	
	52 to years	25,8	1,52 (1,02-2,26)		------	
Marital Status	With partner	20,6	1	0,083		
	Without partner	25,7	1,33 (0,96-1,85)		1,38 (0,97-1,99)	0,070
Lifestyle						
Physical Activity	Active/Very active	16,8	1		1	
	Sedentary/Unregular	23,4	1,50 (0,89-2,52)	0,128	2,14 (1,17-3,93)	0,014
Smoking	No	21,5	1			
	Yes	31,2	1,66 (1,00-2,75)	0,049	1,79 (1,05 – 3,03)	0,031
Anthropometric						
BMI	Proper weight	17,5	1		1	
	Overweight	20,8	1,24 (0,80-1,91)		1,30 (0,80-2,10)	0,280
	Obesity	27,8	1,81 (1,18-2,76)	0,013	1,92 (1,21-3,09)	0,006
AC	Normal	19,7	1		----	-----
	Altered	24,2	1,30 (0,93-1,82)	0,122	----	
Obstetric and clinical factors						
Climateric symptoms	Mild	17,6	1	0,000	1	
	Moderate	28,6	1,87 (1,31-2,67)		1,87 (1,27-2,76)	0,002
	Intense	35,3	2,55 (1,55-4,20)		2,52 (1,48-4,29)	0,001
Episiotomy	No	18,8	1	0,028	1	0,036
	yes	25,1	1,45 (1,04-2,02)		1,47 (1,03-2,12)	
Ovary Cyst	No	20,7	1	0,012	1	0,015
	Yes	30,1	1,66 (1,11-2,46)		1,71 (1,11-2,64)	

Bivariate analysis: independente variable associated to outcome variable to the level of 0,25; OR crude: odds ratio crude; OR adjusted: odds ratio adjusted of multivariate analysis; IC 95%: confidence ;

HEALTH SERVICES AND SURVEYS POSTER PRESENTATIONS

P-25.

Relationship between age at menopause and alcohol consumption: The Korea National Health and Nutrition Examination Survey

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Objective: To investigate the relationship between age at the menopause and alcohol consumption in South Korea by using data from the 2010-2012 Korean National Health and Nutrition Examination Surveys (KNHANES). **Design:** Cross-sectional data of 712 women who became menopausal state within 3 years were analyzed. **Results:** Non-drinker, mild to moderate-drinker and heavy-drinker population were 271 (36%), 426 (61.1%) and 17 (2.9%). After adjustment for body mass index, smoke, and exercise (model 1) or smoke, exercise, education, duration of menopause, age at menarche, age at first and last delivery (model 2), mean age at the menopause of non-drinker, mild to moderate-drinker and heavy-drinker was 51.6 ± 0.2, 50.7 ± 0.2 and 50.5 ± 0.6 years (model 1) and 51.3 ± 0.2, 50.8 ± 0.2 and 50 ± 0.8 years (model 2). The difference of mean age at the menopause among three groups was statistically significant (model 1; $p = 0.0016$, model 2; $p = 0.014$). In the Alcohol Use Disorders Identification Test (AUDIT) score, mean age at the menopause of <5, <10, and ≥10 score groups was 51.2 ± 0.2, 50.6 ± 0.4 and 50.1 ± 0.5 years (model 1) and 51.1 ± 0.1, 50.7 ± 0.4 and 49.6 ± 0.5 years (model 2). The difference of mean age at the menopause among three groups was statistically significant (model 1; $p = 0.014$, model 2; $p = 0.0071$). **Conclusion:** In the Korean women, alcohol consumption was associated with an early age at the menopause.

Sources of Funding: None,

P-26.

Development of a Community Based Menopause Workshop…Menopause Re-Imagined, for the Women of the Upper Cumberland Region of Tennessee

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Objective: Although a natural and normal transition from the childbearing years, menopause is a multifaceted event that affects women physically, mentally, and emotionally. Evidence has shown that a woman's ability to cope with the changes and stresses of menopause can be enhanced through education. Women will spend a third of their life in a post- menopausal state. A successful transition in the individualized yet unique journey of menopause is a women's health management challenge that can be lessened when education about menopause is provided to women by health care professionals possessing creativity, commitment, caring and skill. The positive effects of menopause education have been reported in the literature; however, the United States has a scarcity of research that looks at educational strategies to assist women in increasing their knowledge about menopause. Studies by Tsao & Huang (2003), Udea, Matsuda, Okano, and Suenaga (2009), and Hunter & O'Dea (1999), have shown the lack of knowledge women have regarding menopause as well as the positive effects from menopause education, there is a scarcity of studies or programs in the United States (US) that look at effective educational strategies where women can have fears alleviated, myths debunked, healthy choices promoted, and confidence restored as they learn about this natural transition in their lives. Countries such as Japan, China, Canada, and Korea have published studies espousing the success of educational intervention strategies, yet the US literature reveals a paucity of published work regarding this issue. The purpose of this research project is to create a menopause workshop in the Upper Cumberland Region of Tennessee, where educating women could result in increasing knowledge, decreasing fear and anxiety, decreasing cost of unnecessary medications and treatment, decreasing health related issues, and promoting overall health, well-being and empowerment. Objective #1 is to conduct the initial workshop in the summer of 2016. Objective #2 the workshop post- test will reflect an increase of knowledge in 75% of the attendees compared to the pre- test knowledge. Objective #3 will that 50% of the attendees will indicate an increased level of empowerment following the workshop related to the menopausal transition as identified on the Personal Progress Empowerment Tool (PPS) (Johnson, Worrell, & Chandler, 2005). Objective #4 A post workshop questionnaire demonstrating that 75% of those who successfully completed the menopause workshop were satisfied. **Design:** A one group quasi-experimental design utilizing a pre and post-test format to assess increase of knowledge base as a measurement of success, PPS checking for empowerment increase and a satisfaction questionnaire using a Likert scale of 1-5. An increase of knowledge and empowerment, a decrease in anxiety, fear and confusion, improved utilization of healthcare resources in the community, a decrease in medicalization and related costs and an overall increase in well-being. **Results: A** brief cost effective educational approach might be used to decrease much of the uncertainty, fear, physical and emotional distress related to menopause (Sirtzinger, Robinson, & Crawford, 1992). Education and health promotion related to menopause helped to alleviate negative attitudes (Ayers, Forshaw, & Hunter, 2009). Health education regarding menopause is markedly inadequate compared to that concerning puberty, conception, and birth, leaving menopausal women with feelings of loneliness, anxiety, and confusion (Udea, 2004). Women experience not only the biological changes that accompany menopause but they may experience a loss from their maternal role, youth, beauty, and purpose in life (Bauld & Brown, 2009). Women felt the worst thing about menopause was not knowing about menopause LaRocco & Polit (1980). The workshop will be held in the summer of 2016. **Conclusion:** The workshop will be held in the summer of 2016.

Sources of Funding: None.

P-27.

Post Menopausal Bleeding Assessment Clinic: Audit of a Focused Care Clinic

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Objective: To perform an audit of a novel Post Menopausal Bleeding Assessment Clinic (PMBAC) to determine patient characteristics, diagnostic modalities, outcomes and referral pathways. The overall goal is to provide guidance for improving care for this high risk population in our region. **Design:** A prospective quality assurance project was established for a novel PMBAC that was opened at The Ottawa Hospital in Jan 2014. Data was collected for 2 years until December 2015. The data collected including patient demographics including BMI, risk factors for uterine cancer, pelvic ultrasound reports, endometrial biopsy results and subsequent outcomes. **Results:** Over 2 years, 111 patients were seen in the clinic which limited referrals to post menopausal bleeding only. Patient characteristics included mean age of 63.5 years, BMI of 31 and endometrial echo of 9.6mm. Risk factors included hypertension (37%), diabetes (15%) and tamoxifen use (10%). Initial biopsy were as follows: malignancy in 13 (11.7%), benign in 32 (29%), insufficient sample in 35 (32%), and there were 8 (7%) failed cases. Following initial assessment, 20 patient required hysteroscopic evaluation in the outpatient hysteroscopy clinic, which detected 3 additional malignancies and 3 cases of hyperplasia. Another 14 patients underwent hysteroscopy in the operating room, where one additional case of endometrial hyperplasia was diagnosed. **Conclusion:** A regional referral program for Post Menopausal Bleeding provides focused care for patients at risk of uterine malignancy. While initial assessment and biopsy offers diagnosis in a timely fashion, many patients still require further evaluation in the form of hysteroscopy guided procedures. Access to an outpatient hysteroscopy suite and services are necessary to provide support for evaluation of PMB.

Sources of Funding: none

P-28.

Evaluation of menopausal symptoms in mid-aged South American women using the 10-item Cervantes Scale (CS-10)

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Objective: To evaluate the presence of menopausal symptoms and factors related to intensity in mid-aged women. **Design:** This was a cross-sectional multicentric study in which women aged 40 to 65 from various South American sites were surveyed with the 10-item Cervantes Scale (CS-10) and a questionnaire containing personal data. **Results:** A total of 857 women participated from Cartagena, Colombia (n=215, Afro-Colombian, part of the research project named CAVIMEC (Calidad de Vida en la Menopausia y Etnias Colombianas). Guayaquil, Ecuador (n=195, Mestizo), Cusco, Perú (n=231, Quechua and high altitude) and Asunción, Paraguay (n=216, Mestizo). Median age of all surveyed women was 48 years, with those from Guayaquil being older. A 32.9% were obese (BMI 30 or more), 55.0% being postmenopausal, and 10.8% using menopausal hormone therapy (MHT). Rate of being postmenopausal was evenly distributed among studied sites. Median [IQR] total CS-10 score was 9.0. The top three most frequently reported symptoms were muscle and joint pains (85.4%), hot flashes (75.9%) and heart discomfort (61.5%); with these also being the most frequently rated as severe/very-severe. Higher total CS-10 scores (indicating more severe symptoms) were significantly found among those living high altitude or being indigenous (Quechua) and postmenopausal. No differences were observed in terms of BMI, MHT use or being diabetic or hypertense. **Conclusion:** In this large mid-aged female sample, menopausal symptoms correlated to menopausal status, high altitude and indigenous ethnicity.

Sources of Funding: None

P-29.

Survey of Canadian PGY-4 and PGY-5 Obstetrics and Gynaecology Residents on Knowledge of and Exposure to Premature Ovarian Insufficiency

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Objective: 1. To determine exposure to and general knowledge around premature ovarian insufficiency (POI) among Canadian senior Obstetrics and Gynaecology residents. 2. To identify an opportunity to improve trainee knowledge around and exposure to POI during residency training. **Design:** An electronic survey was administered to senior Obstetrics and Gynaecology residents (PGY-4 and PGY-5) through their residency programs. Survey questions assessed basic POI knowledge and previous exposure (didactic and clinical) to POI. Respondents were asked to indicate comfort level in managing POI patients. Data was summarized descriptively and compared between two trainee groups (PGY-4 and PGY-5) using Chi-square tests. **Results:** Survey responses were received from residents in all sixteen Canadian Obstetrics and Gynaecology residency programs with an overall response rate of 45% (93/207 residents). With respect to basic POI knowledge, 80% (74/93 residents) identified the correct age for diagnosis of POI and 67% (62/93 residents) recognized the most common aetiology. Almost all respondents (99%, 90/91 residents) would prescribe hormone therapy for

POI treatment, with the most preferred option being hormonal birth control (62%, 56/91 residents). Most trainees (61%, 57/93 residents) lack access to a specialized POI clinic at their centre and 63% (58/92 residents) have seen less than six patients with POI during their residency training. Most respondents feel somewhat comfortable managing POI patients (68%, 63/93 residents) but 22% (20/93 residents) feel totally uncomfortable. The majority of respondents (84%, 77/92 residents) indicated they would benefit from additional training in POI. The only statistically significant difference between PGY-4 and PGY-5 trainees was that more PGY-5 residents could identify the correct age for diagnosis of POI compared to PGY-4 residents (91% vs. 70%, p=0.014). **Conclusion:** A significant proportion of trainees lack basic knowledge around POI and most senior Obstetrics and Gynaecology residents in Canada indicate the need for further didactic and clinical exposure to POI during residency training. We identify an opportunity for residency programs to improve curricula around POI. Initiatives may include establishing specialized POI clinics at academic centres, increasing didactic teaching around POI and developing and disseminating clinical practice guidelines for the diagnosis and management of POI.
Sources of Funding: None.

PHYSICAL ACTIVITY AND NUTRITION POSTER PRESENTATIONS

P-30.
Caloric Restriction and Longevity: Should this counseling be included in the care of Postmenopausal Women

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Objective: The first known study to test caloric restriction's influence on senescence was conducted by Thomas B. Osborne, *et al* in 1917. His report, "The Effect of Retardation of Growth Upon the Breeding Period and Duration of Life of Rats", was an unprecedented experiment that showed caloric restriction extending the life of mammals. Numerous studies on caloric restriction conducted since then show decreased signs of aging across eukaryotic life forms. This article reviews the data on whether the age-old practice of caloric restriction should be introduced into the counseling of post-reproductive aged women. **Design:** This review assessed the scientific literature regarding caloric restriction, mTOR, and menopause. **Results:** The data suggest promising results for post-menopausal women who follow a calorically restricted diet. This type of diet inhibits the action of the mTOR pathway, which is linked to ailments of aging such as Alzheimer's disease, cancer, Type-2 diabetes, and heart disease (Blagosklonny, 2006). Caloric restriction weight loss was found to reduce inflammation in post-menopausal women, which is associated with cancer rate reduction (Imayama *et al*, 2012). Inhibition of mTOR via caloric restriction directly reduced mammary tumor growth in mice, supporting the relationship between obesity and breast cancer (Nogueira *et al*, 2012). Another study showed that a reduction of mTOR caused less muscle-deterioration associated with aging, which is important to prevent falls common within the elderly population (Wu *et al*, 2013). A recent paper examined young adults who were calorically restricted for two years and found higher rates of bone loss (Villareal *et al*, 2015). This sheds light on the possible side effects of reducing the mTOR pathway via a calorically restricted diet. **Conclusion:** Much of the data support caloric restriction being associated with increased longevity and decreased illnesses commonly associated with aging. However, there is evidence indicating that caloric restriction could increase chances of osteoporosis, so further testing needs to be done to determine if this can be prevented with exercise. The data suggest that caloric restriction research and counseling be explored in the menopausal population of women, in which weight gain is a major consequence of this life transition.
Sources of Funding: none

P-31.
Addressing Physical Fitness in Postmenopausal Women: A Template from the Military

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Objective: As women enter the menopausal and post-menopausal stages of life, many struggle with the maintenance of their physical fitness. Encouraging women to stay physically fit could have potential benefit not only in the prevention of cardiovascular disease and diabetes, but also in the prevention of certain cancers. Although clinicians stress exercise in this population, the goal of what exercise competence is for a woman to achieve and an appropriate way to measure this fitness level has been not been incorporated into clinical practice. The U.S. military branches provide set requirements for body composition analysis and minimum performance in various physical activities; all service members must meet these standards, which are tailored to age, twice a year. This review compared the standardized physical assessments for older women that are used in each branch of the military to determine which one appeared to be the most efficient for all civilian physicians to utilize when counseling postmenopausal women on physical fitness. In April, 2016 the US Navy updated and implemented revised standards. These updated standards will be reviewed for this abstract. **Design:** Since there are no physical fitness standards for postmenopausal women that are universally used by clinicians that could be found through a literature search, the military standards were explored. Each military branch (Navy, Marines, Air Force, Coast Guard and Army) has a physical fitness standard for women. This paper presents the guidelines from each of these military branches with recommendations of which one appears to be most suited for the midlife and older female population. **Results:** In comparing the physical fitness standards between the branches of the armed forces there were differences that distinguished each set of standards. All branches, with the exception of the USMC utilize push-ups and sit-ups, also referred to as curl-ups, to gauge strength in the individual. The Marines substitute a flexed-arm hang for push-ups in their standards, which may be too difficult for most women. The Air Force, Coast Guard and Navy have a 1.5-mile run as a part of their fitness assessment. The Army has a 2-mile run and the Marines have a 3-mile run, which again may be too difficult for many postmenopausal women. Both the Navy and the Coast Guard also offer a swim as a substitute cardiovascular exercise, whereas the Coast Guard does not offer this. This would be a deterrent to women who cannot run. All branches, except for USMC provide standards for women according to their age. The age stratification in the Navy and Army is 5-year intervals, whereas the Air Force and Coast Guard have ten-year increments. The Navy is the only branch of the military that provides standards up to age 65+, thus providing more guidance specifically for postmenopausal women. The Navy guidelines, therefore appear to be the most adaptable to a civilian clinical practice. **Conclusion:** These data suggest that clinicians should consider utilizing the US Navy's PFA standards to counsel their patients on which exercise regimen they should use. US Navy PFA guidelines can also be used by the postmenopausal woman and clinician to quantify how fit the woman is and whether she is meeting her physical fitness goal.
Sources of Funding: None

P-32.
Studying the impact of exercise on hot flashes using mobile exercise tracker, MENQOL scale and hot flash diary.

