S-1. Breast Adipose Tissue Estrogen Metabolism in Postmenopausal Women with or without Breast Cancer
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Objective: It has been shown that in breast cancer the tumor tissue actively produces and metabolizes steroid hormones. Although adipose tissue is an active endocrine organ, little is known about the possible mechanisms through which the non-estrogenic breast adipose tissue contributes to steroid hormone metabolism in the breast. Thus, we compared the metabolic pathways producing active estradiol in breast subcutaneous adipose tissue of postmenopausal women with or without breast cancer.

Design: We studied the concentrations of estradiol (E2) and inactive estradiol fatty acid esters (E2-FAE) with liquid chromatography-tandem mass spectrometry (LC-MS/MS) in serum and adipose tissue samples from postmenopausal women undergoing mastectomy due to an estrogen receptor-positive breast tumor (N=14) and from women undergoing breast reduction mammoplasty (N=14). Also serum estrone (E1) concentration was determined with LC-MS/MS. mRNA expression of genes encoding aromatase, hormone-sensitive lipase, 17β-hydroxysteroid dehydrogenase (17β-HSD) type 1, 7 and 12, and steroid sulfatase were analyzed with quantitative RT-PCR.

Results: Free E2 and E2-FAE were accumulated in breast adipose tissue compared with serum (P<0.01), both in women with and without breast cancer. Estradiol concentration in non-malignant breast adipose tissue was lower in women with breast cancer than in controls [median(range); 33.3(17.5-81.4) vs. 62.2(16.1-156.5) pmol/kg; P=0.002, ANCOVA, adjusted for age and waist to hip ratio]. For estrone concentrations [19.3(10.0-49.2) vs. 12.2(10.2-39.6) pmol/l; P=0.408] did not differ. Accordingly, the relative expression of mRNA for 17β-HSD type 12, converting E1 to E2, was lower in the adipose tissue of women with cancer compared with controls (0.19±0.10 vs. 0.37±0.21, P=0.018).

Conclusion: Both free E2 and the inactive esterified form levels are higher in the breast adipose tissue than in serum after menopause. However, estrogen metabolism is differently regulated in the adipose tissue of women with or without cancer. In the adipose tissue surrounding a breast tumor 17β-HSD type 12 expression is lower than in controls, which could indicate that the conversion of E1 to E2 is decreased. Further studies are needed to establish the clinical significance of our findings in the development and growth of breast cancer in postmenopausal women.

S-2. Prevalence and Determinants of Lower Urinary Tract Symptoms in Peri- and Postmenopausal Women
Masakazu Terauchi, MD, PhD1, Atsuka Hirose, MD, PhD2, Mikiko Akiyoshi, PhD3, Yoko Owa, MS4, Kiyoko Kato, BS5, Toshiro Kubota, MD, PhD2

1Department of Women’s Health, Tokyo Medical and Dental University, Tokyo, Japan; 2Department of Obstetrics and Gynecology, Tokyo Medical and Dental University, Tokyo, Japan

Objective: This study was undertaken to estimate the prevalence and determinants of lower urinary tract symptoms (LUTS) in peri- and postmenopausal women. Design: The records of 351 women who enrolled in the Systematic Health and Nutrition Education Program at the Menopause Clinic of the Tokyo Medical and Dental University Hospital from November 2007 to December 2012 were subjected to a cross-sectional analysis. The prevalence of frequent urination (“bothered by frequency more than once a week”), nocturia (“wakes up more than once to urinate”), and stress incontinence (“leak urine on the way to the bathroom”), and stress incontinence (“leak urine when I cough, sneeze, or exercise”) was estimated on the basis of their responses to the Menopausal Health, Tokyo Medical and Dental University, Tokyo, Japan

Methods: The prevalence of frequent urination (“bothered by frequency more than once a week”), nocturia (“wakes up more than once to urinate”), and stress incontinence (“leak urine on the way to the bathroom”), and stress incontinence (“leak urine when I cough, sneeze, or exercise”) was estimated on the basis of their responses to the Menopausal Health, Tokyo Medical and Dental University, Tokyo, Japan

S-3. Lower Estradiol and Sex Hormone Binding Globulin Levels are Associated with Higher Volumes of Ectopic Cardiovascular Fat in Women at Midlife: The Study of Women’s Health Across the Nation (SWAN) Ectopic Cardiovascular Fat Ancillary Study
Sam R. El Khoury, PhD, MPH1, Kelly Shields1, Matthew Budoff, MD2, Carrie Hanley1, Emma Barinas-Mitchell1, Inke Janssen3, Susan Everson-Rose2, Karen A. Matthews2

1Epidemiology, University of Pittsburgh, Pittsburgh, PA; 2West Penn Allegheny Health System, Pittsburgh, PA; 3Los Angeles Biomedical Research Institute, Torrance, CA

Objective: Postmenopausal women are at higher risk of cardiovascular disease (CVD) compared with premenopausal women. Growing evidence suggests a role of ectopic cardiovascular fat (ECF), fat surrounding the heart and the vasculature, in the pathogenesis of CVD. Whether volume of ectopic cardiovascular fat depots is related to levels of androgenic hormones in women transitioning through menopause is unknown. We evaluated separately the cross-sectional associations between volumes of epicardial (EAT), pericardial (PAT) and peri-aortic (PVAT) adipose tissues and endogenous sex hormones (estradiol (E2), free androgen index (FAI) and sex hormone binding globulin (SHBG)) in a sample of midlife women. Design: Women who were not on hormone therapy from the SWAN ectopic cardiovascular fat ancillary study at the Pittsburgh and Chicago sites were evaluated. ECF depots were quantified using electron beam computed tomography scans. Both ECF volumes and sex hormones were log transformed to achieve normality and linear regression modeling was used to evaluate associations.

Results: The study included 450 women (37.3% black, 62.7% white; 61.8% pre-/early peri-menopausal and 38.2% late peri-/postmenopausal) aged 46–59 years (mean (SD): 50.7(2.8) years) who had data on any of the 3 ECF depots. In unadjusted models (Table 1), higher levels of E2 were significantly associated with lower EAT and PAT, but not PVAT. Levels of E2 and FAI were significantly associated with lower volumes of all 3 ECF depots, while higher levels of FAI were significantly associated with greater volumes of all 3 ECF depots. In fully adjusted models, higher levels of E2 remained associated with less PAT, higher levels of FAI with higher PVAT, and higher levels of SHBG with lower volumes of all 3 ECF depots. Conclusion: Endogenous sex hormones are associated with volumes of ECF. Certain hormones may be more related to a specific location of ECF than other hormones. Levels of endogenous sex hormones during the menopausal transition may contribute to ectopic cardiovascular fat volumes, which may render women more vulnerable to coronary heart disease at midlife.

Acknowledgments: The Study of Women’s Health Across the Nation (SWAN) has grant support from the National Institutes of Health (NIH), DHHS, through the National Institute on Aging (NIA), the National Institute of Nursing Research (NINR) and the National Institute of Child Health and Human Development (NICHD) Grant RO1 HD050595, AG012531, AG012533, AG012546, AG012553, AG012554, AG012495.

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Table 1. Associations between endogenous sex hormones and ectopic cardiovascular fat volumes

<table>
<thead>
<tr>
<th>Sex Hormone</th>
<th>E2</th>
<th>FAI</th>
<th>SHBG</th>
<th>EAT</th>
<th>PAT</th>
<th>PVAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unadjusted</td>
<td>-0.20</td>
<td>0.29</td>
<td>-0.23</td>
<td>-0.15</td>
<td>0.14</td>
<td>-0.17</td>
</tr>
<tr>
<td>Adjusted</td>
<td>-0.20</td>
<td>0.29</td>
<td>-0.23</td>
<td>-0.15</td>
<td>0.14</td>
<td>-0.17</td>
</tr>
</tbody>
</table>

* Log-transformed

** Separate models. Models were adjusted for study site, race, day of menstrual cycle, age, educational level, difficulty to pay for basics, current smoker, level of physical activity, and obesity (Body mass index ≥ 30 kg/m2)
osteoporotic and 3 had history of a fragility fracture. Sensitivity and Specificity with 95%CI for identifying those women with osteoporosis were 24% (11-40%) and 83% (79-87%) for the USPSTF approach. They were 66% (49-80%) and 62% (58-67%) for the RF based method, 79% (63-90%) and 56% (51-61%) for OST-2. An optimal cut point of BMI=28 was detected from the ROC curve, corresponding to a sensitivity of 95% (82-99%) and specificity of 38% (34-43%), and all three fractures were captured by all screening methods. The BMI threshold for RF based similar to Weight/Gilbert and Weight/Lacona for women with a BMI >18. The BMI threshold was 19.9 kg/m² for men. One of 9, 9, 7 and 7 women to undergo DXA screening, respectively, in order to identify one with osteoporosis. Conclusion: BMI is a very important predictor of osteoporosis in the younger postmenopausal population. Using BMI ≥25 as a cut point corresponds to a much higher sensitivity compared to other screening modalities with no evidence of significantly increasing the cost. Large multicenter prospective studies would be needed to confirm the predictive value of BMI as an osteoporosis screening tool for younger postmenopausal women.

S.6. Pharmacokinetic Studies of Solubilized Estradiol Administered Vaginally in a Softgel Capsule

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Objective: Evaluate the safety and efficacy of a novel vaginal capsule of solubilized bioidentical 17β-estradiol for treating vulvovaginal atrophy (VVA) and compare its bioavailability with that of a vaginal estradiol tablet (Vagifem). Design: Two randomized, single-dose, 2-way crossover pharmacokinetic trials compared the bioavailability of a solubilized vaginal estradiol gel (TX-004HR [Test]) compared to a vaginal estradiol tablet (Vagifem [Reference]) in healthy postmenopausal women (aged 40-65 years; BMI 19.30 kg/m²). In each study, 36 women received a single vaginal dose of the Test capsule or Reference, then a single vaginal dose of the alternate drug after a 14-day washout. One trial examined 10 μg doses, and the other examined 25 μg doses. Blood was sampled pre- and post-insertion at set intervals over 24 hours and analyzed for concentration-time curve (AUC24), peak concentration (Cmax), and time to peak concentration (tmax) for estradiol and estrone. In the randomized pilot study of safety and efficacy (N=50), healthy postmenopausal women (aged 40-75 years; BMI ≤34 kg/m²) with a moderate to severe VVA symptom, superficial cells ≤5%, and a vaginal pH ≥5 received a vaginal gel containing 10 μg of solubilized estradiol (n=24) or placebo (n=24) daily for 14 days. Results: After baseline adjustment, AUC24 values were 63% (10 μg dose) and 69% (25 μg dose) less for estradiol and 50% (10 μg dose) and 70% (25 μg dose) for estrone with Test vs Reference. Cmax values were 29% (10 μg) and 46% (25 μg) less for estradiol and 26% (10 μg) and 55% (25 μg) less for estrone with Test vs Reference (Table 1). Systemic exposure was significantly lower with both doses of the Test drug than with equivalent doses of the Reference drug (Table 2). There were no adverse events (AEs) occurred in either trial. In the pilot study, significantly higher mean percent increases from baseline were observed with Test vs placebo for superficial cells (35% vs 4%, P=0.0002) and intermediate cells (13% vs 4%, P=0.0002) at 2 weeks. The mean percent decrease from baseline in parabasal cells was significantly greater with Test vs placebo (54% vs 5%, P=0.0001), as was the mean decrease in vaginal pH (0.97 vs 0.34, P=0.0002). The Test group also had significantly greater improvements in vaginal epithelial integrity and secretion than the placebo arm. Vaginal symptom improvement was similar between groups, likely due to the study’s small size and short duration. Overall, 1459 (28%) women randomized had 17 treatment-emergent AEs (not all treatment related). For TX-004HR: eye contamination; hypolipidemia; blood pressure increase; vaginal discharge, dysuria, or pruritus; vulvovaginal pain or burning; hot flush and cervical dysplasia. For placebo: pruritis, vaginal hemorrhage, or vulvovaginal discomfort. Most AEs were relatively mild; none were serious. Conclusion: Studies showed 10 μg and 25 μg doses of TX-004HR, a novel estradiol vaginal softgel capsule, were safe and well tolerated. Systemic exposure with both doses was significantly less than with equivalent doses of an approved vaginal estradiol tablet. A 10 μg dose of TX-004HR given daily for 2 weeks significantly improved vaginal cytology and pH compared with placebo, suggesting that TX-004HR may represent another local option for treating menopause-related VVA.