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Objective: During menopause, a common symptom that prompts women to seek medical attention is hot flashes. Seventy five percent of all menopausal women (approximately 50,000,000) will experience hot flashes, and that 15% will be severely affected (1). In addition to hot flashes, other significant climacteric symptoms include depression, insomnia, nervousness, fatigue, arthralgia, headache, vaginal dryness and night sweats. Most clinical trials assessing therapeutic efficacy use subjective reports (eg questionnaires, diaries). The current gold standard for objective assessment of hot flashes is measuring the skin conductance level. However, there is still a relative discordancy between self-reported and objectively detected hot flashes even with the use of skin conductance level. A combination of objective and subjective measures probably constitutes a valid assessment of vasomotor symptoms. Resting energy expenditure decreases with age but also decreases with loss of ovarian function. There is little data on energy expenditure as it relates to the menopause and how influences such as exercise play a role in metabolic rate and how this may play a role in vasomotor symptoms. Mobile exercise tracker is a portable monitor that is used to collect minute by minute data on energy expenditure, physical activity and sleep monitoring. The indirect calorimeter is a handheld device that measures basal metabolic rate. There are also no studies comparing this device to the current subjective evaluative methods like the hot flash diary and quality of life surveys. Our aim is to utilize the mobile exercise tracker as a measure for basal metabolic rate and changes in BMR as it relates to intervention with exercise. **Design:** A prospective randomized observational trial was used to obtain minute by minute data on energy expenditure, temperature changes, and vasomotor symptoms. Participant had an exercise intervention over an eight-week period in which the same outcome measures were used continuously with the wristband, daily with the hot flash diary, weekly with MENQOL scale. The indirect calorimeter was used twice in the trial before and after exercise intervention to measure basal metabolic rate. **Results:** Women were between the ages of 35-60, overweight (BMI=30) and experiencing hot flashes secondary to natural or surgical menopause. One hundred percent were Hispanic. Forty two percent of women at enrollment reported moderate hot flashes with an average of 5 perceived hot flashes per day and a basal metabolic rate from 1320-2340. Those women who did not exercise had a decrease in basal metabolic rate. They continued to have severe hot flashes. **Conclusion:** Our preliminary data imply there is a correlation of improvement of reported hot flash severity when there is an increase in basal metabolic rate with monitored exercise. Subjects had 89% compliance when completing daily diary logs of exercise, hot flashes and a mobile exercise tracker usage during the 14-week study.
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P-33.
Prevalence and factors associated with Metabolic Syndrome climacteric women in Southeastern Brazil

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Objective: To estimate the MS prevalence and identify factors associated in climacteric women. **Design:** Cross-sectional and analytical study, realized in 2014 and 2015. Population of 30.018 women, age of 40 to 65 years registered in 73 Family Health Strategies of Montes Claros, Minas Gerais, Brazil. Sampling type probabilistic, with sample of 895 women. The data collect was by questionnaires (sociodemographic, behavioural, reproductive, gynecologic and clinic), anthropometric rating and blood collect. The dependent variable was the MS, according National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATPIII), which claim the diagnostic, the presence of 3 or more of next factors: waist circumference(≥88 cm), blood pressure(≥130ou≥85mmHg), high density lipoprotein cholesterol(<50mg/dL), triglycerides(≥150mg/dL) and fasting glycemia (≥110mg/dL). Were realized descriptive, biraviate and multiple analysis through hierarchical regression model of Poisson.

The measure of adopted association was the prevalence ratio (PR). **Results:** The MS prevalence was 56,5%. The prevalence rate for MS was presented in women with age of 46 to 51 years (1,32; 95% CI: 1,09-1,61), with 52 to 65 years (1,54; 95% CI: 1,29-1,84), with schooling in high school II (1,08; 95% CI: 0,92-1,29) and elementary school I (1,20; 95% CI: 1,03-1,40). After adjusting for socio-demographic factors, were observed the MS prevalence in women that eat less than 3 fruits a day (1,13; 95% CI: 1,00-1,29), with moderate to severe symptoms during climacteric (1,15; 95% CI: 1,02-1,30) and with early menarche (1,10; 95% CI: 0,83-1,21). And the volunteers already made tubal ligation (0,87; 95% CI: 0,76-0,99) and had late menarche (0,86; 95% CI: 0,75-1,00) were protection factors to the MS presence. For setting proximal level was appointed MS prevalence rate to women with overweight and obesity (1,67; 95% CI: 1,38-2,03) and altered waist-hip ratio (WHR) (1,26; 95% CI: 1,08-1,47). **Conclusion:** The older women, with low schooling level, who eat a few fruits, have moderate to severe climacteric symptoms, with early menarche, with overweight and obesity and with altered WHR presented the biggest MS prevalence and those who already made tubal ligation and had late menarche presented lower prevalence of MS.

Sources of Funding: CAPES

Crude and adjusted rate prevalence according with socio-demographic factors, behavioural, gynecologic, anthropometric and clinic to metabolic syndrome (MS) in climacteric women

Variable		RP (CI95%)	Value p	RP (CI95%)	Value p
		Crude		Adjusted	
Socio demographic factors (distal level)					
Age	40 to 45 years	1,0		1,00	
	46 to 51 years	1,37 (1,12 – 1,66)	0,002	1,32 (1,09 – 1,61)	0,005
	52 to 65 years	1,64 (1,38 – 1,95)	0,000	1,54 (1,29– 1,84)	0,000
Schooling	High school/college	1,0		1,00	
	elementary II	1,17 (0,99 – 1,39)	0,073	1,08 (0,92 – 1,29)	0,336
	elementary I	1,35 (1,17 – 1,57)	0,000	1,20 (1,03 – 1,40)	0,021
Gynecologic and behavioural factors (intermediate level)					
Consumption of fruits	Eat 3 or more a day	1,00		1,00	
	Eat less then 3 a day	1,15 (1,01 – 1,32)	0,042	1,15 (1,01 – 1,30)	0,036
Climacteric symptom	Absent/Light	1,00		1,00	
	Moderate/Severe	1,17 (1,03 – 1,43)	0,015	1,15 (1,02 – 1,30)	0,022
Phases of menarche	12 to 14 years (Normal)	1,00		1,00	
	≤ 11 years (Early)	1,01 (0,85 – 1,21)	0,890	1,00 (0,83 – 1,21)	0,994
	≥15 over years (Late)	0,87 (0,75 – 1,00)	0,050	0,86 (0,75 – 1,00)	0,046
Tubal ligation	Did not	1,00	0,081	1,00	0,045
	Already did	0,89 (0,78 – 1,02)		0,87 (0,76 – 0,99)	
Anthropometric and clinic factors (proximal level)					
BMI	Proper weight (≤ 24,99 kg/m2)	1,00		1,00	
	Overweight/Obesity (≥ 25,00 kg/m2)	1,84 (1,53 – 2,23)	0,000	1,67 (1,38 – 2,03)	0,000
WHR	Normal (< 85 cm)	1,00		1,00	
	Altered (≥ 85 cm)	1,48 (1,28-1,72)	0,000	1,26 (1,08 – 1,47)	0,003

%*: Corrected by the design effect (deff); PR: Crude prevalence rate level in p<0,25 and adjusted level in p<0,05; BMI: Body mass index; WHR: Waist hip ratio; CI 95%: Confidence interval.

P-34.

Grip strength and rapid foot-tapping in relation to the menopausal transition in Campeche, Mexico.

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Objective: Studies have shown reduced hand grip strength from pre- to peri- to post-menopause. One cohort study found the trend explained by body size. Our aim was to test whether grip strength declines with menopausal status among rural and urban women in the state of Campeche, Mexico. In addition, we tested whether foot-tapping -- a measure of muscle and neuron function -- also declines with postmenopausal status. **Design:** Participants aged 40-60 were drawn from the city of Campeche (n=305); semi-rural Mayan communities (Ich Ek and Suc Tuk, n=78); isolated Mayan communities, Hopelchen municipality (n=76); and isolated non-Mayan communities, Calakmul municipality (n=84). In total, 543 women were interviewed; 537 participated in foot tapping, 536 in hand grip strength measures. Grip strength was measured with a digital hand dynamometer (Smedley), two measures with each hand. Rapid foot taps were performed while the participant sat on a chair, heel on the ground, tapping her toe for 10 seconds, twice per foot. The highest grip strength and number of foot taps were used here. Height, weight, waist and hip circumferences, measures of balance and activity were also collected. Menstrual cycles were categorized as pre-menopausal (regular or changes in menstruation, 41%); peri-menopausal (cycles more or less frequent; cycles 6+ days different; or 2+ months without menses, 24%); or post-menopausal (12+ months without menses, 35%). Women were categorized as Maya (55%) or non-Maya (38%) on the basis of last names, language spoken, and place of birth of themselves, their parents, and their grandparents. Some women (7%) could not be clearly classified and, for these analyses, were combined with non-Maya. Health was self-reported and dichotomized into poor/regular and good/very good. An index of socioeconomic status (SES) was computed from 10 culture-specific dimensions, including number of people living in the home, source of water, and type of latrine (range 17-39). Dependent variables were considered in relation to grip strength and foot taps using ANOVA and Pearson correlation. Linear regression models were used to see if menopausal status remained significantly associated with grip strength and foot tapping after controlling for urban/rural residence, ethnicity, and other variables. **Results:** In univariate analyses, grip strength declined from 22.5 kg (pre-menopause) to 21.6 kg (peri) to 20.0 kg (post, $p<0.01$). Foot tapping declined from 35.6 (pre-menopause) to 33.4 (peri) and 33.9 (post, $p<0.05$). Compared to Mayan women, non-Mayan women had greater grip strength and more foot taps ($p<0.05$). Grip strength and foot-tapping increased with better health ($p<0.01$). Foot tapping and grip strength varied significantly across the four sites, and, compared to rural women, urban women had higher grip strength and foot taps ($p<0.01$). Higher levels of grip strength were significantly associated with younger age, higher SES, but not BMI or waist circumference. Higher levels of foot-tapping were significantly associated with younger age, higher SES, lower waist circumference, but not BMI. Grip strength and foot-tapping were correlated (r=0.296, p<0.01). In linear regression models that included all significant variables (except for foot tapping), menopausal status was not associated with hand grip strength. Instead, health, urban/rural residence, and age were significantly associated with grip strength. In models that included all significant variables (except for hand grip strength), menopausal status was not associated with foot tapping. Instead, health, urban/rural residence, and age were significantly associated with foot tapping. **Conclusion:** The findings of this study differed from other studies in that hand grip strength was not significantly associated with menopausal status after controlling for health, urban/rural residence, and age. The findings were similar for foot-tapping. Surprisingly, more active rural women had lower grip strength and foot tapping measures. Health was more important than body size in explaining variation in grip strength and foot tapping.

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P-35.

Effectiveness of a Web-based physical activity promotion program among Chinese American midlife women

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Objective: Asian American midlife women are reportedly at high risk for chronic diseases such as cardiovascular disease, hypertension and diabetes. These prevalence rates of chronic diseases can be effectively reduced by increasing physical activity. However, their participation rate in physical activity is lower than that of White midlife women. Physical activity was devalued in Asian cultures. Thus, it is critical importance to conduct a culturally tailored program for increasing physical activity among Asian American midlife women. The purpose of this pilot study is to evaluate a theory driven Internet intervention that is culturally tailored to Chinese American midlife women. The specific aims of the preliminary study are to evaluate the Web-based physical activity promotion program (WPAPP) through a usability test and to explore the effectiveness of the Web-based physical activity promotion program in improving Chinese American midlife women's physical activity experience. **Design:** The study design was a randomized repeated measures pretest/posttest (pre-test, post 1 month, & post 3 months) control group design. The settings of the study were Internet communities/groups for midlife women (ICMWs) and Internet communities/groups for Asian Americans (ICAAs). The study was announced in the settings through their sites, listservs, and instant messaging. The instruments of the pilot study included: questions on background characteristics, the Physical Activity Assessment Inventory, the Modified Barriers to Health Activities Scale and the Kaiser Physical Activity Survey. The reliability and validity of all the instruments were supported in Asian American midlife women (.69<Cronbach's alpha<.91; Test-retest correlation=0.79 to .91). **Results:** Sixty seven Chinese American women were recruited in this study. After randomly assigned to control or intervention group, participants were measured on three occasions (Time 1:pre-test, Time 2:post 1month, & Time3: post 3 months) regarding their scores on the Modified Barriers to Health Activities Scale (BHAS), Physical Activity Assessment Inventory (PAAI) and Kaiser Physical Activity Survey (KPAS) during the period. Sixteen observations were retained for further statistical analysis, after excluding observations from the intervention group who did not complete any of the post tests, responses having clear patterns, and participants who did not answer the above questionnaires. The mean age for the control group is 45.1 and for the intervention group is 45.83. All participants are married, and they graduated from college or graduate school. Repeated measure ANOVA was used to compare changes in measured variables by time and group after controlling for the pretest data. Results showed that participants in the intervention group than those in the control group significantly decreased their barriers in performing physical activities at Time 1 (F=14.10, p<.001, effect size=.45). Participants in the intervention group scored higher on the KPAS at time 1 than control group with a median effect size (F=2.99, p=.07, effect size=.19). PAAI scores of intervention group increased by time whereas the scores of control group decreased by time although the changes were not significant (F=1.31, p=.29, effect size =.10). **Conclusion:** The WPAPP that was tested in this study is the first theory driven Web-based physical activity promotion program that is culturally tailored to Chinese American midlife women by incorporating ethnic-specific predictors of their physical activity including their cultural attitudes. This study provided a prototype of culturally competent Web based physical activity promotion program for ethnic minority women, which could be immediately extended to other ethnic groups.

This study also provided fundamental knowledge that the field of more-targeted/ tailored Web-based programs can be built, implemented, and disseminated to improve physical activity experience for ethnic specific groups of women.
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REPRODUCTION POSTER PRESENTATIONS

P-36.

Pregnancy Counseling for Post-Menopausal Women

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Objective: Menopausal practitioners rarely ask patients about their desire for pregnancy, since menopause is defined as the loss of functional follicles. Assisted Reproductive Technology and Oocyte Donation/Egg Freezing in the modern era no longer make it a valid reason for practitioners to not bring up the topic. Although pregnancy at a later age is stigmatized as a danger to the baby and mother, recent data suggest that this may not always be the case. In addition, women are living longer, and older mothers' longevity projections still have them seeing their offspring to the age of majority. Population data from 2011-2015 indicates that over 20% of the populations in countries such as Japan and Italy each are above the age of 65, with the average life expectancy of 82 years. Our goal is to evaluate the risks associated with post-menopausal pregnancy and to recommend a counseling strategy by which menopausal practitioners may wish to conduct patient care. **Design:** Peer reviewed journals and guidelines from professional organizations on post-menopausal pregnancy risks and outcomes were examined. Source and experimental construct validity were confirmed in all papers used in this review. Data as confirmed by experimental test-retest reliability indicate the relevance of these findings. **Results:** Available data examined women in the bracket ≥40 yr, therefore making it difficult to extrapolate data at each specific menopausal age. These data suggest that post-menopausal women who are given appropriate counseling do not have statistically increased risks for pregnancy complications when compared to risk stratified pre-menopausal women. In the study by Dietl et al, the CI values for post-menopausal women were generally <0.05 for each pregnancy variable examined. As long as 1) pre-existing chronic diseases were medically and dietetically treated, 2) pregnancy-induced morbidity was monitored and controlled, 3) women attended regular pre-natal check-ups, 4), a healthy life style was adhered to during the pregnancy, and 5) delivery occurred in a perinatal center, post-menopausal women had successful pregnancy outcomes (Dietl et al). Additionally, evidence suggests that Caesarean Section rates may not be increased due to health conditions and obstetrical complications in older women. Regarding spontaneous abortion, the rate following IVF appears to be not significantly different from the rate following natural conception. The rate of spontaneous abortion is associated solely with the mother's age. With oocyte donation, age issues are eliminated. **Conclusion:** Pregnancy counseling for post-menopausal women should be included based on research that suggests that these women are able to have a successful pregnancy outcome. Monitoring the baseline and pregnancy-induced health conditions in an individualized manner is critical to the success of a post-menopausal pregnancy. Research that examines further breakdown of age brackets ≥40 yr needs to be conducted to understand the implications of pregnancy in each age range of older women. Dietl, A., S. Cupisti, M. W. Beckmann, M. Schwab, and U. Zollner. "Pregnancy and Obstetrical Outcomes in Women Over 40 Years of Age." Geburtshilfe Und Frauenheilkunde. Georg Thieme Verlag KG, Aug. 2015.

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P-37.

Implication of structural and transcript alteration in frozen-thawed pre- and peri-menopausal stage murine ovaries: decline in tolerance against cryodamage?

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Objective: Cryopreservation of ovarian tissue is an emerging technique for fertility preservation for reproductive age cancer patients. During freezing, cells or tissues are exposed to harmful environment, which leads to a decline of cellular functionality and alteration in fine structure and gene expression. In this study, we attempted to demonstrate the effects of cryopreservation on structural and gene expression changes in pre- and peri-menopausalstage murine ovaries. **Design:** Ovaries of pre-menopausal (six-week-old C57/BL6 mice, n=20) and peri-menopausal (six-month-old C57/BL6 mice, n=20) were isolated, and were cryopreserved using mass cryopreservation. After thawing, ovaries were fixed for H&E staining and electron microscopy, and were used for the isolation of total RNAs. The expression of specific genes was analyzed using RT-qPCR. Non-cryopreserved, fresh isolated ovaries of each group were used as control. **Results:** Morphological analysis of non-frozen ovaries demonstrated even follicle distribution in pre-menopausal stage and irregular distribution in pre-menopausal stage groups. Cryopreservation decreased the number of follicles located near the epithelia in both groups. The expression of ovarian aging-related genes wasaltered after cryopreservation in both groups as well. The expression of POF5F1, NOBOX, GDF9 were significantly decreased in peri-menopausalstage mice, which was not significant in thepre-menopausal stage mice. **Conclusion:** In conclusion, cryopreservation of ovaries leads to the alteration in structural and molecular signature, indicative of an age-related decline in tolerance against cryodamage. Further studies are needed to elucidate the age-dependent effects of ovarian tissue cryopreservation on non-coding RNA expression involved in folliculogenesis.

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SEXUAL HEALTH POSTER PRESENTATIONS

P-38.

Mature Women's Attitudes About the Impact of Sexual Concerns on Relationship and Sexual Satisfaction

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Objective: Sexual function plays an important role in the lives of many women and is often a key measure in overall quality of life, especially for women in partnered relationships. The aim of this study was to assess the impact of sexual concerns on the quality of romantic relationships and intimacy in women at midlife and beyond. **Design:** This cross-sectional, questionnaire-based survey was conducted online in a convenience sample of 505 women aged 40 to 75+ years in the United States. Respondents were required to have at least one sexual concern and be in a current partnered relationship to complete the survey. The self-administered 50-item questionnaire was distributed and collected by a 3rd party research firm. This questionnaire recorded various parameteters, including sociodemographic information, sexual health concerns and their associated personal impact, help-seeking motivation, and the impact of sexual concerns on relationship quality and sexual intimacy. Respondents were not compensated for their participation in this survey. **Results:** Seventy-five percent of the respondents were aged 40-59 years while 25% were aged 60-75+ years. The majority of women had been in a relationship for greater than 10 years. Diminished or no sexual interest and diminished or inadequate vaginal lubrication were the 2 most common sexual concerns across all age groups. Women in their 40s felt the most negative impact on the enjoyment of their partnered relationship from their sexual concern(s) compared to women in the older age groups. The majority of women agreed with the statement that sexual activity was important to their overall quality of life, except for women in their 70s where the majority disagreed. Sixty-one percent of respondents engaged in sexual activity less than once a month. If the respondents were experiencing painful intercourse, they were most likely to engage in penetrative sex to make their partner happy. Fifty-two percent of the respondents had not discussed their sexual concern(s) with their HCP. When concerns were discussed, it occurred during an appointment for another reason, with 70% of the respondents reporting that they initiated the discussion themselves. Personal lubricants and vibrators were the most commonly reported products used to alleviate sexual concerns. For respondents aged 40-69, feeling better about their body was the most frequent response when asked what would increase satisfaction with their sex life. The majority of women older than 70 were happy the way their sex life was. Among all respondents, sexual concerns only somewhat decreased their ability to enjoy their partnered relationship. **Conclusion:** This survey provides an important overview of the sexual health concerns and their impact on women at midlife and beyond. Although the women in this study felt that their sexual satisfaction could improve, the majority was happy with the quality of their partnered relationships. This study demonstrates that, as women age, sex is still important but becomes less of a determinant of overall relationship satisfaction.

Sources of Funding: Nuelle, Inc.

P-39.

Vaginal Laxity and Female Sexual Function: Minimally Invasive Treatment Options

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Objective: Vaginal laxity and tissue architecture have often been overlooked as contributing etiological factors to female sexual dysfunction. Vaginal looseness can lead to diminished physical sensation during intercourse. This reduction in sensation is often coupled with a reduction in sexual satisfaction, all of which can also impact a woman's sense of sexual self-esteem and her relationship with her sexual partner. **Design:** A review of PubMed using the terms vagina, laxity/loose and sexual function or vaginal relaxation syndrome produced a total of 31 English articles. A review of the ClinicalTrials.gov database was carried out using the terms vagina and laxity/loose and revealed 4 studies, only one of which is currently ongoing **Results:** Treatments for vaginal laxity range from surgery to self-prescribed over-the-counter medications, with varying degrees of clinical evidence associated with each. There are currently a number of energy-based devices being used to treat vaginal laxity in an office-based setting in some areas of the world, e.g., CO_2 laser, erbium laser, unipolar radiofrequency (RF) and monopolar RF with cooling. There are significant differences among the different energy-based devices, which include whether the outcome is oriented towards aesthetic genital appearance or underlying sexual function. Of the 31 articles, only 4 were related to non-surgical vaginal treatment to improve sexual function. One was on the effect of postpartum pelvic floor muscle training on vaginal symptoms and sexual dysfunction. Two were for treatment of vaginal tissue to improve laxity and sexual satisfaction, both using a targeted radiofrequency device with controlled cooling. The remaining study was for the treatment of "vaginal relaxation syndrome" using an Erbium:YAG laser. The devices are further delineated between an improvement in laxity/sexual sensation or purported for other applications. Including GSM. Study design and outcome data

vary between device and outcome data often cannot be compared. There are a variety of patient-reported assessments of vaginal laxity and sexual function reported in the literature or on ClinicalTrials.gov; and not all are validated. **Conclusion:** Vaginal laxity is a real, impactful, medical condition that is underappreciated in the medical community and underreported in the sexual literature. As clinicians discuss benefits and risks with patients for all potential treatments, they are encouraged to be aware of the latest innovative research in the area to ensure the treatments they are advocating are both safe and effective for the patient's specific, primary complaint.
Sources of Funding: This research was sponsored by Viveve Medical Inc.

P-40.

Flibanserin in Postmenopausal Women With Hypoactive Sexual Desire Disorder: Results of the PLUMERIA Study

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Objective: Flibanserin is approved by the US Food and Drug Administration for the treatment of acquired, generalized hypoactive sexual desire disorder (HSDD) in premenopausal women. In the first of two North American studies of flibanserin in naturally postmenopausal women with HSDD (SNOWDROP), significantly greater improvement in number of satisfying sexual events, 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 present report is from the second study conducted to assess the safety and efficacy of flibanserin in this population (PLUMERIA), which was discontinued early by the sponsor for administrative reasons. **Design:** This randomized, double-blind, placebo-controlled, multicenter, 24-week trial was conducted in naturally postmenopausal women with HSDD at 95 sites in North America (United States and Canada; ClinicalTrials.gov registration: NCT01057901). Eligible patients were randomly assigned in a 1:1 ratio to receive once-nightly (qhs) flibanserin 100 mg tablets or matching placebo for 24 weeks. Flibanserin was initially dosed at 50 mg qhs for 14 days and subsequently uptitrated to 100 mg qhs for the remainder of the study. Safety assessment included incidence of adverse events, vital signs, weight, and clinical laboratory measures. Co-primary efficacy outcomes were the number of satisfying sexual events (SSE; count over a 28-day period) and the Female Sexual Functioning Index desire domain (FSFI-d) score. **Results:** The study population (flibanserin, n=376; placebo, n=369) included primarily white women (84.7%), with a mean age of 56.1 years and mean HSDD duration of 5.0 years. When the study was discontinued early by the sponsor, 45.3% of randomly assigned patients had completed Week 16 (which served as the primary analysis time point for the data presented). The most common adverse events (≥5% of patients in either treatment group) in patients receiving flibanserin 100 mg qhs versus placebo, respectively, were insomnia (7.7% vs 3.3%), somnolence (6.9% vs 2.2%), dizziness (6.4% vs 3.5%), nausea (5.3% vs 4.1%), and headache (5.1% vs 6.5%). Overall, 10.4% of patients receiving flibanserin and 7.3% of patients receiving placebo discontinued due to adverse events. The most common adverse events cited for discontinuing flibanserin were insomnia (n=9 [2.4%]), anxiety (n=8 [2.1%]), and headache and somnolence (n=4 each [1.1%]). Improvement from baseline to Week 16 (last observation carried forward) in FSFI-d score was significantly greater for flibanserin compared with placebo (P=0.0108); however, the between-group comparison for SSE did not reach statistical significance. **Conclusion:** Although not approved for use in postmenopausal women, a previous study demonstrated the efficacy and tolerability of flibanserin in postmenopausal women with HSDD. In the present study, flibanserin was generally well tolerated. Flibanserin was associated with significantly greater improvement in sexual desire (as measured by the FSFI-d) compared with placebo; mean improvement in number of SSE was numerically greater with flibanserin but not statistically different from placebo. Despite the greatly reduced power in this study to detect improvement relative to placebo, results suggest that flibanserin may be efficacious in the treatment of HSDD in naturally postmenopausal women.
Sources of Funding: Boehringer Ingelheim; Valeant Pharmaceuticals North America LLC

P-41.

A Brazilian Population-Based Study Of Age At Menopause And Sexual Dysfunction

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Objective: To evaluate the association between age at menopause and sexual dysfunction in women aged 45 to 60 years in a cross-sectional population-based study in a particular Brazilian city. It was also evaluated the association between age at menopause and the components of sexual function. **Design:** Cross-sectional population-based study conducted with 749 women (household survey), representative of a population of 257,434 women, to obtain data on age at menopause and sexual dysfunction, as part of a broader study on women's health. The instrument used to evaluate sexual dysfunction was SPEQ. Associations were determined between age at menopause and sexual dysfunction and sexual dysfunction and demographic, behavioral and medical characteristics. The statistics analysis was performed using the chi square test. **Results:** Age at menopause was not associated with sexual dysfunction. Arousal was the only component of sexual dysfunction that was associated with age at menopause < 40 years (p=0.01). Sexual dysfunction was related to time more than 10 years since menopause (p=0.008), history of myocardial infarction (p=0.009), hypertension (p=0.03), depression/anxiety (p=0.002), vaginal dryness (p=0.02), menopause rating symptoms (MRS)>8 (p<0.001) and sexual problems of the partner (p=0.005). Having physical activity ≥3 times a week (p<0.001), passion with the partner as a lover (p<0.001) and satisfaction with the partner (p<0.001) were protective factors for sexual function. **Conclusion:** Arousal dysfunction was associated with premature menopause. Longer time since menopause, poor health and sexual dysfunction of the partner were associated with sexual dysfunction. On the other hand, physical activity and good relationship with the partner were factors related to a better sexual function. These findings highlight the importance of a better assessment of the association of female sexual dysfunction with longer time since menopause, poor health, lubrication, and partner sexual problems.
Sources of Funding: The Foundation for Research Support of the State of São Paulo - FAPESP, Case No. 2011 / 14526-9.

SLEEP AND MOOD POSTER PRESENTATIONS

P-42.

Dysfunctional beliefs about sleep in women who develop insomnia in the context of the menopausal transition: a target for treatment

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Objective: The prevalence of insomnia increases as women approach menopause, partly in association with the emergence of sleep-disruptive hot flashes, with 40-56% of women having insomnia symptoms and 26% meeting criteria for a clinical insomnia disorder. Sleep-related cognitions, such as faulty beliefs and excessive worry about the potential consequences of insomnia on daytime functioning, are an important factor that can perpetuate insomnia. Here, we aimed to investigate beliefs about sleep in women who had developed insomnia disorder in the context of the menopausal transition (MTI). **Design:** Women in the menopausal transition (MT), defined according to Stages of Reproductive Aging Workshop criteria, were recruited from the community and had a structured clinical interview including a module about sleep. 57 women who met DSM-IV criteria for insomnia disorder that had developed in the context of the MT and with no current depressive or anxiety disorders and no prior history of insomnia, were classified as MTI (age: 49.6±3.4y, BMI: 23.9±3.3Kg.m^{-2}). Forty five women in the MT without insomnia disorder were included as controls (MTC, age: 49.2±3.1y, BMI: 24.4±3.7 Kg.m^{-2}). All women completed questionnaires including the Dysfunctional Beliefs and Attitudes about Sleep (DBAS) scale, a validated measure of 16 items of sleep-disruptive cognitions. **Results:** Women with MTI were more likely to report hot flashes (p<0.001), with greater hot flash interference (p<0.01), more subclinical depressive symptoms (p< 0.001), and a poorer menopause-specific quality of life in vasomotor, psychological, and physical domains (p<0.05) than MTC. They had higher total DBAS scores, reflecting more disruptive sleep-related cognitions than MTC (p<0.001), and also reported higher levels of pre-sleep cognitive and somatic arousal (p<0.01). Analysis of the subscales of the DBAS revealed specific clinically relevant maladaptive cognitions, with MTI women being more likely than MTC to endorse worrying about losing control over their ability to sleep, the unpredictability of having a good or poor night sleep, and attributing suboptimal daytime functioning to a poor night sleep (all p<0.001). The groups did not differ on some other subscales, including the belief that they need 8 hours of sleep to function well. **Conclusion:** Women with insomnia that developed in the context of the MT have more dysfunctional beliefs about sleep than women without insomnia, which may perpetuate or even exacerbate insomnia symptoms. Treating these maladaptive beliefs and attitudes about sleep may lessen the disruptive effect of hot flashes on sleep and assist women in coping with sleep disruption and its impact on daily functioning in the MT.
Sources of Funding: This study was supported by NIH, Bethesda, MD, USA; Grant HL103688 to FCB

P-43.

Altered nocturnal cardiovascular profile in women who develop insomnia in the approach to menopause

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Objective: Insomnia disorder is a strong independent risk factor for cardiovascular (CV) disease (CVD). The prevalence of insomnia substantially increases as women go through the menopausal transition (menopausal transition insomnia, MTI) and goes beyond women's perception of poor sleep. Our previous findings indicated a dramatic reduction in time spent asleep and alterations in sleep microstructure in MTI compared to controls (MTC). A clinical diagnosis of insomnia in conjunction with objective evidences of alteration in macro and micro-structure of sleep may put MTI women at high risk for developing CVD. We aimed to determine the night-time CV functioning in MTI using indices derived by the heart rate variability (HRV) analysis and beat-to-beat blood pressure (BP) monitoring, accounting for menstrual cycle phases, hot flashes, sleep stages and hours across the night. **Design:** Twenty-one MTI (49.0±3.0y) and twenty-five MTC (48.8±2.6y) women had between one and three PSG recordings during the follicular and luteal phases of their menstrual cycles. Serum levels of follicle-stimulating hormone (FSH), estrogen and progesterone, and nocturnal time and frequency-domain heart rate variability (HRV) indices were obtained. In a subgroup of twelve MTI and eleven MTC, beat-to-beat blood pressure (BP) was continuously recorded. Physiological

hot flashes were identified from fluctuations in sternal skin conductance. **Results:** In both groups, FSH and progesterone levels were higher in the luteal compared to the follicular phase of the menstrual cycle ($p<0.001$). Heart rate (HR) was significantly higher and total and vagal-related high frequency HRV were lower in the luteal phase compared to the follicular phase of the cycle ($p<0.05$). Independently of the phase effect, HR was significantly elevated in MTI compared to MTC (~4bpm) in both follicular and luteal phases, across hours of the night, including during undisturbed periods of sleep ($p<0.05$). MTI also showed a trend for reduced total and vagal-related frequency- and time-domain HRV indices. Both MTI and MTC showed a decrease in BP in the first part of the night, however, nocturnal systolic and diastolic BP patterns diverged later, with BP remaining low in MTC but increasing in the second part of the night in MTI ($p<0.05$). In addition, in both groups rapid-eye-movement (REM) compared to non-REM sleep was characterized by increases in BP and HR, coupled with decreased vagal modulation and increased sympathovagal balance ($p<0.01$). **Conclusion:** MTI showed an adverse nocturnal CV profile, with a higher HR and BP than MTC. The marked cardiac acceleration (38% of MTI patients had an average nocturnal HR greater than 70 bpm) and depressed HRV, which was more pronounced in the luteal phase of the cycle, coupled with an altered nocturnal BP profile indicates a high CV risk profile in insomnia developed in the context of menopause.
Sources of Funding: Grant HL103688 (FCB).

P-44.

Impact of Tryptophan Depletion on Sleep Efficiency during the Menopausal Transition while on Estrogen Therapy: Preliminary Results

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Objective: Estrogen therapy (ET) is widely used to alleviate both mood and vasomotor symptoms (VMS) in women during the menopausal transition, with sleep disturbance being one of the most frequently reported problems (Gass et al., 2012). Previous research on sleep efficiency (SE) during the menopausal transition has shown that ET does not improve overall sleep efficiency and no significant correlation between objective and subjective measures of sleep (Regestein et al., 2004; Tansupswatdikul et al., 2015). Previous studies show that the acute tryptophan depletion (ATD) paradigm does not alter total sleep time or SE during a 24 hour period (Landolt et al., 2003). The purpose of this study was to determine whether ATD affects SE in perimenopausal women on ET with and without history of major depressive disorder (MDD) during a 72 hour period. **Design:** Nine women (mean age 52.67 ± 3.67) were assessed with the MINI International Neuropsychiatric Interview (MINI) and categorized into 3 groups: current major depressive episode (MDE), currently non-depressed (euthymic) but with past MDD, and healthy control (HC). All women received transdermal estradiol (E2) for 12 weeks. Between weeks 9 to 12, subjects completed the ATD paradigm which consisted of 2 full test days: on day 1 subjects received the ATD drink containing large neutral amino acids (LNAAs), excluding tryptophan (Trp); on day 2 subjects received a SHAM drink, which contained the same LNAAs including Trp. The order of test days was randomized. Subjective measures included the Profile of Mood States (POMS), the Pittsburgh Sleep Quality Index (PSQI), and the Hot Flash Related Daily Interference Scale (HFRDIS), which were collected at 4 time points: baseline, while on ET, post ATD and post SHAM. At the end of each test day subjects were affixed with an actigraph watch for 72 hours to measure their activity, sleep patterns and exposure to light. **Results:** In a linear regression model including subjective and objective measures of sleep efficiency (PSQI and actigraph, respectively) as response variable and POMS and HFRDIS as predictors we found that POMS predicted subjective SE (beta coefficient = -0.20, $R2 = 0.15$, $p = 0.01$) but not objective SE. Hot flashes alone were not a predictor of SE as measured by PSQI or actigraph. No correlation between subjective and objective measures of SE was found. No difference was found between the 3 groups or at SHAM and ATD. **Conclusion:** Corroborating previous studies, we found a correlation between depressive symptoms and subjective SE. Also, ATD did not seem to adversely affect SE after 72 hours and there were no significant changes in subjective or objective measurements of SE across any of the time points or within groups.
Sources of Funding: None.

P-45.

Validation of the Menopause Visual Analogue Scale in Determining Mood and Physical Symptoms of Perimenopausal Women on Estrogen Treatment

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Objective: Fluctuations in estrogen levels during the perimenopausal period have been linked to changes in mood as well as physical symptoms (Nelson, 2008). To assess these changes, clinicians have used a variety of self-reported tools to assess symptom severity and determine priorities in terms of therapeutic options. Visual analogue scales have shown promising results, particularly in patients with depression and pain. We propose here a visual analogue scale specific to the perimenopausal period. Our objective was to validate whether the Menopause Visual Analogue Scale (MVAS) can accurately assess mood and physical symptoms in perimenopausal women receiving estrogen therapy as compared to the Greene Climacteric Scale (GCS). **Design:** 73 perimenopausal women were recruited at the Women's Health Concerns Clinic at St. Joseph's Hospital, Hamilton. At study entry, all subjects were administered the MVAS and GCS. Fourty-seven of these women were then treated with 17 β-E2 (100 μg /day) and the MVAS and GCS were re-administered 8 weeks into treatment. At each assessment, we compared the total mood (MVAS-M) and physical (MVAS-P) sub-scores of the MVAS, respectively, with the total mood (GCS-M) and physical (GCS-P) sub-scores of the GCS by using Pearson's correlation with $\alpha=0.05$. **Results:** At baseline, the MVAS-M was significantly and positively correlated with the GCS-M ($r=0.755$; $p<0.01$). Furthermore, the correlation between MVAS-P and GCS-P demonstrated similar findings ($r=0.739$; $p<0.01$). After 8 weeks of treatment, correlations between the MVAS-M and the GCS-M ($r=0.551$), and between the MVAS-P and GCS-P ($r=0.464$) also remained significant ($p<0.01$ and $p=0.001$, respectively). **Conclusion:** The MVAS may be a valid tool in assessing both changes in mood and physical symptoms in perimenopause and among women receiving estrogen therapy. Also, initial feedback from participants describes the MVAS as a user-friendly tool and requiring less time for completion than the GCS.
Sources of Funding: None.