Table 1. Mean Estrogen Values in the Pharmacokinetic Trials

<table>
<thead>
<tr>
<th>PK Parameter</th>
<th>Estradiol</th>
<th>Estrogen</th>
<th>Test vs Reference</th>
<th>Cmax</th>
<th>fmax</th>
<th>AUC0-24</th>
<th>Cmax</th>
<th>fmax</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 μg Dose</td>
<td>Ref</td>
<td>Test</td>
<td>tmax</td>
<td>1.75</td>
<td>24.24</td>
<td>5.15</td>
<td>6.83</td>
<td>9.07</td>
</tr>
<tr>
<td></td>
<td>9.92</td>
<td>0.97</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25 μg Dose</td>
<td>Ref</td>
<td>Test</td>
<td>tmax</td>
<td>1.85</td>
<td>50.22</td>
<td>10.69</td>
<td>11.48</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.06</td>
<td>16.40</td>
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<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Table 2. Test-to-Reference Ratios for Estrogens in the Pharmacokinetic Trials

<table>
<thead>
<tr>
<th>PK Parameter</th>
<th>Test vs Reference</th>
<th>10 μg Dose</th>
<th>Cmax</th>
<th>95% CI</th>
<th>Test vs Reference</th>
<th>25 μg Dose</th>
<th>Cmax</th>
<th>95% CI</th>
</tr>
</thead>
</table>

* Statistically significant by ANOVA (P<0.05). In the 10 μg arm, 34 women were analyzed for estradiol and 33 for estrone.
S-7. Improvement in Female Sexual Function by Ospemifene Treatment Is Not Associated with Changes in Serum Hormones in Postmenopausal Women with Vulvar and Vaginal Atrophy
Raymond Kingsberg1, Shelli Graham2, Ginger D. Constantine, MD3, 4New England Research Institutes, Watertown, MA; 1Case Western Reserve University, Cleveland, OH; 2Siongoi Inc, Florham Park, NJ; 3EndoRheum Consultants, Malvern, PA
Objective: Ospemifene is an oral tissue selective estrogen agonist/antagonist that was approved in 2013 by the US Food and Drug Administration (FDA) for the treatment of dyspareunia, a symptom of vulvar and vaginal atrophy (VVA), in postmenopausal women. In Phase 3 studies, ospemifene improved objective measures and visual exam findings of VVA, and reduced the severity of other bothersome symptoms of menopause. In addition, ospemifene significantly improved female sexual function assessed with the Female Sexual Function Index (FSFI), as previously reported (Kingsberg et al, ISSWSH 2014 abstract). The objective of this report is to evaluate the effects of ospemifene 60 mg/day on serum hormone levels and possible correlation with FSFI scores in postmenopausal women with VVA. Design: In a Phase 3 randomized, double-blind, placebo-controlled trial, subjects in two strata reporting MBS of moderate to severe dyspareunia or vaginal dryness, respectively, at baseline were randomized 1:1 to receive OSP 60 mg/day or PBO for 12 weeks. Main enrollment criteria were postmenopausal women, age 40 to 80, and diagnosis of VVA. Subjects completed the 19-question FSFI questionnaire at baseline and Week 4 and 12. Serum specimens were collected at baseline and Week 12. Serum hormone levels were measured in a central laboratory using standard methods. Correlation between FSFI score and serum hormone levels was analyzed using Pearson’s correlation coefficient. Results: 919 women were randomized in this trial, with 605 in the dyspareunia stratum (ospemifene n=303; placebo n=302) and 314 in the dryness stratum (ospemifene n=160; placebo n=154). As shown previously, women randomized to ospemifene had significantly greater FSFI total score improvement vs placebo at Week 4 (P=0.001) and Week 12 (P<0.001); all 6 domains of FSFI were significantly improved at Week 12. Serum levels of the following hormones were measured: estradiol (E2), total testosterone (total T), free testosterone (free T), follicle-stimulating hormone (FSH), luteinizing hormone (LH), and sex hormone binding globulin (SHBG). In the ospemifene group, both mean FSH and LH levels decreased slightly from Baseline to Week 12 while remaining well within the normal range for postmenopausal women. There were no clinically relevant changes in mean E2 after ospemifene treatment. Mean SHBG level increased, but remained within the normal range at Week 12. Total testosterone levels increased slightly in the ospemifene group; however, mean free testosterone levels remained unchanged. No significant correlations were observed between changes in FSFI scores and either baseline levels or changes in serum sex hormones. Conclusion: Ospemifene significantly improved female sexual function assessed by FSFI scores in a Phase 3 randomized placebo-controlled trial. Changes in serum sex hormones were within the normal range and were considered not clinically relevant. Improvement in FSFI scores did not appear to be correlated with serum hormone levels.

S-8. Soy Isoflavones for Reducing Bone Loss (SIRBL) Study: Effect of a three-year trial on hormones, adverse events, and endometrial thickness in postmenopausal women
D. Hofmann1, Andrew Bushmakin2, Marta D. Van Loan, PhD3, Bonnie S. Beer, MD4, Laura N. Hanson4, Charles T. Peterson5, Mandy S. Kurzer, PhD6, NCCAM, National Institutes of Health, Bethesda, MD; 7Statistics, Iowa State University, Ames, IA; 8USDA, ARS, Western Human Nutrition Research Center, Davis, CA; 9OB/GYN, Yale School of Medicine, New Haven, CT; 10University of California, San Francisco, CA; 11East Bay Physicians Medical Group, Berkeley, CA; 12Pfizer Inc, New York, NY; 13Pfizer Ltd, Tadworth, United Kingdom; 14Pfizer Inc, Groton, CT
Objective: To assess the overall safety and potential endometrial stimulation of soy isoflavone tablets consumed (3-year) by postmenopausal women. To determine the endometrial thickness response-to-treatment among compliant women, taking into account hormone concentrations and other hypothesized modifying factors. Design: We randomized healthy postmenopausal women (45.8-65.0 years) to placebo control or two doses (80 or 120 mg/day) of soy isoflavones at two sites. We used intent-to-treat (N=224) and compliant (<95%; N=208) analyses to assess circulating hormone concentrations, adverse events, and endometrial thickness (via transvaginal ultrasound). Results: Mean endometrial thickness (mm) declined from baseline through 36 mo. Nonparametric ANOVA for treatment differences among groups showed no differences in absolute (or percentage change) endometrial thickness at any time point (Chi-Square p-values ranged from 0.12-0.69), nor in circulating hormones at any time point. A greater number of endometrial thickness values (mm) declined from baseline through 36 mo. The model predicting the endometrial thickness response-(using natural logarithm)-to-treatment with compliant women across time points was significant (p<0.0001), indicating that estrogen exposure (p=0.0013), plasma 17b-estradiol (p=0.0086), and alcohol intake (p=0.023) contributed significantly to response. Neither the 80 (p=0.57) nor 120 (p=0.45) mg/day dose exerted an effect on endometrial thickness across time. Conclusion: Our RCT verified the long-term overall safety of consuming soy isoflavone tablets in postmenopausal women who displayed excellent compliance. We found no evidence of a treatment effect on endometrial thickness, adverse events, or circulating hormone concentrations, most notably thyroid function, during a three year period.