P-46.

Differential Item Functioning of the Psychological Domain of the Menopause Rating Scale (MRS)

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Objective: To establish the DIF of the psychological domain of the MRS in Colombian women. **Design:** A total of 4,009 women with ages between 40-59 years, who participated in the CAVIMEC (Calidad de vida en la Menopausia y Etnias Colombianas) project were included in this study. The average of age was 49.0±5.9 years. Of the total of the population, 45.1% were mestizo, 32.1% were afro-colombian and 22.8% of women were indigenous. The indigenous women were resident in three settlements in La Guajira, Córdoba and Amazonas. The MRS was applied to all the participants and it is a self-applied scale, completed in a voluntary and anonymous way. Nevertheless, in the participants with limitations for reading in Spanish, a nurse with skills in the community language helped women to understand the form in their native dialect. The MRS consists of 11 items, four of them belonging to the psychological domain, that evaluate the presence of depressive mood, irritability, anxiety and physical and mental exhaustion, classifying them if they were absent, mild, moderate, severe and very severe. In this study, averages (X) and standard deviation (SD) of the scores were compared according to the ethnic group using the ANOVA test. P values < 0.001 were accepted as statistically significant. Spearmans correlations (rs) were calculated between the score of each item and ethnic group; rs=0 showed non-differential functioning. In addition, the classic reliability and validity tests, to quantify internal consistency, Cronbachs alpha and McDonalds omega were calculated **Results:** In mestizo women, the highest average score and standard deviation was obtained in the physical and mental exhaustion (0.86±0.93) and the minor one was in the presence of anxiety (0.44±0.79). In afro-colombian women, a similar situation was presented, obtaining an average of 0.99±1,07 for physical and mental exhaustionand an average of 0,63±0,88 for anxiety. And in indigenous women, there was obtained an average score more raised for the presence of physical and mental exhaustion not only (1.33±0.93) between indigenous if not also with regard to other women of the study and the minor score was evidenced in the depressive mood (0,50±0,81), which is contrary to the demonstrated in mestizo and afro-colombian women ($p<0,001$). See table below. **Conclusion:** The psychological items of the MRS show differential functioning according to the ethnic group, which may induce systematic error in the measurement of the construct or lack of adjustments to the linguistic particularities of every ethnic Colombian group. The socio-cultural context influences the score assigned to each symptom for what it is necessary to make a refinement of the theoretical underlying construct from the perspective of the psychometrics.
Sources of Funding: none

AVERAGE (SD) OF THE PSYCHOLOGICAL ÍTEMS OF THE MRS ACCORDING TO THE ETHNIC GROUP**

Item	Mestizo	Afro-colombian	Indigenous	Total
Depressive mood	0,76 (0,97)	0,74 (0,93)	0,50 (0,81)	0,70 (0,93)
Irritability	0,56 (0,85)	0,67 (0,88)	0,85 (0,74)	0,66 (0,84)
Anxiety	0,44 (0,79)	0,63 (0,88)	0,55 (0,80)	0,53 (0,83)
Physical and mental exhaustion	0,86 (0,93)	0,99 (1,07)	1,33 (0,93)	1,01 (0,99)
** p value<0.001				

P-47.

Sleep Quality and Hot Flashes in a Group of Climacteric Women in the Colombian Caribbean

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Objective: To estimate the prevalence of women with worse sleep quality according to hot flashes. **Design:** Descriptive, cross-sectional and comparative study carried out between mestizos women aged 40-59, residents in Cartagena, a city located in the Colombian Caribbean area. This study is part of the research project named CAVIMEC (Calidad de Vida en la Menopausia y Etnias Colombianas). A form with questions about sociodemographic data and other validated scales about quality of life and sleep quality were applied to those women by pollsters in door-to-door visits in 2015. The presence or absence of hot flashes (HF) was determined with the first item of the Menopause Rating Scale (MRS) and the sleep quality was assessed with the Pittsburgh Sleep Quality Index (PSQI); a total score of this scale ≥5 identifies women with sleep disturbances. The participation in the study was volunteer, anonymous and with prior informed consent. A sample size was estimated in 400 women. Data analysis was performed using the EPI-INFO 7 statistical program. A p value of < 0.05 was considered as statistically significant. Cronbach's alpha for PSQI: 0.85. **Results:** 413 women participated in the study. 102 (27.1%) of them did not have HF and 311 (75.3%) manifested HF. Average age: 52 [9] and 47 [7] years, respectively. In the group without HF, 37.6% were between 55-59 years; while in the group with HF, 37.2% were between 45-49 years. In both groups, half of the population were married, while 40% were employees of different jobs. Also, 18.3% [CI95%14.2-23.1] of women without HF indicated not to have smoking habits and 20.6% [CI95% 13.2-29.7] of women with HF were smokers. Between the last ones, 42.2% [CI95%: 32.4-52.3] were in perimenopausal status and 12.7% [CI95%:6.9-20.8] were in postmenopause. Between women without HF 72.0% [CI95%:66.6-76.8] were in perimenopause and 2.9% [CI95%:6.9-20.8] in postmenopause. There were not found significant differences between the two groups with regard to number of children, coffee consumption, use of energy drinks, alcohol consumption, and the use of hormonal therapy, to have diabetes, depression or arterial hypertension, to walk, to do exercise or to bike riding. The median of the total PSQI score was 4 [6]. For the group without HF, the total PSQI score was 3[5] and to those women with HF the total score was 6[7], p<0.001. The most affected components in women with HF were "sleep latency" and "daytime dysfunction" with higher score and statistically significance with regard to women without HF. 43.3% of all the studied population had poor sleep quality, with a higher prevalence in women with HF and with statistical significance. Some factors were associated with poor sleep quality: The presence of HF OR: 3.9 [CI95%:2.3-6.6] and coffee consumption, OR: 1.9 [CI95%:1.1-3.3]. Items as to walk, to do exercise, to be in overweight or obesity and to be in postmenopause were not statistically significant. **Conclusion:** Six of each ten women with HF have poor sleep quality while three of each ten women without hot flushes have poor sleep quality. To feel HF was risk factor to have poor sleep quality

Sources of Funding: None

PREVALENCE OF GOOD OR POOR SLEEP QUALITY ACCORDING TO THE PRESENCE OF HOT FLUSHES (HF)

Sleep quality	All population N=413	Women without HF N=311	Women with HF N =102	p
Good	234 (56.7) [51.7-61.5]	200 (64.3) [58.7-69.6]	34 (33.3) [24.3-43.4]	< 0.001
Poor	179 (43.3) [38.5-48.3]	111(35.7) [30.4-41.3]	68 (66.7) [56.6-75.7]	< 0.001

P-48.

Impact of Anxiety in the Sleep Quality of Climacteric Women of a City in the Colombian Caribbean Coast

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Objective: To evaluate the sleep quality according to the presence of anxiety in climacteric women. **Design:** Cross-sectional study carried out in mestizo women between 40 and 59 years, in the Cartagena (Colombia) in 2015, who reported presence of anxiety when they were assessed with the Menopause Rating Scale (MRS). Professional pollsters applied a questionnaire with sociodemographic data and the Pittsburgh Sleep Quality Index (PSQI) to assess the quality of sleep. A total score ≥ 5 in the last scale indicates poor sleep quality. The participation in this study was anonymous and voluntary. Data analysis was performed using the EPI-INFO 7 and STATA statistical programs. A p value of < 0.05 was considered as statistically significant. This study is part of the research project named CAVIMEC (Calidad de Vida en la Menopausia y Etnias Colombianas). **Results:** 423 surveys were included for the analysis. 13.3% (55) of the women reported presence of anxiety according to the findings in the Menopause Rating Scale (MRS). The average age was 49.2± 4.9 years and 50.6 ± 5.7 years for women with and without anxiety, respectively. The half of women with anxiety were between 40 and 49 years. There were not significant differences in level of education between the both groups. 6 of each 10 women with anxiety still have a job, while 4 of each 10 women without anxiety were pensioners or housewives. There were not found differences in the marital status. Women without anxiety smoked more than women with anxiety (20.6% vs 7.4%, respectfully), p=0.02. 50% of all women were in overweight. There were not found significant differences between coffee consumption, energy drinks and physical activity in both groups. 7 of each 100 women with anxiety was in treatment with hormonal therapy while 1 of each 100 women without anxiety used it (p 0.001). 7% and 1% of women reported depression with and without anxiety respectively (<0.001). For the PSQI, a Cronbachs alpha was calculated in 0.85. Women with anxiety had an average score of 6.9 ± 3.3 and women without anxiety 4.4 ± 4.1 (p <0.001). In the quality components "duration and sleep disturbances", women with anxiety had a higher average score than the other one (p <0.001). 7 of each 10 women with anxiety had poor sleep quality in comparison to 3 of each 10 women without anxiety. Anxiety could increase 2.6 times the risk of poor quality of sleep in comparison to women without anxiety (aOR 3.3) [CI95% 1.9-5.7]. **Conclusion:** The prevalence of anxiety in midlife women could influence in the sleep quality in menopause.

Sources of Funding: None

Sleep quality	All population n=413	Without Anxiety n=358	With Anxiety N =55	p
Good	216 (52.3) [47.4-57.2]	220 (61.5) [56.2-66.5]	14(25.5) [14.7-38.0]	<0.0001
Poor	197 (47.7) [42.8-52.6]	138 (38.5) [33.5-43.8]	41(74.5) [61.0-85.3]	<0.0001

TREATMENTS POSTER PRESENTATIONS

P-49.

Effects of isoflavones, 17β-estradiol and combined therapy in uterus, mammary glands and liver of diabetic rat models induced by streptozotocin (STZ)

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Objective: We hypothesize here that 1) small leucine rich proteoglycan (SLRPs) is diminished in menopause, leading to dysregulation of matrix extracellular and collagen; 2) isoflavone can re-establish the regulation (SRLPS) and collagen through the activation of decorin, biglycan, lumican and fibromodulin in the uterus and mammary glands, resulting in alleviation of menopause symptom and 3) the peroxisome proliferator-activated receptor γ (PPARγ) is deactivated in diabetic condition, leading to dysregulation of lipid metabolism and isoflavone can re-establish the lipid homeostasis through the re-activation of PPARγ in the liver. It was also demonstrated that isoflavone interacts with PPARγ, a key molecule involved in the insulin resistance. **Design:** To examine the hypothesis we used non–diabetic: GI (n=10) Sham control animals ovariectomized; and GII (n=10) control ovariectomized that received propylene glycol vehicle. Diabetic: GIII (n=10) Sham control diabetic animals ovariectomized; GIV (n=10) control ovariectomized diabetic animals receiving propylene glycol vehicle; GV (n=10), ovariectomized diabetic animals treated with soy isoflavones (150mg/kg by gavage); GVI (n=10) ovariectomized diabetic rats treated with estrogen (17β-estradiol, 10mg/kg, subcutaneously); GVII (n=10), ovariectomized diabetic animals treated with soy isoflavones (150mg/kg by gavage) and with combination therapy estrogen (17β-estradiol, 10mg/kg). Rats were monitored daily. Body weight and food consumption were calculated weekly. Serial collection of blood samples were obtained from the leg vein at 0, 5, 10, 20, 40, 80 and 160 min upon human insulin (0.2U/100g) administration and plasma glucose were determined by glucose test strips. The insulin sensitivity index KITT was calculated and lower KITT implies lower insulin sensitivity or higher insulin resistance. Uterus, mammary glands and liver were collected and processed for morphology analysis (HE and Picro sirius red staining) and lipid quantification analysis (number and size of lipid droplets) using Oil red staining **Results:** Our results showed that non diabetic treatment not markedly increased body weight of female rats (p<0.01). In diabetic condition, the groups of isoflavones, 17β- estradiol and combined therapy significantly decreased body weight (p <0.01). Considering that no differences were found in food intake in any of the groups, this reduction in body weight in diabetic condition, isoflavone group is mainly due to 17β- estradiol and the combination of therapy effects. Diabetes condition also significantly decreased the KITT insulin sensitivity (p<0.001) in all diabetics treated rats compared with non-diabetics, but only isoflavone group significantly increased the insulin sensitivity or decreased insulin resistance compared with other groups (p<0.01). In fact, one month of diabetic condition significantly reduced the weight and size of the mammary glands (p<0.01), but isoflavone did not rescue the normal mammary glands phenotype as well as the other tested treatments (p<0.01). However, lipid quantification analysis showed the accumulation of lipids in the liver (p <0.01) in diabetic condition treated rats, whereas isoflavone and therapic combination significantly decreased it (p <0.01). On the other hand, it was observed that (SLRPS) gene expression and protein analysis also ameliorated when animals were treated with 17β-estradiol (p<0.001). The expression of the same genes in the groups treated with isoflavone was relatively minor. **Conclusion:** Isoflavone favors the lipid metabolism of diabetic rats in comparison with those treated with17β- estradiol or combined therapy. Further biochemical analysis allowd us to verify the role of isoflavone in re-activation of PPARγ in diabetic rats model and in depth mechanistic function of isoflavone in menopause, particularly its effect on SLRPs.

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P-50.

Effects of natural and plant-based therapies on menopausal symptoms: a systematic review and meta-analysis

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Objective: The proportion of women in Western countries who use complimentary therapies to manage menopausal symptoms is estimated to be 40-50%. We aimed to determine the impact of natural and plant-based therapies on the presence and severity of menopausal symptoms. **Design:** The electronic databases MEDLINE, EMBASE, and Cochrane Central were systematically searched to identify appropriate studies published up to December 16th 2015. We included randomized controlled trials (RCTs) and observational studies that assessed natural or plant-based therapies in relation to the presence of one or more menopausal symptoms, including hot flashes, night sweats, vaginal dryness and Kupperman Index. Reference lists of the included studies were searched for further identification of relevant studies. **Results:** In total, 119 articles based on 113 unique studies (101 RCTs and 12 prospective non-randomized intervention or observational studies) were identified, including a total of 12,443 individual women. Based on meta-analyses of the findings from RCTs, use of phytoestrogens significantly reduced the reported number of daily hot flashes [pooled mean difference of changes: -1.26 (95%CI: -1.87, -0.65)] and significantly improved vaginal dryness score [pooled mean difference of changes: -0.31 (-0.52, -0.10)]. Individual phytoestrogen interventions such as dietary and supplemental soy isoflavones were beneficial for menopausal outcomes in general, and for number of night sweats in 24 hours in particular. Additionally, behavioral therapies, acupuncture, and several herbal remedies improved overall menopausal symptoms as measured by the Kupperman Index [pooled mean differences: -11.10 (-17.17, -5.03), -8.41 (-11.81, -5.0), and 6.72 (-8.10, -5.33), respectively]. There was substantial diversity in quality across the available studies. **Conclusion:** Findings indicate that composite and certain specific phytoestrogen supplementations may confer a benefit of reducing menopausal symptoms in women. Additionally, several other plant-based and natural therapies may also effectively improve menopausal symptoms. However, owing to a generally sub-optimal quality and the heterogeneous nature of the current evidence, further rigorous studies are needed to determine their impact on menopausal health and symptoms alleviation.

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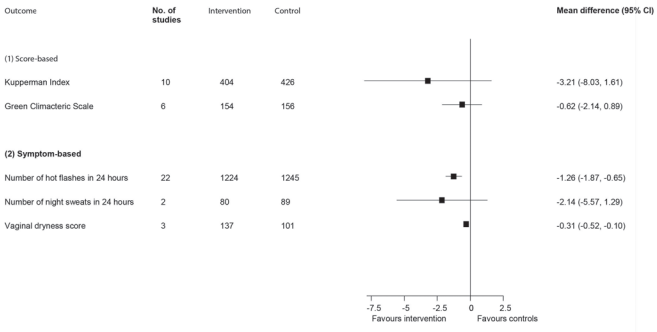
Figure 1. Effects of Phytoestrogens supplementation on menopausal outcomes in the available randomised controlled trials



P-51.

Breast Cancer Risk and Menopausal Hormone Therapy: Does type of progestin matter?

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Objective: Risks of menopausal hormonal therapy and breast cancer have been studied, with two large randomized controlled trials (RCTs), the Heart Estrogen/Progesterone Replacement Study (HERS) and Women's Health Initiative (WHI) sginificantly adding to the world literature on this subject. Except for the estrogen only arm in the WHI, both reported an increased risk of breast cancer with menopausal hormonal therapy. The WHI data suggested that the progestin with the estrogen may have increased the relative risk of breast malignancy. However, there continues to be controversy on the role of progestin in breast cancer when used with systemic estrogen therapy. The question is whether all progestin structures (synthetic and natural) have the same impact on postmenopausal mammary gland tissue. This review evaluated the disparities between synthetic progestins and progesterone in menopausal hormonal therapy with respect to risk for breast cancer. **Design:** Published studies were identified from PubMed/MEDLINE, Google Scholar, and Cochrane databases, which included keywords associated with medroxyprogesterone acetate (MPA), synthetic progestins, progesterone, micronized progesterone, bioidentical progesterone, menopausal hormonal therapy, and breast cancer. **Results:** In an animal study using a monkey model there was a difference in proliferation of breast tissue (99%, 58% and 194% in estrogen alone, estrogen +micronized progesterone and estrogen + MPA respectively). In women, a few publications suggest that the relative risk of breast cancer correlates with the type of progestin used. However, other data did not report a correlation with progestin type and risk of breast cancer. **Conclusion:** The data are not definitive on progestin type and breast cancer risk. Further randomized controlled trials are needed to delineate whether progestin type plays a role in breast cancer risk, as well as what impact progestin dose, route of delivery and time frame in the woman's life cycle when it is used has on the risk of this malignancy.

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P-52.

Influence of Menstrual Cycle on Pharmacokinetics of Ciprofloxacin. *Sandhya Rani Guggilla, Swathi Konda, Sarangapani Manda.1 Post Doctoral fellow, university college of pharmaceutical sciences, kakatiya university sandhyaguggilla9@gmail.com.918897474898 1 Professor, university college of pharmaceutical sciences, kakatiya university

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Objective: The aim of the present research work is to study the influence of menstrual cycle (i.e., follicular phase, ovulatory phase and luteal phase) on pharmacokinetic parameters of Ciprofloxacin in patients. **Design: PATIENTS AND METHODS** The study protocol was approved by the Institutional Ethical Committee. Patients with regular menstrual cycle, not suffering from any other chronic disease not using any other drug except Ciprofloxacin were included in the study. **Patient selection** The female patients were selected from the patients who visited antibiotic department as out patients in the Warangal General Hospital, Warangal, after taking due permission from that department and written informed consent was obtained from all the patients who were willing to participate in the study. 12 female patients who complied inclusion criteria and on long term oral Ciprofloxacin therapy (not less than 2 years) with prescribed dosage regimen as per physician's prescription 500mg were selected for the study. Plasma samples were collected from each patient prior to the morning dose (0 h) and at the time points of 1, 2, 3, 4, 6, 8 & 12 hours after dosing. Plasma samples were collected after cleaning the tongue debris and mouth every time before sampling, which were stored at -80°C until further analysis. The retention times were 5.1 min. and 6.0 min. for Oflaxacin and Ciprofloxacin respectively. The peak area ratios obtained at different concentrations of the drug were plotted against the concentrations of the drug. The slope of this plot was calculated by least square regression analysis and was used to calculate Ciprofloxacin concentration in unknown plasma samples. Data was analysed for pharmacokinetic parameters by using WINNONLINE software. **Analysis of blank blood samples for hormones** The blank blood samples were collected from the patients before administration of the drug (0h) and analysed for concentrations of estrogen and progesterone hormones by the Chemiluminisence method. **Results:** Ciprofloxacin levels were higher in the Follicular phase than in ovulatory and luteal phases and its levels in the ovulatory phase were lower than follicular and luteal phase. Mean concentrations of estrogen and progesterone in three phases of menstrual cycle are summerised. The mean levels of estrogen were 29.2 ± 15.5, 99.5 ± 110.7 and 112.26 ± 65.7 pg/ml in follicular, ovulatory and luteal phases respectively. The mean levels of progesterone were 0.5 ± 0.5, 3.5 ± 3.8 and 9.8 ± 9.2 ng/ml in follicular, ovulatory and luteal phases respectively. Mean values of various pharmacokinetic parameters of Ciprofloxacin obtained in three phases were compared with the values obtained in other two phases and for the calculation of percentage increase or decrease, follicular phase was treated as reference. The mean Vd/f value was increased by 53.56% in the ovulatory phase and 9.31% in luteal phase compared to follicular phase. The difference between mean Vd/f values for follicular versus ovulatory phase ($P < 0.01$) and luteal versus ovulatory phase ($P < 0.05$) was statistically significant. The mean $V_{ss/f}$ value was increased by 50.71% in the ovulatory phase and 6.3% in the lutealphase compared to follicular phase. The difference between mean $V_{ss/f}$ values for follicular versus ovulatory phase ($P < 0.01$) and luteal versus ovulatory phase ($P < 0.01$) was statistically significant. **Conclusion:** From the above observations it can be concluded that, phase specific menstrual hormonal changes influenced Ciprofloxacin pharmacokinetics to a lesser extent and $V_{d/f}$ and $V_{ss/f}$ were significantly altered. Mean plasma concentrations of Ciprofloxacin were higher in follicular phase than in ovulatory and luteal phases. Estrogen and progestirone levels also may influence the cmax of Ciprofloxacin.

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P-53.

The comparison of the efficacy between the tibolone and transdermal estrogen for the menopausal symptoms in Korean menopausal women

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Objective: The aim of the study was to compare the efficacy between tibolone and transdermal estrogen for the menopausal symptoms in Korean menopausal women. **Design:** At Korea university anam hospital obstetrics and gynecology department, 44 Patients were recruited as tibolone group, who started Tibolone as their first HRT and 49 as transdermal estrogen group, who started estrogen as their first HRT from March 2013 to February 2016. To compare the menopausal symptoms, MRS score was checked on their first outpatient visiting day, and 3 months after. Excluding 11 patients who did not complete MRS score, and 25 patients who completed MRS score only once, Tibolone group included 26 patients and Transdermal estrogen group included 31 patients. **Results:** Demographic characteristics showed a statistically significant difference in body weight and BMI. Hot flashes, Sweating, Heart discomfort, Sleep problems, Dryness of vagina were significantly improved in Tibolone group, and of the respective dimension of symptoms, somato-vegetative symptomes, urogenital symptoms were also significantly improved. In Transdermal estrogen group, Hot flashes, sweating, Sleep problems, Depressive mood, Irritability, Physical and mental exhaustion, Sexual problems, Bladder problems, Joint and muscular discomfort were significantly improved, including all

somato-vegetative symptoms, psychological symptoms, urogenital symptoms. However, Hot flashes, sweating and sleep problems, which showed a significant improvement in both groups, did not show a significant difference between the groups. **Conclusion:** As a result of comparing tibolone and transdermal estrogen using MRS score difference, transdermal estrogen group showed a statistically meaningful improvement in more items of the MRS questionnaire. However, there was no significantly difference between tibolone group and transdermal group. We thought this result came from the difference of demographic characteristics and the degree of menopausal symptoms at the time of the therapy start.
Sources of Funding: None

P-54.

Physicians' Perceptions of Estrogen Agonist/Antagonists in Menopausal Health: An Opportunity to Address a Triad of Concerns in the Menopause

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Objective: Estrogen agonists/ estrogen antagonists have been used in obstetrics and gynecological care for several decades. Both clomiphene and tamoxifen are well utilized in gynecological care however the use of SERMS in postmenopausal care has been limited yet they are gaining in popularity in menopause health care since they can effectively address a constellation of symptoms, including bone health, vaginal integrity as well as impact breast chemoprevention. In the era of value-based care, simultaneous treatment of multiple issues with one medication is a potential cost-effective method of achieving optimal health care utilization. Many postmenopausal woman desire a reduction in breast cancer dignosis, treatment of bone health and improvement in the genitourinary syndrome of menopause (GSM). We conducted a self-administered internet survey to assess the current treatment trends for the use of SERMS by health care professionals for postmenopausal patients, specifically for the treatment of osteoporosis/ osteopenia and symptoms of vulvovaginal atrophy (VVA). **Design:** We conducted a self-administered web-based survey for physicians who were potential prescribers of SERMS. One hundred and eight (n=108) health care professionals were surveyed. Both Obstetrician /Gynecologist (n= 53) and primary care specialists (n= 55) were included. Eligibility criteria included: Primary specialty of OB/GYN or Gynecology for "OB/GYNs," Family Practice, General Practice or Internal Medicine for "PCPs". All health care providers were those in full-time clinical practice and actively managing menopausal women and had at least two and not more than 30 years of clinical practice experience. Clinicians were currently working in a community-based clinical practice and were known to treat a minimum number of postmenopausal patients per month for both osteopenia/osteoporosis and vulvovaginal atrophy (VVA). **Results:** Most physicians in this study evaluate and treated between 100-250 postmenopausal patients per month. Although not statistically significant, OB/GYNs reported a higher monthly average volume of postmenopausal patients (186 patients) versus PCPs (140 patients). SERMs currently capture a relatively small share of physician prescriptions; on average, 10% of VVA patients are reported to be treated with Ospemifene and 6% are treated with BZA and CEE. Nearly half of the physicians (48%) reported that the number of their postmenopausal patients who are receiving prescriptions for for the prevention of osteoporosis are increasing and bone health remains an important concern for this growing segment of their clinical practice. For a novel SERM under investigation, the features that were perceived as most favorable included: reduction of vertebral fracture by 42% and non-vertebral fracture by 26% (76%), an 80% reduction in incidence of ER+ breast cancers at 5 years (74%) and no significant drug-drug interactions (72%). Also valued by the participants was 5-years of efficacy and safety data from a placebo-controlled fracture study (70%). The concept that a drug could also treat vaginal symptoms was also viewed favorably by both OBGYs and PCPs. **Conclusion:** Clinicians are becoming more aware of SERMS as a clinical option and support the concept of a therapeutic benefit for the menopausal woman who are concerned with a triad of issues including breast cancer risk reduction, GSM treatment and bone health management
Sources of Funding: This research was funded by Sermonix Pharmaceuticals.

P-55.

Climacteric amenorrhea in post-operative tamoxifen users: A comparative hormone study with eumenorrheic control

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Objective: Tamoxifen has been used to prevent recurrence of breast cancer, however, tamoxifen-users frequently experience amenorrhea and it can be confused from amenorrhea associated with other hormonal abnormalities. In amenorrheic patient without breast cancer, clinicians usually measure the level of hormones, which is known to be associated with ovarian function or menstruation. We aimed to investigate the feature of several hormones associated with ovarian function or menstruation in climacteric breast cancer patients receiving tamoxifen treatment. **Design:** The medical records of fifty-nine climacteric breast cancer patients who received tamoxifen treatment were retrospectively reviewed. Serum hormone levels were measured either specifically between cycle days 2 and 5 in menstruating patients or at any time in amenorrheic participants. Women with previous history of chemotherapy or serum follicle stimulating hormone (FSH) levels higher than 30 mIU/ml were excluded from the study because they were at risk of incipient menopause. **Results:** The study population consisted of amenorrheic patients (n=36) and patients with menstruation (n=23). Serum level of lutenizing hormone and estraiol were not statistically different based on the pattern of menstruation. Serum FSH level was significantly higher in amenorrheic patients (8.09 mIU/ml) than those in menstruating subjects (5.06 mIU/ml) (P=0.01). Serum concentration of thyroid stimulating hormone was lower in patients with amenorrhea, although the prevalence of hypo- or hyperthyroidism was not different according to the pattern of menstruation. **Conclusion:** The hormone levels may be influenced by tamoxifen treatment in climacteric breast cancer patients.
Sources of Funding: None

P-56.

Assessing the humanistic burden of menopausal symptoms and estrogen-progestogen therapy side effects among postmenopausal women in the US

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Objective: Postmenopausal (PM) women can experience bothersome symptoms including hot flashes/night sweats. Estrogen plus progestogen therapies (EPT) represent the current standard of care but can cause side effects including breast pain/tenderness and vaginal spotting/bleeding. The objective of this study was to assess the humanistic burden of menopausal symptoms and EPT side effects in a large sample of PM women in the US. **Design:** This was a multi-center observational study with 352 PM women. The sample included: PM women taking EPT with side effects (side effects sample; n=202); PM women taking EPT without side effects (control sample; n=75); PM women not taking EPT with menopausal symptoms (untreated sample; n=75). The following Patient-Reported Outcome (PRO) instruments were completed by all women at baseline: Breast Sensations Impact Questionnaire (BSIQ), Post-Menopausal Bleeding Impact Questionnaire (PMBIQ), Menopause-Specific Quality of Life questionnaire (MENQOL) Menopause Rating Scale (MRS) and EuroQoL Five Dimension Five Level questionnaire (EQ-5D-5L). The Menopause Symptoms Treatment Satisfaction Questionnaire (MS-TSQ) was completed by side effects and control samples only. Two electronic daily diaries (eDiaries), the Breast Pain and Tenderness Daily Diary (BPT-DD) and Vaginal Bleeding and Spotting Daily Diary (VBS-DD), were completed by the side effects sample daily for 28 days post baseline. Descriptive statistics (mean, SD) and repeated-measures models were used to examine differences between various groups of participants. **Results:** Health status, as assessed by the EQ-5D-5L (possible score range: -0.109 to 1.000), was highest for the control sample who had no EPT side effects (0.93), followed by the side effects sample (0.85) and lowest for the untreated sample (0.84), with significant differences among the groups ($p<0.001$). In the side effects sample, average frequency of vaginal spotting/bleeding, as measured by the VBS-DD (possible score range: 0-100%), was less than 30% across each seven-day period; women aged 40-50 years reported more frequent vaginal spotting/bleeding than older age groups with significant differences between the groups (mean percentage range: 19.7-28.8% vs. 13.8-17.6% [51-60 years] and 4.4-15.2% [≥61 years]; $p<0.05$). The side effects sample reported greater impacts from vaginal spotting/bleeding on each domain of the PMBIQ compared to the control sample ($p<0.001$). Women aged ≥61 years reported lower impacts from vaginal spotting/bleeding than younger participants, with significant differences between the age groups (1.2 [≥61 years] vs. 1.4 [40-50 years] and 1.4 [51-60 years]; with a possible score range of 1-5; $p<0.05$). Mean scores of breast sensation severity, as measured by the BPT-DD (possible score range 0-10), ranged from 1.3-1.5 across each seven-day period with no significant differences between age groups. Impacts from breast sensations, as measured by BSIQ, were comparable among all groups, with no significant differences between samples or age groups. Severity of menopausal symptoms, as measured by the MRS, was significantly higher in the untreated sample compared to the side effects and control samples ($p<0.001$). Menopausal symptoms, as measured by the MENQOL, were higher in the untreated sample compared to the side effects and control samples, with statistically significant differences among the groups ($p<0.001$). The control sample reported significantly greater treatment satisfaction on each domain and total score of the MS-TSQ compared to the side effects sample ($p<0.001$). Participants aged ≥61 years reported greater satisfaction on the MS-TSQ 'administration' and 'tolerability' domains compared to younger participants, with significant differences among the three groups ($p<0.05$). **Conclusion:** Both menopausal symptoms and EPT side effects can be burdensome for women, impacting multiple domains of HRQoL. Findings highlight the need for effective hormone therapy without burdensome side effects.
Sources of Funding: Pfizer Inc

P-57.

Effects of Estrogen on Hearing Impairment

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Objective: Estrogen 17b-estradiol (E2) is a steroid hormone whose actions involve genomic and non-genomic mechanisms. It is generally accepted that a majority of its effects are mediated *via* two estrogen receptors (ERs), ER-α and ER-β, which belong to a nuclear receptor superfamily, by regulating nuclear estrogen responsive genes. The purpose of the present study is to investigate the protective effect of E2 against hydrogen peroxide-induced toxicity in organotypic cultures of cochlear explants from three-day postnatal rats. **Design:** We examined the expression of ER-α and ER-β protein in the inner ear of mice by immunohistochemistry **Results:** Pre-treatment with E2 ameliorated cell death induced by hydrogen peroxide in organotypic cultures of Corti's organ. Pretreatment with E2 also significantly suppressed hydrogen peroxide-induced increases in the intracellular accumulation of calcium. Treatment with E2 resulted in an increased expression of ER-α and ER-β. **Conclusion:** In the current study, to examine the protective effects of estrogen against the functional impairments of the inner ear, we treated the organ of Corti with H_2O_2. Thus, we attempted to induce the damage

to the auditory cells and clarify the protective effects of estradiol and the relevant mechanisms. To summarize, our results are as follows: In the current study, to examine the protective effects of estrogen against the functional impairments of the inner ear, we treated the organ of Corti with H_2O_2. Thus, we attempted to induce the damage to the auditory cells and clarify the protective effects of estradiol and the relevant mechanisms. To summarize, our results are as follows: 1. Estrogen receptor-α and -β (ER-α and ER-β) proteins were expressed in the stria vascularis of the external wall of the cochlea in the inner ear, the spiral ligament, the spiral ganglion, the saccule of the vestibular organ, the utricle and the ampulla of the semicircular canal. 2. H_2O_2 induced the damage to the auditory cells in the organ of Corti in the inner ear in a dose-dependent manner. But this was prevented with the pre-treatment with estradiol. 3. Estradiol inhibited H_2O_2-induced decrease in the expression of estrogen receptor-α and -β in the auditory cells. 4. Estradiol inhibited H_2O_2-induced increase in the expression of ERR-β in the auditory cells.. 5. Estradiol inhibited H_2O_2-induced Ca^{2+} deposition in the auditory cells.

Sources of Funding: None

P-58.

Highly concentrated palmitoleic acid proving the safety and efficacy of Provinal® for cardiometabolic disorders and dry eye syndrome.

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Objective: The purpose of this study is to conduct a review to determine whether supplementation with omega-7 has some influence on the dryness of mucous membranes (dry eye and vaginal dryness) and cardiometabolic risk, both common features postmenopausal stage. **Design:** Palmitoleic acid (C16:1 n-7) or Omega-7 is a monounsaturated fatty acid. It is biosynthesized from palmitic acid by the action of the enzyme delta-9 desaturase. It can also be obtained from sea buckthorn (*Hippophae rhamnoides*), macadamia nuts (*Macadamia integrifolia*) and marine sources (menhaden and anchovies). The nutritional and biological functions of palmitoleic acid are complex and scientific understanding of the biological significance on human health is limited. Palmitoleate may increase cell membrane fluidity, attenuate insulin resistance, and reduce inflammation associated with diabetes and heart disease (Prog Lipid Res 2012;51:340-9). **Results:** Multiple studies have demonstrated the health benefits of palmitoleic acid over the last decade. They have shown beneficial effects on regeneration of skin and mucous membranes (Maturitas 2014; 79:316-321), and improving immune functions, reducing oxidation and strengthening cardiovascular health (J. Nutr. Biochem. 1999; 10,622-630). B. Yang and E. Erkola demonstrated beneficial effects of Omega-7 from SBA 24® on the overall condition of the mucous membranes of patients of Sjögren's syndrome (*Proceedings of the 97th Annual Meeting of American Oil Chemists Society*. April 30-May 3, 2006, St Louis. Abstract). In 2014, P. Larmo and B. Yang, showed Omega-7 beneficial effects, on vaginal health, indicating it is as a potential alternative for mucosal integrity for those women not able to use estrogen treatment for vaginal atrophy (Maturitas 2014; 79:316-321). These results have provided enough data to justify further research on a higher purity palmitoleic acid extract (Provinal®) (Lipid Technology 2015;27(5):107-11) void of the high levels of palmitic acid (saturated fat <1%) naturally found in *H. rhamnoides*. Sea buckthorn and macadamia oils typically contain around 9% to 40% palmitic acid, the negative effects (*Molecules* 2015, *20*(9):17339-17361) of which can negate the benefits of the omega-7 (J Agric Food Chem. 2001; 49(4):1939-47). **Conclusion:** Purified palmitoleic acid (Provinal®) has shown a potent antiinflamatory and lipid-modulating effect compared with placebo in a double-blinded, placebo controlled trial (J Clin Lipidol. 2014; 8:612-617; Lipid Technology 2015; 27(7):155-160). Further studies with promising results are being published using purified palmitoleic acid (Provinal®) in dry eye, prevention of metabolic syndrome, including cardiovascular disease and insulin resistance.