S-9. Relationship Between Knowledge of Hormone Therapy Clinical Trial Results for Management of Menopausal Symptoms and Enthusiasm for Hormone Therapy Prescribing
Raymond Kingsberg1, Shelli Graham2, Ginger D. Constantine, MD3, Corrado J. Altomare4, Lucy Abraham5, Andrew Bushmakin6, Susannah Cort7, OB/GYN, Yale School of Medicine, New Haven, CT; 8University of California, San Francisco, CA; 9East Bay Physicians Medical Group, Berkeley, CA; 10Pfizer Inc, New York, NY; 11Pfizer Ltd, Tadworth, United Kingdom; 12Pfizer Inc, Groton, CT
Objective: To better inform about results of large, published MHT clinical trials (eg, WHI) are more or less likely to prescribe MHT compared with physicians who have less accurate knowledge of the trial results. The objective of the current physician survey was to examine whether prescribers who are more knowledgeable and enthusiastic about prescribing MHT for menopausal symptoms. Design: United States obstetricians/gynecologists (OB/GYNs) and primary care physicians (PCPs) completed an anonymous 15 to 20 minute internet-based survey of MHT clinical trial knowledge and attitudes about menopause and MHT. Knowledge was assessed via 9 statements about MHT trials, with a response scale of true, false, or don’t know (range: 0-9; enthusiasm was assessed via 6 case studies with a 7-point response scale of “extremely likely” to “extremely unlikely” in relation to how they would treat each patient (range: 6 to 42). Higher scores on each scale correspond to greater levels of knowledge and enthusiasm, respectively. The primary analysis examined the correlation between MHT clinical trial knowledge and enthusiasm for initiating/continuing MHT. Secondary analyses gauged knowledge and enthusiasm based on type of practice (OB/GYN or PCP), gender, years in practice, and MHT prescriber status. Results: Among 501 surveyed physicians (median age: 51.0 years; median years in practice: 19.0 years), MHT knowledge (mean [SD] 3.8 [2.3]) and enthusiasm (mean [SD] 24.5 [6.5]) exhibited a statistically significant, moderate positive correlation (0.30, 95% CI 0.21, 0.37, P<0.001), indicating that higher knowledge was associated with greater enthusiasm for prescribing MHT for menopausal symptoms. OB/GYNs (vs PCPs) were significantly more knowledgeable and enthusiastic about prescribing MHT for menopausal symptoms with effect sizes ranging from moderate to large in magnitude (Table). Knowledge and/or enthusiasm also significantly varied according to gender and length of time in practice (Table). Enthusiasm (but not knowledge) was significantly higher among male (vs female) physicians. Knowledge (but not enthusiasm) significantly increased as a function of time in practice. As expected, MHT prescribers were significantly more knowledgeable than nonprescribers (mean [SE]: 3.3 [0.25] vs 2.1 [0.56], P<0.015; effect size: 0.54). Conclusion: Knowledge of the results of large, published clinical trials of MHT was positively associated with enthusiasm for prescribing MHT for managing menopausal symptoms, with OB/GYNs significantly more knowledgeable and enthusiastic than PCPs.

S-10. Linear Mixed-Effects Longitudinal Model*: Endometrial Thickness Response Across Time Points (N=208, compliant model)

<table>
<thead>
<tr>
<th>Outcome Variable</th>
<th>Independent Variable</th>
<th>Parameter Estimate</th>
<th>Standard Error</th>
<th>p-Value**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endometrial Thickness</td>
<td>Hormone</td>
<td>-0.041</td>
<td>0.152</td>
<td>0.317</td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>0.515</td>
<td>0.580</td>
<td>0.369</td>
</tr>
<tr>
<td>Treatment (80mg)</td>
<td>Treatment</td>
<td>0.032</td>
<td>0.096</td>
<td>0.57</td>
</tr>
<tr>
<td></td>
<td>Treatment (120mg)</td>
<td>0.043</td>
<td>0.055</td>
<td>0.43</td>
</tr>
<tr>
<td></td>
<td>Time (min)</td>
<td>-0.008</td>
<td>0.001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>Estrogen Exposure**/cy</td>
<td>0.022</td>
<td>0.007</td>
<td>0.0013</td>
</tr>
<tr>
<td></td>
<td>Plasma 17Beta-Estradiol (pg/mL)</td>
<td>0.006</td>
<td>0.002</td>
<td>0.0006</td>
</tr>
<tr>
<td></td>
<td>Alcohol Intake###/g (g/day)</td>
<td>-0.001</td>
<td>0.004</td>
<td>0.023</td>
</tr>
<tr>
<td></td>
<td>Serum Thyroid-Stimulating Hormone (mU/L)</td>
<td>-0.000</td>
<td>0.001</td>
<td>0.86</td>
</tr>
</tbody>
</table>

**Overall model vs. model with design variables only: likelihood ratio = 12.149; df = 4; P<0.001. Likelihood ratio based on maximum likelihood estimation; estimates and significances based on restricted maximum likelihood estimation
^Natural logarithm of endometrial thickness as variance stabilizing transformation
###P values based on asymptotic normality of t-distribution; variables left in model were significant at p<0.10 level (acceptable Type I error rate in modeling endometrial thickness). Additional variables (i.e., body weight, lactation duration, etc.) did not remain in model. Interaction between treatment and time (log likelihood ratio=3.996; df=2) was not significant (p=0.14).
##Calculated at baseline, estrogen exposure in years = age at menarche - age at menopause; estrogen exposure was not related to plasma 17-beta estradiol (Pearson correlation coefficient = -0.05)
###Represents usual weekly alcohol intake at baseline, which was assessed at baseline from a dietary questionnaire.
Nese Yuksel, BScPharm, PharmD, Laetitia Brochu, Bushra Malik, Arienne Bayot. Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta, Edmonton, AB, Canada.
Objective: To assess the quality of information presented and the claims made on websites offering bioidentical hormone therapy (BHT) products or services. Additionally, we wanted to describe marketing strategies employed by these websites. Design: Websites offering BHT products or services were identified through Google (Google Inc Canada) September 16, 2013. Search terms included “bioidentical hormone therapy”,”services or doctors” and “purchase or buy”. Websites were excluded if they were video or discussion forums, only provided information on where to buy BHT, were duplicates, required membership and were not in English. A quantitative content analysis was performed on a convenience sample of 100 websites meeting study criteria. Criteria for content analysis were predetermined by study investigators. The DISCERN instrument was used to determine the quality and reliability of the health information. Websites were analyzed separately by two coders; discrepancies were resolved by a third coder. Results: Websites were from Canada (60%), United States (38%), and other (2%). Majority of websites were from health care providers either recommending BHT or offering to prescribe BHT (89%). Websites originated from medical clinics (49%), naturopathic/health care providers either recommending BHT or offering to prescribe BHT (89%) and nurse practitioners (19%). Most common words to promote BHT were natural (70%), treat hormone imbalance (56%), anti-ageing (50%), promote sexual health (25%), and pain (18%). Websites overall claimed that BHT was safer than conventional HT in general (46%) and had less side effects (56%). Websites that made a specific safety claim, claimed that BHT had less risk of breast cancer (28%) and associated cardiovascular risk (28%) in comparison to conventional HT. Saliva testing to measure hormone levels was mentioned in 42% of websites. Fifty-percent also promoted other services such as weight loss programs (43%), botox (21%), laser (18%), skin care/wrinkles (15%) and spa (8%). Most common words to promote BHT were natural (70%), treat hormone imbalance (56%), anti-ageing (50%), promote sexual health (25%) and for wellbeing (18%). Although all of the websites were directed for women, 62% also targeted men. Most profiles showed primarily white females (70%) or couples (33%). Upper 4% of websites had a disclaimer from a regulatory body such as FDA or Health Canada. Based on the DISCERN instrument the quality and reliability of the information on the website was poor, with 20% providing a clear sources of information or when information was presented (20%) and only 2% were balanced/unbiased. Conclusion: The way BHT is promoted and the claims that are made on internet websites are not consistent with current evidence based recommendations from professional organizations. Understanding the mixed messaging regarding BHT that patients may be exposed to on the internet, can help health care professionals when educating their patients.