Sources of Funding: None

P-59.

The Effect of Body Position on the Pharmacokinetics of TX-004HR, Estradiol Vaginal Softgel Capsule

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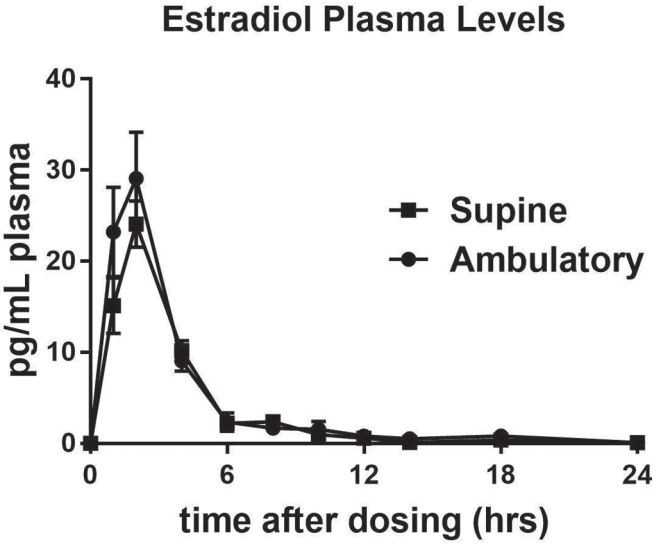
Objective: TX-004HR is a soluble estradiol vaginal capsule under development for the treatment of moderate to severe dyspareunia, a symptom of vulvar and vaginal atrophy, due to menopause. TX-004HR was designed to be convenient for the patient, fast acting, and have low systemic estradiol exposure. This analysis was undertaken to evaluate the impact of normal daily activities for 4 hours post dose versus remaining in the supine position for 4 hrs post dose on the pharmacokinetic (PK) profile of TX-004HR 25 mcg. **Design:** In two studies, at the same site, the same sixteen healthy postmenopausal female subjects were fasted for at least 10 hrs prior to dosing through 4 hrs following dosing. Subjects received TX-004HR 25 mcg administered intravaginally by trained female study personnel. Following their first dose, the subjects were required to remain in a supine position for 4 hrs following dosing. Following the second dose, after 5 mins resting time, the subjects were instructed to be ambulatory in the clinic and refrain from reclining for the 4 hrs following dosing. Blood samples were collected at pre-defined intervals up to 24 hrs after dosing. Plasma samples were analyzed for estradiol using LC-MS/MS. PK parameters were calculated on an individual and group mean basis with baseline correction. **Results:** The mean C_{max} and AUC_{0-24} of estradiol was not significantly different with ambulation than with supination. On an individual subject basis, the majority showed similar C_{max} and AUC_{0-24} levels with ambulation as with supination. There were no signs of posture having an effect on absorption rate as evidenced by the similarity in group average and individual subject t_{max}. In addition, there was no difference between the group mean profiles when compared on an individual time point basis, further demonstrating that posture had no effect on absorption of clearance. **Conclusion:** Based on these PK results, the systemic exposure of estradiol in TX-004HR 25 mcg was generally low and occured regardless of whether the subjects were ambulatory or supine for 4 hrs after dosing. Showing that activity level does not results in meaningfully different systemic absorption of estradiol from TX-004HR, gives the patient more flexibility with her dosing regimen.

Sources of Funding: TherapeuticsMD, Inc.



Baseline corrected estradiol levels after dosing of TX-004HR 25 mcg. Subjects were either supine or ambulatory for 4 hrs after dosing. Mean ± SE.

P-60.

Resting-state fMRI after Acute Tryptophan Depletion in Perimenopause Women on Estrogen Therapy: Preliminary Results

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Objective: Estradiol (E2) exerts modulatory effects on serotonergic (5HT) neurotransmission by regulating the density and turnover of 5HT receptors and synthesizing enzyme activity. Acute Tryptophan depletion (ATD) is a useful paradigm to study 5HT transmission in mood disorders. Little is known about the effect of ATD in perimenopausal women with a history of MDD on resting state functional connectivity (Rs-FC). Here, we examined the impact of ATD on Rs-FC in perimenopausal women with and without a history of MDD receiving hormone therapy. **Design:** Eighteen perimenopausal women on estrogen-based hormone therapy were scanned using eyes-open resting-state fMRI 5-6 hours after sham and ATD conditions (order of scans were randomized and subjects and researchers were blind for condition). Women were categorized into three groups based on their clinical history of MDD (Healthy Controls = 7, Past History MDD = 7, Current MDD = 4). Regions established as dense in 5HT and E2 receptors (frontal cortex, limbic system and cerebellar vermis) were used as region of interest seed points in Rs-FC analysis. **Results:** There were no differences in Rs-FC between the SHAM and ATD conditions in healthy controls. Among women, who were not depressed but reported past history of MDD, increased functional coupling was found during ATD compared to SHAM, between the anterior temporal fusiform cortex and left primary somatosensory cortex (p=0.03), right somatosensory association cortex (p=0.03) and left somatosensory association cortex (p=0.04). Women with current MDD displayed increased functional coupling ATD compared to SHAM between cerebellar vermis and right premotor cortex (p=0.03) and cerebellar vermis and the left cerebellum crus (p=0.01). All results are FDR-corrected for multiple comparisons. **Conclusion:** These preliminary results suggest that manipulation of the 5HT system may lead to acute changes in functional connectivity (FC) in patients with a history of MDD. Further, results suggest a difference in the mechanism underlying neuromodulatory effects of E2 in women with current versus past MDD. These changes in FC may reflect the neural component of transient changes in mood experienced when ATD is applied. Further research is needed to elucidate differences in Rs-FC associated with ATD in this population.

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

P-61.

Effect of oral hormone therapy on oxidative stress produced by hot flashes in postmenopausal women

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Objective: One of the most common and distressing symptoms of menopause are hot flashes (HFs) that occur in over 75% of menopausal women, and continue for nearly 5 years after menopause. Also in the postmenopausal period the marked reduction in estrogens has been shown to increase levels of oxidative stress (OS); in addition, it is probably that vasomotor episodes contribute to OS production. Hormone therapy (HT) is used to diminish HFs intensity and frequency, but it is unknowing if this treatment has effect on OS associated to HFs, therefore this is the aim of this study. **Design:** A randomized, double-blind placebo controlled trial was carried out in 100 women with age 48-57 years, amenorrhea ≥12 months and without contraindications for use of HT. They were evaluated with the item about vasomotor symptoms, rated according to its severity on a 4-point scale, in the somatic subscale of Menopausal Rating Scale to assess HF intensity and strengthen the concepts pictorially. Participants were allocated at random to receive either 0.625 mg/d of synthetic conjugated estrogens plus 5 mg/10d of medroxyprogesterone (HT) or placebo (n=50 each) during 6 months, with assessments at initial and final moments. We measured lipoperoxides levels (LPO) by TBARS assay, erythrocyte superoxide dismutase (SOD), glutathione peroxidase (GPx) and total plasma antioxidant status (TAS) using Randox Laboratories kits, and we calculated SOD/GPx ratio and antioxidant gap. Alternative cut-off values of each parameter were defined on the basis of the 90th percentile of young healthy subjects, and a stress score (SS) ranging from 0 to 7, represented the severity of the markers modifications was computed. **Results:** Five women of HT and 8 of placebo groups dropped out in different time. Women with HFs had a SS higher than those without HFs (4.3±1.3 vs. 3.5±1.7, $p<0.05$). After 6 months, SS was diminished in HT groups, but more significant in women with HFs with an increment of GPx and decrement in LPO and SOD/GPx (Table), it showing low OS. In placebo groups there are not changes. **Conclusion:** Our findings suggest that HT decreases OS in postmenopausal women with HFs.

Sources of Funding: This work was supported by grant DGAPA-UNAM IN224115.

Table. Oxidative stress markers at basal and 6 months in women without/with hot flashes using hormone therapy, (mean ± SD)

Oxidative stress marker	Hormone Therapy Without hot flashes (n = 12)			Hormone Therapy With hot flashes (n = 33)		
	Basal	6 months	p value*	Basal	6 months	p value*
Stress score	3.6±1.2	3.1±1.1	0.309	4.6±1.3	2.6±1.3	<0.0001
Lipoperoxide (µmol/L)	0.320±0.06	0.292±0.06	0.241	0.367±0.05	0.297±0.06	<0.0001
SOD (U/gHb)	1.29±0.14	1.30±0.15	0.663	1.24±0.22	1.19±0.13	0.160
GPx (U/gHb)	58.3±19.5	74.3±29.6	0.027	53.7±20.5	66.5±18.1	0.007
SOD/GPx ratio	0.024±0.01	0.019±0.01	0.040	0.026±0.01	0.019±0.01	0.003
TAS (mmol/L)	977±297	935±175	0.694	1041±202	1093±322	0.471

***Paired t test.**

P-62.

Responder Analysis of Estradiol Spray for the Treatment of Vasomotor Symptoms: A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study

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Objective: Estradiol transdermal spray is approved for treatment of moderate to severe vasomotor symptoms due to menopause. Estradiol spray (1 to 3 sprays) decreased the frequency of hot flushes ≥50% from baseline in 74.3% to 85.5% of patients compared with 46.1% of patients receiving placebo (pooled) at Week 12. The aim of this post hoc responder analysis was to examine efficacy during 12 weeks of treatment. **Design:** Post hoc responder analysis of healthy postmenopausal women ≥35 years of age who experienced ≥8 moderate to severe hot flushes daily (≥56/wk) in a randomized, double-blind, multicenter, parallel-group, phase 3 study was conducted. Patients were randomized to 1, 2, or 3 sprays of estradiol (1.53 mg estradiol/90 µL spray) or placebo to the inner forearm (multiple adjacent sites for 2 or 3 sprays) each morning for 12 weeks. The percentage of patients with ≥50%, ≥75%, and ≥90% decrease from baseline in the number and severity of moderate to severe hot flushes was calculated using the weekly change from baseline in frequency and severity of hot flushes. A severity score was calculated by: 2 x number moderate hot flushes (ie, sensation of heat with sweating, able to continue activity) + 3 x number severe hot flushes (ie, sensation of heat with sweating, discontinuation of activity)/number moderate + number severe hot flushes. Blood samples were collected 2 to 6 hours postdose to determine serum estradiol concentrations by high performance liquid chromatography with tandem mass spectrometric detection at baseline and Week 12. **Results:** The post hoc responder analysis included 454 women (age range, 36-76 y; 70% white) randomized to receive estradiol spray (n=226) or placebo (n=228). Responder analyses demonstrated that a greater percentage of patients receiving estradiol spray (pooled) had a decrease from baseline ≥50% (Table), ≥75%, and ≥90% in the daily frequency of moderate to severe hot flushes compared with placebo from Weeks 1 to 12. The severity of moderate to severe hot flushes was improved from baseline ≥50%, ≥75%, and ≥90% in a greater percentage of patients receiving estradiol spray versus placebo at Weeks 2 to 12. Median serum estradiol concentrations in patients who achieved a decrease from baseline ≥50% in the daily frequency of moderate to severe hot flushes were greater versus patients who did not achieve this response with estradiol spray at 12 weeks (median, 24.2 vs 18.2 pg/mL, respectively). **Conclusion:** Estradiol spray improved the daily frequency and severity of moderate to severe hot flushes during 12-week treatment. Serum estradiol concentrations were greater in patients with decreased daily frequency of hot flushes compared with nonresponders.

Sources of Funding: Perrigo Company

Table. Percentage of Patients With Reduction From Baseline ≥50% in Daily Frequency or Severity of Moderate to Severe Hot Flushes

	Decrease in Daily Frequency of Hot Flushes, n (%)		Improvement in Severity of Moderate to Severe Hot Flushes, n (%)	
Time	Estradiol (n=226)	Placebo (n=228)	Estradiol (n=226)	Placebo (n=228)
Week 1	59 (26.1)	42 (18.4)	11 (4.9)	7 (3.1)
Week 2	92 (40.7)	61 (26.8)	18 (8.0)	13 (5.7)
Week 3	117 (51.8)	71 (31.1)	24 (10.6)	13 (5.7)
Week 4	136 (60.2)	78 (34.2)	35 (15.5)	14 (6.1)
Week 5	155 (68.6)	87 (38.2)	51 (22.6)	22 (9.6)
Week 6	161 (71.2)	89 (39.0)	63 (27.9)	21 (9.2)
Week 7	167 (73.9)	94 (41.2)	64 (28.3)	22 (9.6)
Week 8	176 (77.9)	104 (45.6)	69 (30.5)	24 (10.5)
Week 9	172 (76.1)	100 (43.9)	76 (33.6)	25 (11.0)
Week 10	178 (78.8)	104 (45.6)	78 (34.5)	26 (11.4)
Week 11	184 (81.4)	108 (47.4)	84 (37.2)	25 (11.0)
Week 12	178 (78.8)	105 (46.1)	89 (39.4)	32 (14.0)

VAGINAL HEALTH POSTER PRESENTATIONS

P-63.

WITHDRAWN BY AUTHORS

P-64.

Comparative study of vaginal danazol vs diphereline (a synthetic GnRH agonist) in the control of bleeding during hysteroscopic myomectomy in women with abnormal uterine bleeding: a randomized controlled clinical trial

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Objective: To compare the usefulness of vaginal danazol and diphereline in the management of intra-operative bleeding during hysteroscopy. **Design:** Randomized controlled clinical trial. **Results:** One hundred and ninety participants of reproductive age were enrolled for operative hysteroscopy. Thirty women were excluded from the study. One hundred and sixty participants with submucous myomas were allocated at random to receive either vaginal danazol (30 days before surgery) or intramuscular diphereline (twice with a 28-day interval). Overall, 145 patients completed the study. In the danazol group, 78.1% of patients experienced no intra-operative uterine bleeding, and 21.9% experienced mild bleeding. In the diphereline group, 19.4% of patients experienced no intra-operative uterine bleeding, but mild, moderate and severe bleeding was observed in 31.9%, 45.8% and 2.8% of patients, respectively. The difference between the groups was significant. A clear visual field was reported more frequently in the danazol group compared with the diphereline group. The mean volume of infused media was 2 liters in both groups. The success rate was 100% for both groups with no intra-operative complications. **Conclusion:** Both vaginal danazol and diphereline were effective in controlling uterine bleeding during operative hysteroscopy. However, vaginal danazol provided a clearer visual field.

Sources of Funding: None

P-65.

Elevation of collagen and proteoglycan in diabetic rat vaginas treated with soybean isoflavones, 17β-estradiol and combined therapy

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Objective: To analyze the interactions of the small leucine rich proteoglycan (SLRPs) in the vagina of diabetic rats treated with 17β-estradiol, isoflavones, and the combination therapy. **Design:** Non–diabetic: GI (n=10) Sham control animals ovariectomized; and GII (n=10) control ovariectomized that received propylene glycol vehicle. Diabetic: GIII (n=10) Sham control diabetic animals ovariectomized; GIV (n=10) control ovariectomized diabetic animals receiving propylene glycol vehicle; GV (n=10), ovariectomized diabetic animals treated with soy isoflavones (150mg/kg by gavage); GVI (n=10) ovariectomized diabetic rats treated with estrogen (17β-estradiol, 10mg/kg, subcutaneously); GVII (n=10), ovariectomized diabetic animals treated with soy isoflavones (150mg/kg by gavage) and with combination therapy estrogen (17β-estradiol, 10mg/kg). The treatment lasted 30 days. At the end of the experiment the rats were killed under deep anesthesia, the vaginas were dissected out and processed for RT reaction (RT-PCR) and Western blotting techniques. Another part of the vagina was immersed in 10% formaldehyde for subsequent histological studies of Picro Sirius Red. The results were analyzed by one-way ANOVA followed by the Bonferroni posttest. **Results:** The morphological data showed the groups treated with 17β -estradiol had the vagina more developed with thicker layers of stratified epithelium than those treated with isoflavone after ovariectomy ($p<0.001$). The same was observed for gene expression and protein analysis that was also higher when animals were treated with 17β-estradiol ($p<0.001$). The expression of the same genes in the groups treated with isoflavone was relatively lower. **Conclusion:** Isoflavone improves collagen formation and proteoglycans dposition in the vagina of diabetic rats, but this effect is not so higher when compared to those treated with 17β-estradiol or combination therapy.

Sources of Funding: This study was supported by Fundação de Amparo à Pesquisa do Estado de São Paulo - FAPESP.

P-66.

Painful Vaginal Penetration (MPVP) Model: From Empirical Generalization to Testable Model

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Objective: Objective: Sexual health concerns are among the most commonly reported concerns of female cancer survivors. Dyspareunia and decreased desire are the most frequently reported concerns that interfere with quality of life among female cancer survivors as well as women in general. Many women with a history of cancer, especially a hormone receptive cancer, are reluctant to use prescribed therapies such as local estrogen to reduce pain with penetration that may be caused by vaginal atrophy, vaginal dryness, or decreased elasticity. Healthcare providers are well positioned to help women overcome problems of dyspareunia and decreased desire by prescribing nonpharmacological self-care practices and/or the use of over-the-counter products. However the knowledge needed to prescribe non-pharmacological interventions to manage dyspareunia and decreased desired tends to be scattered and disorganized. The Minimizing Painful Vaginal Penetration Model (MPVP) described provides a useful guide for organizing one's thinking about the causes of painful vaginal penetration as well as interventions to minimize painful penetration and the effect of these interventions on the female sexual response. Importantly, this model also provides a framework to address arousal and desire based on the work of Rosemary Basson. The MPVP model is presented as a useful guide for healthcare professionals to use while discussing vaginal pain, arousal, and decreased desire. Research is needed to test the proposed relationships depicted in the model. **Design:** Design: The MPVP model emerged through a synthesis of concept mapping with inputs from empirical observation and the literature. The relationships between the recommended interventions as they relate to reducing vaginal pain with penetration are described. Literature support is provided for each relationship to provide the framework for the model. The relationships between vaginal pain with penetration, vaginal pain and arousal, and arousal and desire are also described and supported by literature. Importantly, the relationships between arousal and desire are based on the work of Rosemary Basson and others and further support the importance of addressing vaginal pain with penetration leading to a heathy sexual response. **Results:** Results: According to Basson, sexual response outcomes such as increased arousal and desire are essential aspects of a woman's sexual response. Repeated clinical (empirical) observation suggests a patterned relationship between pain with vaginal penetration and decreased arousal and desire. Women who report pain with vaginal penetration frequently have symptoms of vaginal atrophy, vaginal dryness, or decreased elasticity. Over time, repeated use of self and/or partner administered interventions such as increasing lubrication, vaginal stimulation, and vaginal stretching, minimize vaginal pain with penetration. Clinically, women report increased arousal and desire when pain from vaginal penetration is minimized. Therefore, selected theoretical outcomes (arousal and desire) seem to be achieved with some degree of regularity when clinical symptoms such as painful penetration, vaginal atrophy and vaginal dryness are managed effectively. **Conclusion:** Discussion:. The MPVP model can be thought of as a graphic representation of an empirical generalization. Empirical generalizations can be understood as patterns of regularity that occur repeatedly under different circumstances. They become useful to science and practice when depicted mathematically, graphically or symbolically as in a model or conceptual framework depicting relationships from which potentially testable hypotheses can be derived. It is hoped that use of the model for research and practice might accelerate the pace of knowledge development and lead to more efficacious treatments for painful vaginal penetration Conclusion/Implications: Importantly, the MPVP model links clinical concepts and interventions to quality of life outcomes. Providing a framework based on relationships between clinical concepts and theoretical concepts supported by the literature enables healthcare providers to organize their thinking and engage in a more thorough discussion with their patients. In addition, a the MPVP model provides a framework to guide practice and future research regarding healthy sexual response is described

Sources of Funding: None

P-67.

Vulvar Opinions on Washes Survey (VOWS); Preliminary Report

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Objective: Introduction: Vulvar care and hygiene is an often-neglected topic of discussion between the health care provider and their female patients. With increasing non-hormonal products on the market for the treatment of genitourinary syndrome of menopause, vulvar hygiene products, wipes, and cleansers are becoming more widely recommended and utilized by women of all ages. In order to better understand the misunderstanding the present vulvar care habits of women, this survey was completed. **Design:** Methods: This is an in-office survey that was a random sampling of women who attended a community based gynecology office. A total of fifty women were asked to complete the survey while waiting for their regularly scheduled office appointment. Surveys were completed on paper, in person and participants were not compensated for their time. All answers were anonymous. **Results:** Preliminary Results: Fifty women (ages 23-73) were randomly selected to compete a short office bases survey concerning Vulvar Hyiene. Current vulvar care products included: OTC body soap (n=37), water (n=18), specialized feminine cleanser (n=7), nothing (n=2). When asked about where they received information concerning vulvar care they received their information from their : Mother (n=15), no one (n=14)- nine (9) said they saw it on the pharmacy shelf, where as five (5) figured it out on their own and only 3 three received information from their gynecologist (n=3), While 31/50 or 62% of women were aware of vulvar cleansers, only 7/50 (14%) actually utilized a vulvar cleanser. Approximately 60% of women would consider utilizing a specialized cleanser for the intimate vulvar area and the majority would pay between 10-20 dollars for such a care product. In addition the majority of women were familiar with potential irritants as common ingredients within genital products including: parabens, glycerin, fragrances, colors, bacteriocides and spermicide. **Conclusion:** Conclusions. Vulvar hygiene is an area of growing concern especially with the new all encompassing new definitions of GSM. Patients need to be sufficiently educated when it comes to selection of vulvar hygiene product. Larger Studies are needed to further evalauted the issues of vulvar hygiene and care products within a diverse patient demographic.

Sources of Funding: This research was unsupported by pharmaceutical support.

P-68.

Raising Awareness … Starting the Conversation

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Objective: Our **primary goal** was to **change clinician behavior** to increase appropriate management of symptomatic vulvovaginal atrophy (VVA) to result in an improvement in the quality of life for women ages 35-80. Measure #1: Increase in the frequency of the

diagnosis of VVA found through chart review. Measure #2: Increase in the documentation in the medical record (measured pre vs post) of evaluation and treatment for VVA in patients with diagnosis. Our **secondary outcome** was to measure how systems changed as a result of this project by measuring what practices said they would do differently and what they actually did do differently. **Design:** We developed an internet-based VVA Shared Decision Making (SDM) decision aid and educational interventions to teach SDM methods to clinicians and change clinician behavior, resulting in an increase in appropriate management of symptomatic VVA. The educational interventions included spaced education about VVA and SDM as well as on-site academic detailing and practice facilitation. We evaluated methods to increase recognition and management of symptomatic VVA in family medicine and OB/GYN clinics through raising awareness of patients, clinicians and clinic staff about the impact symptomatic VVA has on patient quality of life. This intervention took place in family medicine and OB/GYN clinics in Wisconsin and North Carolina. Data was collected using pre and post intervention surveys on clinicians, staff, and patients as well as through electronic health record data extraction and manual chart review. **Results:** All education and patient enrollment is complete. Post chart review data and data collation is ongoing. In summary, nine Primary Care and five Gynecology clinics participated in the study, including 42 clinicians seeing patients. An additional 55 clinicians participated in some aspect of the education. Preliminary findings: Clinicians self-reported screening patients for VVA (42% pre- and 74% post-intervention). Clinicians similarly reported adding VVA to the problem list (52% pre-, 74% post-intervention). The majority of learners completing the VVA spaced education activity found the content (69%) and usefulness (71%) excellent/very good and 48% anticipated making changes as a result of the activity. Learners completing the SDM activity also found the content (60%) and usefulness (55%) very good/excellent and 55% anticipated making changes as a result of the activity. After completing all educational activities, 97% of clinicians intended to use SDM with patients with symptomatic VVA and 84% intended to use SDM with patients with other diagnoses in the future. Of the 201 enrolled patients originally a part of the study, 160 (76%) accessed the online SDM decision aid (DA) with 72% viewing at least 50% and 68% viewing all sections. Additionally, 3% of enrolled patients reported viewing the DA whose scores were not on file. Seventy-two patients initially declined to be a part of the study when approached by their clinician, however, 88% of them still wanted a DA access code. 35% of those patients accessed the DA with 73% of them viewing 50% and 55% viewing all sections. 130 (65%) patients completed the entire study, rating their symptom management post study. Participant ages ranged from 42 to 76 with the average age being 58. After the study, 76% of patients recommended using the internet VVA program and 85% recommended participating in a shared decision making process with their clinician. The completion of our data collection and evaluation will provide additional results. **Conclusion:** Lessons learned developing and implementing this novel educational program can be applied to many medical topics in the future. Our methods of education and facilitating practice change were successful in a variety of practice sites in multiple health systems located in 2 states, in 2 regions of the country, suggesting our results can be generalized and reproduced elsewhere.

Sources of Funding: We were funded by Pfizer with an Independent Grant for Learning and Change.

P-69.

Fractional CO_2 Laser Treatment for the Symptoms of Vulvovaginal Atrophy in Postmenopausal Women

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Objective: Current research suggests that vulvovaginal atrophy (VVA) is a common and underreported condition that can affect the sexual health of women. Fractional laser systems with dedicated gynecological handpieces have become available as a nonsurgical and non-hormonal approach for treatment of vaginal symptoms associated with this condition. Here we present data on the effects of fractional CO_2 laser in postmenopausal women treated by resurfacing and coagulation of the vaginal canal tissue and mucosal tissue of the introitus. **Design:** Postmenopausal women with symptoms of VVA, who were not able to or not interested in using local estrogen therapy, were recruited for fractional CO_2 laser system treatment. The Vaginal Health Index (VHI) was used by the investigator to assess changes in vaginal elasticity, fluid volume, vaginal pH level, epithelial integrity and moisture. Subjects self-reported on vaginal symptoms of dryness, dyspareunia, burning, itchiness and dysuria, using a numerical scale from 0=no symptoms to 10=worst possible symptoms. A similar numerical scale was used to measure discomfort associated with treatment. In this ongoing study, subjects will be assessed at one, three, six and 12 months post final treatment. **Results:** Currently, 36 females (mean age 56±8 years; mean weight 70.5±16 kg; Fitzpatrick Skin Type I-VI and 86% Caucasian) have undergone three CO_2 laser treatments and were assessed at 1-month after the third treatment. Vaginal health improved with successive treatments with 89% and 97% of subjects showing highly significant improvement in the VHI scale after the first and second treatments, respectively ($p<0.001$). At one month following the third treatment, all 36 patients (100%) showed a statistically significant improvement in the VHI scale ($p<0.001$), with an average improvement of 9.7±3.2 points compared to mean baseline score of 10.9±2.9. Improvement in VHI remained significant ($p<0.001$) for all 19 subjects evaluated at the 3-month follow-up with a mean VHI score of 20.3±2.8. The most prominent vaginal symptoms at baseline also improved significantly with treatment with 86% of subjects self-reporting improvement in dryness ($p<0.001$), 78% in dyspareunia ($p<0.001$) and 64% in burning ($p<0.001$) at the 1-month follow-up. Itching and dysuria were mild at baseline (score <2) with significant improvement in 44% of subjects for itching ($p<0.01$), while there was no significant improvement in dysuria ($p=0.18$) at the 1-month follow-up. Most patients reported that probe insertion (93%), movement (95%) and laser application (97%) were accompanied with none to mild pain. Immediate treatment responses for the 108 laser procedures were transient and included: mild to moderate erythema (55%) and edema (56%) and mild vaginal bleeding (2%) and tissue retraction (1%). Four subjects reported on mild to moderate vaginal itchiness, spotting or dysuria following the procedure that resolved without intervention. One subject reported on vaginal itchiness that was relieved with ice pack and topical analgesic gel application. **Conclusion:** In this postmenopausal population, fractional CO_2 laser treatment was associated with improvement of vaginal health and amelioration of symptoms of vulvovaginal atrophy. There was minimal discomfort and adverse effects associated with treatment. Investigation of long-term clinical outcome is underway and may support the use of fractional CO_2 laser as a non-hormonal treatment option for sustained relief of VVA symptoms.

Sources of Funding: Study equipment was provided by Syneron Candela Corp.

P-70.

Milli™ A Novel Patient Controlled Expanding Dilator

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Objective: Vaginal dilators are currently prescribed as adjunctive supportive treatments for a variety of genitopelvic conditions including but not limited to genitourinary syndrome of menopause (GSM), vulvovaginal atrophy (VVA), pelvic floor hypertonus, lichen sclerosis and provoked vestibulodynia. In addition, many women may use dilators as bridging exercises if there is a long period of abstinence without penetrative sexual intercourse. Dilators may help with reconditioning for the woman who may also have anticipatory anxiety about intravaginal penetration. Dilators are also a helpful adjuncts to desensitization protocols that help women transition away from painful intercourse. Changing dilator sizes in an abrupt, stepwise fashion may be considered time consuming and often invokes apprehension for patients. Compliance may be compromised causing discontinuation of instructional dilators due to concerns over minimal progress, and that larger sizes appear daunting. Patients may surmise that the next size dilator is a goal that maybe unreachable. One of the limitations of current vaginal dilators is that they are static in size, and it is often difficult and intimidating for a patient to remove a dilator size and replace it with the next size up. Materna Medical has created a specialized electronic expanding dilator to solve many of these issues, which may lead to more rapid vaginal health recovery and less patient apprehension or anxiety. **Design:** Milli ™, The Materna Medical Pelvic Health Device, is a specialized designed unique dilator to provide easier more convenient treatment when vaginal dilation is necessary as part of the overall treatment paradigm. The Materna Device is designed to slowly expand in small controlled increments, which could allow the user to increase the diameter in a more comfortable and less intimidating way. The Milli ™ device features a constant shape insertion tip, with a dilating device, which can expand in 1mm increments controlled by the user. The handle has buttons that can increase or decrease the diameter of the device while the device is still inserted. The patient, herself, is able to comfortably control their own dilation, progressing through their treatment more effectively and at her own pace. The gradual increase in diameter allows for one insertion and a progressive stepwise dilation without removal of static devices. **Results:** A pilot, pre-marketing, in office trial of the novel device was used in 10 patients at 2 medical offices. Participants had previously used a variety of vaginal dilators from multiple sources including (Berman dilators, Vaginismus.com and Soul Source). Participants suffered from a variety of underlying pelvic conditions and all complained of some degree of pelvic floor hypertonus for approximately four years. The device trial was for 20-30 minutes, under direct care and supervision of a health care professional (HCP). All participants completed the in office trial after proper evaluation, education and assessment with water-based lubricant. There were no serious adverse events or device complications reported. All reported that the device was superior to conventional available dilators that are currently available on the market. All participants reported that the device expanded with ease and comfort. Most reported that the device was easy to clean and all were satisfied with the device. Positive comments included: expands easily, very easy to use, and less anxiety to implement. Incremental control was noted to improve confidence and the gentle expansion, especially while the device remained inserted, was a positive experience. **Conclusion:** Milli ™ offers excellent promise as a novel dilator device that the patients can self control, and by slow incremental control progress at her own pace towards her goals. The need to change dilators will help decrease patient anxiety and may improve compliance. Larger long-term interventions, with larger numbers combined with a standard dilation program are planned post marketing to further support these hypotheses.

Sources of Funding: Dr. Michael Krychman and Stephanie Prendergast, PT are paid consultants for Materna. This research was unsupported by Materna.

P-71.

The EMPOWER Survey: Women's Knowledge and Treatment of Vulvar and Vaginal Atrophy (VVA) Remains Low Years after Previous Surveys

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Objective: Postmenopausal women's knowledge about VVA, a component of genitourinary syndrome of menopause (GSM), and available treatment options has historically been low. Recent direct-to-consumer marketing and educational efforts would be expected to have increased understanding of the condition and treatment

options. The results of the EMPOWER survey of postmenopausal women with VVA were examined in comparison with past VVA surveys to assess progress in women's understanding and approaches to treatment of VVA. **Design:** The EMPOWER survey, an internet based survey of US postmenopausal women with symptoms of VVA, assessed women's awareness of VVA and their behaviors and attitudes associated with treatment of symptoms. The EMPOWER results were compared with results from 6 surveys evaluating knowledge, behavior, and attitudes associated with VVA among US postmenopausal women: REVEAL (Wyeth 2008), VIVA US (Simon et al 2013), Healthy Women #1 (HealthyWomen.org 2011), REVIVE (Kingsberg et al 2013), CLOSER North America (Simon et al 2014), and Healthy Women #2 (HealthyWomen.org 2015). **Results:** The EMPOWER survey was consistent with all 6 past VVA surveys, and showed that postmenopausal women generally failed to recognize VVA and its chronic, progressive course and were reluctant to discuss vaginal or sexual symptoms with their health care providers (HCPs). Women consistently lacked knowledge concerning prescription therapeutic options and often were engaging in painful intercourse. In the EMPOWER survey, 81% were not aware that VVA is a medical condition; while in REVEAL, 43% were not aware that VVA symptoms were associated with menopause. In the VIVA survey, 90% of women experiencing vaginal symptoms failed to attribute the symptoms to VVA and 43% failed to recognize VVA as a chronic condition. Similarly, 70% of the women in Healthy Women #2 were unfamiliar with VVA as a medical condition. More than two-thirds of the EMPOWER respondents were not familiar with most of the prescription VVA products; while almost half (46%) in Healthy Women #1 were not aware that prescription treatments were available for VVA. Prescription therapy use in the CLOSER survey was more prevalent (31%) than in the EMPOWER survey (7%). Women in the REVIVE survey included in their concerns and dislikes of currently available treatments a perceived lack of efficacy (69%) and cost (32%), while in the EMPOWER survey, 26% changed products due to lack of efficacy and only 12% because of cost. Concerns regarding hormone safety and exposure were a top reason respondents in the REVIVE survey (76%) disliked currently available vaginal estrogen preparations. In EMPOWER, 59% rated the risk of systemic absorption a negative attribute of VVA prescription treatments; messiness associated with the application of a vaginal cream and the necessity to reuse an applicator were also considered negatives (both 64%). Similarly, 20% of women in the REVIVE survey found prescription vaginal products messy and 41% thought product administration was inconvenient or annoying. **Conclusion:** The results of the EMPOWER survey demonstrate and reinforce that even with multi-media marketing and educational strategies in the years following other major VVA surveys, minimal progress has been made toward increasing women's awareness or understanding of VVA. Women remain naïve to the safe and effective treatment options that are currently available. All studies reiterate that postmenopausal women with symptoms of VVA remain under-informed and under-treated. The results of these surveys indicate that women strongly desire accurate medical information about VVA from their HCPs. Thus, HCPs should be aware of this unmet medical need. The results of these 7 surveys clearly demonstrate that HCPs should be concerned with initiating education and discussions with postmenopausal women for them to better understand VVA as a medical condition, symptoms associated with VVA and the risk benefit ratio regarding treatment options.

Sources of Funding: TherapeuticsMD

P-72.

Abdominal ultrasound to assess vaginal wall and vaginal mucosal thickness: an innovative way to quantify vaginal atrophy?