S.11. Preventing Dyspareunia with Self-applied Topical Anesthetic Improves All Aspects of Sexual Function in Menopausal Survivors of Breast Cancer: a Randomized Controlled Trial
Martha F. Goetsch, MD, MPH1, Jillian Romm1, Jeong Y. Lim2, Aaron B. Caughey1. Obstetrics & Gynecology, Oregon Health & Science University, Portland, OR; Public Health & Preventive Medicine, Oregon Health & Science University, Portland, OR; Obstetrics & Gynecology, UC San Diego Health, University of California, San Diego, CA.
Objective: Dyspareunia associated with vulvovaginal atrophy is especially difficult for women with a history of breast cancer because they are warned not to use estrogen, the most effective therapy. This population is known to have a high rate of sexual dysfunction due to their menopausal status. Data from validated sexual function questionnaires have not been published about this population. The objective of this study was to evaluate domains of sexual function at baseline and after the intervention of self-applied topical anesthetic to the introitus to determine if domains beyond the pain domain changed with effective pain relief. Design: In a randomized controlled trial, breast cancer survivors in long-term relationships who had moderate or severe entry pain or pelvic floor myalgia were randomized to apply either liquid lidocaine 4% or saline to the vulvar vestibule for three minutes immediately prior to coitus. Each was provided with study liquid and silicone lubricant for penetrative activities, and each agreed to use vaginal penetration weekly for either a tandem or monogamous relationship, and to keep a pain diary. Each subject completed the Sexual Function Questionnaire (SFQ) at baseline, after one month of blinded pre-coital and after two further months of open-label lidocaine use. The SFQ measures domains of desire, subjective arousal, lubrication, orgasm, cognitive and emotional function, pain, enjoyment and partner concern. Comparisons were made with the Wilcoxon-rank sum test with significance set at p<0.05.
Results: Forty-six survivors with entry dyspareunia, severe vulvovaginal atrophy and vestibular tenderness had median intercourse pain scores of 8 (interquartile range 7-9) (range 1-25) at baseline. At baseline median SFQ scores improved in all domains. As treatment time increased and scores improved, there was not a statistical difference at study conclusion between the median scores of those using lidocaine for 2 months versus 3 months, except for marginally better cognitive arousal with longer lidocaine use (p=0.049). Serial SFQ scores suggested that increasing proportions of subjects had normal sexual function. By study conclusion the proportion with normative scores had increased to 44% for desire, 7% for subjective arousal, 21% for cognitive arousal, 20% for orgasm, 0% for pain, 4% for enjoyment and 65% for partner concerns. Conclusion: Breast cancer survivors with moderate and severe dyspareunia had severely abnormal sexual function in all domains measured by the SFQ. Subjects could readily learn to self-apply topical anesthetic to the vulvar vestibule immediately prior to coitus, achieving significant reductions in pain. In the course of a few weeks, SFQ scores in all domains improved when pain was prevented. Scores continued to improve with longer use of intravaginal lidocaine and data regarding final levels of sexual function achievable with lidocaine will require longer follow-up. Preventing intimacy pain and providing adequate lubrication resulted in improvement in all domains of sexual function since continued severe vulvovaginal atrophy and low estrogen status.
S-13. USPSTF Osteoporosis Screening Strategy: Confirming its predictive ability may prove challenging?
Xuezhi Jiang, MD1,2, Lauren Good1, Peter F. Schnatz, D.O. 1,2. 1Department of ObGyn, The Reading Hospital, West Reading, PA; 2Department of ObGyn, Jefferson Medical College of Thomas Jefferson University, Philladelphia, PA

Objective: The U.S. Preventive Services Task Force (USPSTF) recommends osteoporosis screening for those younger postmenopausal women (age < 65) whose 10-year major osteoporotic fracture risk by FRAX without BMD is greater than 9.3%. This study was designed to examine how well the USPSTF strategy identifies osteoporosis screening candidates among women aged 50-64 years.

Design: Postmenopausal women aged 50-64 years presenting for a screening Dual-energy X-ray absorptiometry (DXA) screening test were recruited between January 1, 2007, and March 1, 2009. The phone survey was conducted after their recruitment and consent. Survey questions included age, weight, height, race, history of a fragility fracture (including the spine or hip) that occurred after age 50 years, a parental hip fracture, ever or current long-term use of steroids, current smoking, and a medical history of rheumatoid arthritis. Using DXA results as the gold standard, the predictive accuracy (sensitivity, specificity, positive predictive value [PPV], and negative predictive value [NPV], area under the receiver operating characteristic curve [AUC]) for the USPSTF strategy to identify younger postmenopausal women with osteoporosis was determined.

Results: Of 445 postmenopausal women aged 50-64 years, 38 were identified as osteoporotic by DXA (T-score ≤-2.5). Only 9 out of 38 (24%) were correctly identified for BMD testing by the USPSTF strategy. Sensitivity, Specificity, PPV, NPV, and AUC with 95% CI for identifying those younger postmenopausal women with osteoporosis were 24% (94-160%), 83% (79-87%), 12% (5-21%), 92% (89-95%), and 0.62 (0.52-0.72), respectively.

Conclusion: The USPSTF strategy only identified about 25% of women aged 50-64 years with osteoporosis. The predictive accuracy of this strategy was only modestly better than chance alone (AUC=0.5).