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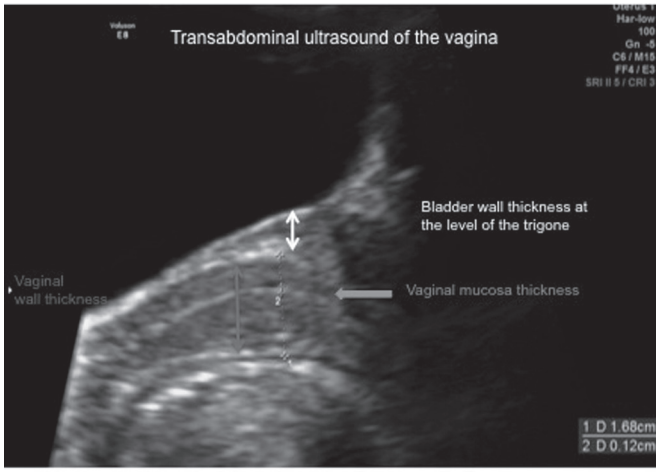
Objective: As life expectancy increases, the number of women reporting adverse vulvovaginal symptoms from menopause, including vaginal dryness and sexual pain, will also increase. Currently, objective assessments of vaginal atrophy, such as vaginal pH and maturation index are indirect measures. The purpose of this study was to assess the use of abdominal ultrasound as a noninvasive method to quantify vaginal wall and vaginal mucosal thickness, measurements which may correlate with vaginal atrophy. **Design:** Abdominal ultrasound measurements, including vaginal wall thickness, vaginal mucosal thickness, and bladder wall thickness at the trigone were taken on women presenting to the Gynecologic Ultrasound Program. Exclusion criteria included: recently pregnant, use of hormone therapy, or a previous oophorectomy or hysterectomy. Measurements were performed by the same team using GE Voluson E8, abdominal probe 2-8 MHz. *Vaginal wall thickness* was defined as the measurement between the outer layer of the anterior vaginal wall to the outer layer of the posterior vaginal wall at the level of the bladder trigone. *Vaginal mucosal thickness* was defined as a hyper-echogenic layer measured between the inner layer of the anterior vaginal wall to inner layer of the posterior vaginal wall at the level of the bladder trigone. Data was analyzed using linear regression with IBM SPSS. **Results:** 44 women, (age range: 22-66; 42.2 +/-10.2; Mean +/-SD), were included. The data from the ultrasound measurements showed that there were no age related changes in vaginal mucosal measurements in this cohort (Range: 0.9-2.2 mm; Mean: 1.47mm). However, in the women ages 40 and above, there was a slight decline measured in the vaginal wall thickness (Range: 7.6-25.9 mm; Mean: 15.7). This decline was a trend; it did not reach statistical significance. The median of the bladder wall thickness at the level of trigone (trigone thickness) measured abdominally was 6.5 mm, which correlates with previously published data. **Conclusion:** Results from this study suggest that the *vaginal wall* thickness can be measured by abdominal ultrasound and may correlate with age related atrophic vaginal changes. However, this same trend in declining thickness of the *vaginal mucosa* with age was not noted in the age range of women studied in this trial. More postmenopausal patients are needed to further assess vaginal wall thickness as a measure of vaginal atrophy and as noninvasive evaluation comparable with endometrial thickness use.

Sources of Funding: None



P-73.

Clinical Application of Probiotic Products for Vaginal Health: review of published evidence for specific probiotic products available in Canada

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Objective: This guide is designed to translate scientific evidence available for probiotic supplements into practical, clinically relevant information, enabling clinicians to easily select the appropriate product, dose, and format for a specific indication. **Design:** Published data or studies with defined clinical outcomes for probiotic strain(s) were searched, using defined inclusion criteria. Commercially available products containing said strain(s) were identified, and the levels of evidence were used to rate the strength of the recommendation. This information was compiled into a chart form, it was assessed by independent expert reviewers. This guide is meant to be used as a clinical decision making tool to assist health care professionals in providing evidence based recommendations for their patients. In the case of probiotics, the clinical evidence supports only certain formulations/brand names of the probiotics (including the genus, species, alphanumeric designation or strain, number of live bacteria present, the blend of probiotic strains present and finally, the non-active ingredients present). Every attempt was made by the author and the reviewers to include the published clinical data for the available probiotic formulations. No bias is intended toward any specific formulation. Abbreviations CFU = Colony forming units, L.= Lactobacillus INCLUSION CRITERIA AND LEVELS OF EVIDENCE 1. Commercially available in Canada as a supplement or probiotic-containing food 2. Generally Regarded as Safe status (FDA) and/or Natural Product Number (Health Canada) for probiotic strain(s) used in the products 3. Favourable published clinical evidence for the particular strain(s) present in each product/food - For products containing multiple strains, evidence must be for the specified combination and not for the separate probiotic strains Expression of Strength of Evidence LEVEL I: Evidence obtained from at least one properly-designed randomized trial. LEVEL II: Evidence obtained from well-designed controlled trials without randomization/Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one centre or research group/Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled trials might also be regarded as this type of evidence. LEVEL III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees. **Results:** In the clinical guide, the available strains were organized based on probiotic strain(s), doses, and evaluated levels of evidence based on our pre-defined criteria. This is further illustrated in the table included with this submission. **Conclusion:** There is evidence to support the use of oral and vaginal probiotic products for vaginal health, however applications and results are strain-specific. Lack of adverse effects supports the wide use of these products, and further investigation is recommended.

Sources of Funding: None

Probiotic Products for Vaginal Health (Adapted from "Clinical Guide to Probiotic Supplements Available in Canada, 2016 Edition")

Brand Name	Probiotic Strain(s)	Dosage Form	CFU per dose	Number of doses per day	Vulvovaginal candidiasis	Bacterial vaginosis
Fem-Dophilus®	L. rhamnosus GR-1 2.5B L. reuteri RC-14 2.5B	Oral capsule	5B/capsule	1 capsule	I (115,116)	I (117-119)
ProB ™ (RePhresh ProB)	L. rhamnosus GR-1 2.5B L. reuteri RC-14 2.5B	Oral capsule	5B/capsule	1 capsule	I (115,116)	I (117-119)
Probaclac BV®	L. acidophilus A-212 0.4B L. rhamnosus A-119 6.8B S. thermophilus A-336 0.8B	Vaginal capsule	8B/capsule	1-2 capsule		II(120)
Provacare ™	L. rhamnosus Lcr35	Vaginal capsule	3.41B/capsule	2 capsules	I (121)	I (122-124)
Purfem ™	L. rhamnosus PBO1 1B L. gasseri EN-153471 (EB01) 1B	Vaginal ovule	2B/ovule	1 ovule		I (125,126)
UltraFlora™ Women's	L. rhamnosus GR-1 1B L. reuteri RC-14 1B	Oral capsule	2B/capsule	2 capsules	I (127)	I (128,129)

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P-74.

100% Natural Vaginal Lubricant Usage in Women With Gynecologic Cancer Receiving Irradiation

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Objective: Vaginal lubricants containing hyaluronic acid are indicated for menopausal vaginal dryness. The objective was to conduct a pilot to evaluate whether a completely natural vaginal lubricant containing hyaluronic acid (Mae by Damiva) is safe and effective in women with severely compromised vaginal health due to radiation therapy to treat gynecologic cancer. A secondary objective was to identify whether the natural vaginal lubricant could be used with a dilator. **Design:** This non-interventional, open-label pilot trial was conducted at the BC Cancer Agency in British Columbia, Canada. The information was collected by survey in women treated for gynecologic cancer receiving irradiation. Women were provided with samples of natural lubricant and asked to complete a survey after usage. Women were informed that they could use the lubricant in advance of intercourse, with a dilator and/or for general vaginal comfort. The survey results were reviewed with an oncologist during a follow-up meeting. **Results:** We summarize the results of a pilot non-interventional, open-label, non-controlled study of use of a completely natural plant-based vaginal lubricant in six (6) women who have received gynecologic radiation therapy in British Columbia, Canada, and were under the care of an oncologist. Women used a 100% natural vaginal suppository that contains hyaluronic acid and is pH balanced to 3.7. Other suppository ingredients include cocoa butter, mangosteen butter, sea buckthorn extract, vitamin E and sucrose. Hyaluronic acid has been used in clinical trials to improve symptoms of vaginal atrophy (Ref 1). The results of the trial indicate that all women who used the natural lubricant found at least one benefit of decrease in vaginal discomfort, improvement in intercourse comfort, improvement in ease of dilator insertion and increase in vaginal health and well-being. Four women found two or more benefits and two women benefitted in all areas (discomfort, intercourse, dilator usage and well-being). Out of the six women surveyed, five indicated they would use the natural lubricant again. Half of women were also using another vaginal product at the same time. The one woman who indicated "not sure" still received benefit, however, she was also using another product and had discomfort, not described nor elaborated. Women were using the natural lubricant for different and multiple purposes. Four were using the lubricant for intercourse, one woman for both intercourse and dilator usage, one woman for general comfort and one woman used it only with a dilator. The utilization within a one month period ranged from <1 to between 9 and 15 times a month. Ref 1: Constantino, D. and Guaraldi, C., "Effectiveness and safety of vaginal suppositories for the treatment of the vaginal atrophy of postmenopausal women: an open, non-controlled clinical trial." European Review for Medical and Pharmacological Sciences 2008; 12: 411-416. **Conclusion:** No adverse events were reported with usage. Despite the small sample number, we conclude that a natural lubricant appears to be safe and may be shown to provide benefit to women who have received radiation therapy after gynecologic cancer. The lubricant may also be utilized in conjunction with a dilator. Dilator usage helps prevent vaginal closure due to scarring after radiation therapy.

Sources of Funding: None

P-75.

Changes in Maturation Index after Treatment of the Vagina with a Fractional CO2 Laser.

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Objective: Atrophic vaginitis is a common problem in post-menopausal women. Subjective measures can include dryness, soreness, and dyspareunia. Objective measures can include changes in vaginal pH and maturation index. Maturation index looks at the percentage of parabasal cells, intermediate cells, and superficial cells. Proliferation of parabasal cells indicates lack of estrogen stimulation whereas a predominance of superficial cells indicates stimulation by estrogen. First line treatments for atrophic vaginitis include personal lubricants and moisturizers. Estrogen is the next-line therapy. However, women with estrogen-dependent tumors are unable to utilize estrogen therapy. Fractional CO2 laser therapy is a new FDA-approved treatment for atrophic vaginitis which can be utilized for women who are unable to, or prefer not to, use hormonal therapy. **Design:** A retrospective chart review of women receiving intra-vaginal laser treatments for atrophic vaginitis was conducted. At the time of data collection thirty women were in the process of being treated with the fractional CO2 laser. Treatments were performed in an outpatient private office with approximately six weeks between each treatment according to manufacturer's recommendations. A maturation index was performed prior to each treatment to assess for changes in parabasal, intermediate and superficial cells. **Results:** At the time of analysis thirty women had undergone treatment with the fractional CO2 laser. Six women were excluded due to lack of collection of maturation index or invalid results. Analysis of the remaining twenty-four patients was performed. Number of treatments ranged from one to three treatments. Mean and median ages were 57.1 yo and 57 yo respectively. The mean decrease in parabasal cells after one treatment compared to baseline was 8.5% ($p = 0.31$, N=13). After two treatments, the mean decrease in parabasal cells compared to baseline was 1.7% ($p = 0.19$, $N = 9$). After three treatments, the mean decrease in parabasal cells compared to baseline was 20% ($p = 0.57$, N=2). The mean increase in superficial cells compared to baseline after one, two, and three treatments was 0% ($p = 1$, $N = 13$), 6.1% ($p = 0.56$, $N = 9$), 5% ($p = 0.7$, N=2) respectively. **Conclusion:** Maturation index is a non-invasive objective tool to assess cellular changes in vaginal mucosa. Analysis of this cohort shows a decrease of parabasal cells after one, two, and three treatments and an increase of superficial cells after two and three treatments. This study is limited by the sample size and a larger cohort is needed to determine if these changes are statistically significant. Also, maturation index is a test that is used to assess presence of estrogen stimulation. Treatment with fractional CO2 laser may induce changes to the vaginal mucosa through a different mechanism than estrogen administration. The most important end point is patient satisfaction. Correlation with improvement in dyspareunia and other associated symptoms of atrophic vaginitis should be assessed.

Sources of Funding: None

P-76.

Vulvar Abscess in Premenopausal and Postmenopausal Patients: A Retrospective Cohort Study

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Objective: The aim of this study was to determine the prevalence of vulvar abscess in a population of adult women, and to describe characteristics of patients with length of stay (LOS) ≥ 1 day. **Design:** A retrospective cohort of vulvar abscess cases treated at a single tertiary care center between August 2011 and August 2013 was identified through administrative claims data. Analyses were completed on two groups: menopausal transition and early postmenopausal women (40-60 years old) and postmenopausal women (≥ 61 years old). Descriptive statistics summarized patient characteristics and the prevalence of vulvar abscess. Univariate analyses examined factors associated with increased length of stay (LOS). Associations were tested using Spearman correlations for ordinal variables and Pearson correlations for interval variables. **Results:** A total of 250 patients with vulvar abscess were identified. Of those, 54 (24.1%) were pediatric patients with a mean age of 5 (SD 5.6) years, and 196 (75%) were adults with a mean age of 43 (SD 17.8, range 18-95) years. Among these, 66 women were in the menopausal transition or early menopause and 45 women were postmenopausal. The prevalence of length of stay ≥ 1 day was 27% in the younger women and 37% in postmenopausal women, with the majority being treated as outpatients. Characteristics predicting LOS ≥ 1 day were ≥ 2 operative procedures for all women > 40 years (OR 2.07, 95% CI 1.59-3.37), and ≥ 7 comorbidities for postmenopausal women (OR 4.9, 95% CI 6.64-8.00). An increasing trend between Charlson comorbidity scores and number of procedures performed was demonstrated ($r = 0.497$, $P=0.01$). Comorbidities affecting LOS ≥ 1 day included hypertension ($r=0.96$, $P=0.01$), diabetes ($r=0.85$, $P=0.01$), obesity ($r=0.13$, $P=0.01$), cellulitis ($r=0.39$, $P=0.01$), tobacco use ($r=0.09$, $P=0.03$), age ($r=0.39$, $P=0.02$) and Charlson index ≥ 2 ($r=0.44$, $P=0.01$). Inpatient treatment occurred in 42 of 111 (38%) patients and was predicted by the number and type of medical comorbidities. **Conclusion:** This study identified a subset of high risk patients with vulvar abscess who would benefit from earlier treatment and more specialized gynecologic services and interventions. The data gathered in this study may help develop a Service Line or Treatment Pathway for women presenting with vulvar abscess.

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Table 1: Comorbidity Correlations

Variable	Spearman's Rho (r)	Inpatient Length of Stay	P
Hypertension	0.96	0.12	0.01
Diabetes	0.85	0.39	0.01
Cellulitis	0.39	0.34	0.01
Obesity	0.13	0.21	0.01
Tobacco use	0.09	0.13	0.03
Age	0.39	0.15	0.02
Charlson Index	0.44	0.31	0.01

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Local Estrogen or Systemic Opsemifene for Treatment of Vulvovaginal Atrophy and Their Effects on Mammographic Density

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Objective: Since even small increases in serum estrogen may be detrimental for cancer patients on aromatase inhibitors, nonhormonal therapies remain first-line for the treatment of vulvovaginal atrophy (VVA) in women with estrogen-dependent breast cancer. However, improvement of urogenital symptoms with nonhormonal therapies is limited. Low-dose vaginal estrogen and alternative systemic therapies such as ospemifene have been proven to be effective in the treatment of VVA, but their effect on mammographic breast density has not yet been studied. High mammographic density is a well-established, independent risk factor for breast cancer development. The purpose of this study is to provide a background for future research in the hormonal treatment of VVA in survivors of hormone-positive breast cancers and to provide a preliminary description of the effects of vaginal estrogen therapy on the mammograms of healthy postmenopausal women. **Design:** A summary of the existing literature on the effects of local vaginal hormonal therapy and systemic ospemifene on risk of breast cancer recurrence was performed. The mammograms of postmenopausal women without prior history of breast cancer actively using vaginal estrogen, prior to and after one or more years of therapy, were examined using a retrospective chart review between April 2013 and December 2015 at a single practitioner's clinic. Mammographic change was determined via the BI-RADS score and radiology read on mammogram images. **Results:** All modalities of low-dose vaginal estrogen result in increases of circulating estradiol within normal menopausal range, but this increase in serum estradiol is of unclear clinical significance. For breast cancer patients taking endocrine therapy such as tamoxifen and aromatase inhibitors, research regarding breast cancer risk with use of low-dose vaginal estrogen is sparse. One case-control study showed no increase in cancer recurrence compared to non-use despite known transient increases in serum estradiol levels during the first few weeks of vaginal estrogen use. A promising alternative hormonal therapy for vulvovaginal atrophy, ospemifene has been found to have estrogenic effects on vaginal epithelium and bone, but anti-estrogenic and anti-proliferative effects in breasts of postmenopausal women. Recent clinical trials have found that one-year ospemifene therapy yields no increased breast cancer risk in postmenopausal women over a period of 5 years follow-up. Our retrospective chart review yielded 13 healthy postmenopausal women whose ages ranged from 46 to 61. Vaginal estrogen therapies included estradiol vaginal creams, tablets, and rings. On average, vaginal estrogen therapy was used for 4.5 years (SD 4.7). All thirteen women showed no change in mammographic BI-RADS score or change from BI-RADS 2 (Benign Finding) to BI-RADS 1 (Negative) after one or more years on vaginal estrogen. Notably, two additional women, who underwent early menopause due to breast cancer, had no changes in mammographic BI-RADS scores after 4 and 1.5 years, respectively, on vaginal estrogen. One of the breast cancer survivors used ospemifene in combination with vaginal estradiol tablets with good efficacy. **Conclusion:** In the coming months, we plan to complete our retrospective chart review on the effect of vaginal estrogens on mammographic density in healthy postmenopausal women with the hope of studying their effect in breast cancer survivors. Further research is necessary to assess the effect of various therapies for VVA on mammographic density as a marker for breast cancer risk. Ospemifene, in particular, is under-studied and may be an ideal alternative therapy for hormone-responsive breast cancer patients undergoing treatment with aromatase inhibitors.

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