S-14. Effect of Estrogen and Menopausal Status on the Histology and Gene Expression in the Labia Majora and Vaginal Introtus
Murray A. Freedman, MS, MD1, Raphael Warren, Ph.D.2, Kailash B. Sharma, MD1, Miranda A. Farage1, Robert L. Binder1, Jay P. Tiesman1, Yu Wang1,2, David B. Moore1, Chelsea Combs1, Robert J. Isfort1, Charles C. Bascom1. 1Obstetrics & Gynecology, Georgia Regents University, Augusta, GA; 2Feminine Care, The Procter and Gamble Company, Cincinnati, OH; 3Global Biotechnology, The Procter and Gamble Company, Cincinnati, OH

Objective: Hormone replacement therapy (HRT) has been approved for prevention of vasomotor symptoms, osteoporosis and vulvovaginal atrophy. Previous studies have documented the efficacy of estrogen therapy in preserving the structural integrity of the vagina but there is little documentation of its effect on the introitus and labia. This study was designed to evaluate the histological and transcript biological profiles of the introitus and labia majora in three cohorts of women: hypoestrogenic postmenopausal women, postmenopausal women treated with HRT, and pre-menopausal women.

Design: Selection criteria for each cohort were based on clinical examination of vaginal morphology and vaginal pH. Vaginal atrophy was determined using a 3 point scale (mild, moderate or severe) for each of the following criteria (a) hymenal rugation, (b) elasticity at the introitus, (c) patulousness of urethra, (d) “telescoping” of the vestibule, and (e) color (presence of petechiae and or erythema). Vaginal pH was measured using pH paper.

Criteria for the “Atrophic” postmenopausal women included a clinical score of ≥6 and a vaginal pH ≥ 5.5. Post-menopausal women on HRT (oral or nonoral) had clinical scores of < 6 and a vaginal pH < 5.0. All premenopausal women recruited had a clinical score of ≤ 5 and a vaginal pH < 5.0. In addition to serum hormone status (including estrogen, testosterone, and SHBG) paired biopsies were obtained at 1) the level of the hymen at the fourchette and 2) at the mid-point of the labia majora. One biopsy was directed to histology and the paired biopsy was prepared for transcriptomic analysis on Affymetrix HG-U1219 GeneChips. In addition, symptoms of vulvovaginal atrophy (i.e., dryness, pruritus, dyspareunia) were recorded on a 5 point scale ranging from none to unbearable.

Results: The introitus revealed significant histological changes associated with estrogen status compared to the labia majora. Both pre-menopausal and post-menopausal estrogenized women showed an abundance of glycogen enriched superficial epithelial cells and rete pegs at the dermal-epidermal junction while features were essentially absent in the hypoestrogenic post-menopausal cohort. Scores for clinical atrophy correlated closely with vaginal pH (r2=0.77) but less closely with vaginal dryness (r2=0.46) and dyspareunia (r2=0.29).

Post-menopausal women with vaginal atrophy showed profound changes in gene expression at the introitus compared to pre-menopausal women and post-menopausal women on HRT. The GeneChip used contains 49,293 probe sets, corresponding to ~22,000 genes, and ~2465 probe sets are expected to be significant by chance alone at p<0.05. As can be seen in Table 1 there were many more changes than expected by chance at the introitus. There were fewer changes in the labia majora of women with atrophy compared to pre-menopausal controls and the HRT groups, but more than expected by chance. Hierarchical clustering revealed that the gene expression changes occurring in the atrophied introitus were nearly completely reversed in women on HRT.

Gene ontology enrichment analysis revealed that the gene expression changes in the post-menopausal introitus were associated with processes likely to be important in atrophy including aging, tissue remodeling, collagen fibril organization, cell cycle, cell death and vasculature development. Overall, the transcriptomic results were consistent with the histologic changes in each cohort. Conclusion: The introitus in hypoestrogenic post-menopausal women demonstrates similar anatomic and histologic atrophy as seen in the vagina. These changes are associated with profound changes in gene expression and correlate well with vaginal pH.

Table 1. Number of Probe Sets Significant at p<0.05

<table>
<thead>
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<th>Site</th>
<th>Comparison</th>
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<tr>
<td>Perimenopausal vs. Menopause + HRT</td>
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<td>Introtus</td>
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<td>Yes</td>
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<tr>
<td>Menopause vs. Menopause + HRT</td>
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<tr>
<td>Menopause vs. Menopause + HRT</td>
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S-15. Most Otherlyome in Women with Vulvar-Vaginal Atrophy as a Moderator of Treatment Effects
JoAnn V. Pinkerton4, Andrew Bushmakin4, Lucy Abraham1, Joseph Cappelleri3, Barry Kommin1, 4PRO Center of Excellence, Pfizer Ltd, Tadworth, United Kingdom; 2University of Virginia Health System, Charlottesville, VA; 3Pfizer Inc., Groton, CT; 4Pfizer Inc., Collegeville, PA

Objective: This post-hoc analysis evaluates treatment effects for conjugated estrogens/ bazedoxifene (CE/BZA) by most bothersome symptom (MBS) of vulvar/vaginal atrophy (VVA). Design: The dataset was from a 12-week randomized, double-blind, placebo-controlled phase 3 clinical trial to evaluate the effect of CE/BZA on VVA. Subjects were postmenopausal women with a uterus (N=664, Mean Age=56.3) experiencing moderate-severe symptoms of VVA. At baseline, women indicated which VVA symptom (dryness, itching/irritation or pain with intercourse) bothered them most. Linear models were used to explore treatment effects of CE 0.45 mg/BZA 20 mg and CE 0.625 mg/BZA 20 mg compared to PBO while accounting for baseline MBS. Assessments included the Menopause-Specific Quality of Life (MENQOL) questionnaire, the Arizona Sexual Experiences Scale (ASEX), the Menopause Symptoms Treatment Satisfaction Questionnaire (MSTSQ) and the International Continence Society (ICS) sexual function and for vaginal pH. Results: At baseline, 52% of women selected pain with intercourse as their MBS, 35% selected dryness and 13% selected itching/irritation. Results showing standardized effect sizes (ES) and statistical significance are presented in Fig 1. All 3 groups saw statistically significant improvements in MENQOL sexual functioning, and overall MSTSQ, at one or both doses, with sizable ES. Improvements in lubrication compared to PBO were statistically significant for both lower and higher doses for those with painful intercourse as their MBS, and the lower dose for dryness. At both doses those with dryness as MBS had statistically significant changes in their parabasal cells while those with pain with intercourse as MBS had statistically significant and very large ES in superficial cells. Conclusion: Women with VVA most frequently selected pain with intercourse as MBS. For these women, treatment with both doses of CE/BZA provided significant improvements in lubrication and sexual functioning. Regardless of MBS, women taking the FDA-approved dose of CE 0.45 mg/BZA 20 mg saw improvements in sexual functioning, MENQOL, and clinical parameters. While significant improvements across outcomes were seen more frequently with the higher dose, both doses were effective.
ABSTRACT PRESENTATIONS

S-16. The Day-to-day Impact of Vaginal Aging (DIVA) Questionnaire: A New Multidimensional Self-Report Measure of the Impact of Vaginal Symptoms in Postmenopausal Women of Diverse Backgrounds

Alison Huang, MD, MAS1, Steven Gregorič2, Miriam Kuppermann3, Sanae Nakagawa4, Stephen Van Den Eeden5, Jeanette Brown1, Louise Waller1, Anita Stewart1,6, 1University of California San Francisco, San Francisco, CA; 2Kaiser Permanente Division of Research, Oakland, CA

Objective: To develop and validate a new self-report measure of the impact of vaginal symptoms on functioning and well-being in postmenopausal women, and to explore differences in the self-reported impact of postmenopausal vaginal symptoms by age and race/ethnicity. Design: Structured self-report items were developed to address the impact of vaginal symptoms such as dryness, soreness, itching, and pain with sexual intercourse on functioning and well-being, based on findings from focus groups with racially/ethnically diverse, symptomatic postmenopausal women. Items were refined after cognitive interview pre-testing and then field-tested among symptomatic postmenopausal women enrolled in a multiethnic cohort study in California. Model fit was examined during confirmatory factor analysis by assessment of the comparative fit index (CFI). Additional evidence of construct validity was obtained via examination of correlations with other measures of related constructs. Internal consistency was assessed using Cronbach’s alpha. Age- and race/ethnicity-related trends in impact scores were examined using multivariable models controlling for partner status and general health. Results: Of the 796 symptomatic postmenopausal women completing the draft questionnaire, mean (SD) age was 56.2 (8.5) years (total range of 41 to 81 years), and 60% were racial/ethnic minorities (including 21% Black, 25% Latina, and 20% Asian women). The refined 19-item questionnaire included four multi-item scales addressing symptom impact on: 1) activities of daily living, 2) emotional well-being, 3) sexual functioning, and 4) self-concept and body image. The four factor model provided good approximate fit (CFI = 0.987, SRMSR = 0.038). Correlations with other measures of symptom bothersomeness, sexual function, depression, and anxiety conformed to hypotheses. Cronbach’s alpha ranged from 0.82 to 0.93. Younger age was associated with higher impact scores on the DIVA sexual functioning and emotional well-being domain scales, after adjustment for race/ethnicity, partner status, and general health (p<0.05). White race was associated with higher impact scores on the DIVA sexual functioning and self/body image scales, after adjustment for age, partner status, and general health (p<0.05). Conclusions: The Day-to-Day Impact of Vaginal Aging questionnaire is a new self-report measure of the impact of vaginal symptoms on activities of daily living, emotional well-being, sexual functioning, and self-concept and body image in postmenopausal women, with good construct validity and internal consistency reliability in women across a range of ages and racial/ethnic backgrounds. Younger age and white race may be associated with greater impact of vaginal symptoms across multiple domains important to postmenopausal women.

S-17. Ospemifene Improved The Severity of Vulvar and Vaginal Atrophy Symptoms In Postmenopausal Women In Phase 3 Randomized, Placebo-Controlled Trials

Ginger D. Constantine, MD1, Risa Kagan, MD2, Sarah Berga2, Shelli Graham3, Ginger D. Constantine, MD. 1University of California San Francisco, East Bay Physicians Medical Group and Sutter East Bay Medical Foundation, Berkeley, CA; 2Columbia Center for Women’s Health Research, Columbia, OH; 3Eastern Virginia Medical School, Norfolk, VA; 4Kaiser Permanente Division of Research, Oakland, CA; 5Eastern Virginia Medical School, Norfolk, VA

Objective: To evaluate subjective endpoints of VVA using a patient-reported MBS as well as all moderate to severe symptoms of VVA. Design: Two Phase 3 randomized, double-blind, placebo-controlled trials evaluated the efficacy and safety of ospemifene and were included in this analysis. In Study A, participants were randomized 1:1:1 to receive ospemifene 30 mg/day, 60 mg/day or placebo (PBO) for 12 weeks. In the second trial (Study B), subjects in two strata reporting MBS of moderate to severe dyspareunia or vaginal dryness at baseline, respectively, were randomized 1:1 to receive ospemifene 60 mg/day or PBO for 12 weeks. Main enrollment criteria were similar in both studies: postmenopausal women, age 40 to 80, and diagnosis of VVA. VVA symptoms assessed in the trials included vaginal dryness, dyspareunia, vulvar and/or vaginal irritation/itching, difficult and/or painful urination, and vaginal bleeding associated with sexual activity. Symptoms were self-reported at Week 4 and Week 12, and those reported as moderate to severe at baseline were included in this analysis. Change in the severity of VVA symptoms from Baseline to Week 4 or 12 was analyzed using Cochrant-Mantel-Haenszel (CMH) row mean scores test. Results: Study A randomized 276 women to OSP 60 mg/day and 268 women PBO. OSP 60 mg/day demonstrated statistically significant superiority over PBO for all four co-primary endpoints, including Change from Baseline to Week 12 in severity of MBS of vaginal dryness (mean change -1.19 vs -0.89; p= 0.023) or MBS of vaginal dryness (mean change -1.26 vs -0.84; p=0.021). Change from Baseline to Week 4 in severity of MBS of dyspareunia or MBS of vaginal dryness was numerically but not statistically improved in OSP 60 mg group vs PBO. For VVA symptoms regardless of being reported as MBS, OSP 60 mg showed statistically significant superiority over PBO in improving vaginal dryness at Week 4 (p<0.05) and Week 12 (p<0.001), and dyspareunia at Week 12 (p=0.05). Difficult/painful urination was numerically improved in OSP 60 mg group vs PBO at Week 12 (p=0.052). Study B randomized 919 women, with n=605 in the dyspareunia stratum (OSP n=303; PBO n=302) and n=314 in the dryness stratum (OSP n=157; PBO n=157). In the dyspareunia stratum, change in the severity of dyspareunia at Week 12 was significantly different between OSP and PBO groups at Week 12 (p=0.001), and numerically different at Week 4 (p=0.0698). In the vaginal dryness stratum, change in the MBS of vaginal dryness did not reach statistical significance at Week 4 (p=0.1886) and Week 12 (p=0.0803). For VVA symptoms that were moderate or severe at baseline regardless of being reported as MBS, OSP was significantly better than PBO in reducing the severity of dyspareunia at both Weeks 4 and 12 (p<0.001). The severity of dyspareunia and vaginal and/or vaginal irritation/itching were significantly decreased in the OSP 60 mg group vs PBO at Week 4 (p=0.0421), and at Week 12 (p=0.0264), respectively. In both studies baseline severity differences were observed. Conclusions: Ospemifene, an oral tissue-selective estrogen agonist/antagonist, was approved by the US Food and Drug Administration (FDA) in 2013 for the treatment of dyspareunia, a symptom of VVA, in postmenopausal women. Parameters to assess the efficacy of VVA treatments include both objective measures (e.g., percentage of superficial and parabasal cells, vaginal pH) and subjective measures (e.g., self-reported VVA symptoms). A responder analysis that combines both objective and subjective measures may be useful in characterizing the efficacy profile of VVA treatment. The objective of this presentation is to report the results of exploratory responder analyses from two phase 3 ospemifene clinical trials. Design: Two Phase 3 randomized, double-blind, placebo-controlled trials evaluated the efficacy and safety of ospemifene and were included in this analysis. In Study A, participants were randomized 1:1:1 to receive ospemifene 30 mg/day, 60 mg/day or placebo for 12 weeks. In Study B, participants in two strata reporting most bothersome symptom (MBS) of moderate to severe dyspareunia or dryness at baseline, respectively, were randomized 1:1 to receive ospemifene 60 mg/day or placebo for 12 weeks. Main enrollment criteria were similar in both studies: postmenopausal women aged 40 to 80 years with a diagnosis of VVA as assessed by vaginal pH, maturation index in the vaginal smear, and reporting VVA symptoms at baseline. A responder was defined a priori as a woman who had all of the following: a) a 10-unit increase in the percentage of parabasal cells; b) an increase in the percentage of parabasal cells; c) a decrease in the severity of VVA MBS by at least 1 point from baseline. Participants of responders at Week 12 or last observation carried forward (LOCF) were compared between groups using Cochran-Mantel-Haenszel (CMH) general association test controlling for study center and uterine status (Study A), or CMH row mean score test controlling for stratum (Study B) for VVA symptoms. In Study A, the percentage of responders at Week 12/LOCF was 20.6% (58/282) in the ospemifene 30 mg group, 33.7% (93/276) in the ospemifene 60 mg group, 38.7% (103/278) in the ospemifene 60 mg group, 38.7% (103/278) in the ospemifene 30 mg group, and 33.7% (93/276) in the ospemifene 60 mg group, respectively.
compared to 3.4% (9/268) in the placebo group. Both osnepime groups had higher significant responder rates than the placebo group (p=0.001); osnepime 60 mg group was also significantly better than 30 mg group (p=0.001). An exploratory analysis was done to assess the percentage of participants who met individual criteria in the natural trend of a responder. For MV, 20.9%, 48.9% and 54.0% of participants were MV responders in the placebo, osnepime 30 mg and 60 mg groups, respectively (p=0.001 vs placebo). In study B, for the ITT population, the percentage of responders at Week 12/LOCF was 39.7% (184/463) in the osnepime 60 mg group, significantly higher than that in the placebo group (5.5% [22/400]; p<0.0001). The percentages of MV responders were 75.7% in the osnepime 60 mg group vs 23.0% in the placebo group (p=0.0001); the percentage of MV responders were 70.4% and 34.9% in the osnepime and placebo groups, respectively (p=0.001).

Conclusion: In two Phase 3 randomized placebo-controlled trials, osnepime demonstrated significantly higher responder rates than placebo in postmenopausal women with VVA, and 60 mg osnepime was significantly better than 30 mg. Most of osnepime’s effect on responder rates may be attributed to improvement in vaginal physiology (MV and pH).

FRIDAY CONCURRENT SESSION #2

S-19. The Association between Vasomotor Symptoms and Hemostatic Factors in Postmenopausal Women

Laura B. Hinson, MPH1, Jacques E. Rossouw, MD2, Mary Cushman, MD, MSc3, Marc Blond6, Andrew Kaukinis, MD1, Barbara McKnight4, Susan R. Heckbert, MD, PhD1, Nancy F. Woods, PhD, RN, FAAN1, Andrea LaCroix2, Matthew A. Allison, MD, MPH1, Lisa W. Martin, MD1, Karen C. Johnson, MD3, Nicholas L. Smith, PhD2, Elizabeth Eng, MD, MPH, University of Michigan, Ann Arbor, MI; 1Department of Medicine, University of Vermont, Burlington, VT; 2Department of Biostatistics, Boston University, Boston, MA; 3Obstetrics, Gynecology and Reproductive Health, University of Washington, Seattle, WA; 4Department of Urology, University of North Carolina at Chapel Hill, Chapel Hill, NC; 5Medicine, University of Virginia, Charlottesville, VA; 6Noven Pharmaceuticals, Inc., New York, NY

Objective: Brisdelle (osnepime) 7.5 mg capsules is a non-hormonal agent approved in the US for the treatment of moderate to severe vasomotor symptoms (VMS) associated with menopause. The efficacy of osnepime 7.5 mg was evaluated in two multicenter, double-blind, randomized, placebo-controlled phase 3 trials of 12 and 24 weeks’ duration. Statistically significant reductions in VMS were achieved as early as Week 1 and 2, respectively. Herein we evaluate the onset and durability of response with paroxetine 7.5 mg. Design: Postmenopausal women aged 40-60 years with moderate to severe VMS (>/=7-8 hot flashes [HF]/d; >/=50-60/week) entered a 12-day single-blind placebo-run-in period and received VMS in daily electronic diaries. Compliance participants were randomized 1:1 to receive once-daily paroxetine 7.5 mg or placebo at bedtime. Co-primary endpoints were mean change from baseline (BL) to Weeks 4 and 12 in frequency and severity of moderate to severe VMS. Duringable response, a post hoc exploratory analysis, was defined as patients achieving a50% reduction in frequency of moderate to severe HF’s that continued for a3 or a4 consecutive weeks. Results: Data from 606 women were included in efficacy calculations in the 12-week study (osnepime 7.5 mg, n = 301; placebo, n = 305) and from 568 women in the 24-week study (osnepime 7.5 mg, n = 284; placebo, n = 284). Kaplan-Meier estimates of time to durable response indicate that a greater proportion of women treated with paroxetine 7.5 mg achieved a50% reduction in VMS for a3 weeks compared with placebo (Table). More women in the paroxetine 7.5 mg treatment groups also achieved a50% reduction in VMS for a4 weeks. Median time to durable response using the 3-week definition was ~8 weeks for paroxetine-treated women but was not reached by the placebo groups. Median time to durable response using the 8-week definition was not reached in any group. For most women, responses persisted to the end of the study (12 or 24). Conclusion: A substantial proportion of women were considered responders (using the 3-week definition) ~8 weeks after initiating treatment with paroxetine 7.5 mg, and this response persisted for up to 24 weeks.

S-20. Paroxetine 7.5 mg Provided a Rapid and Durable Reduction in Vasomotor Symptoms Associated With Menopause Following Treatment Initiation

Dawn Burton1, JoAnn V. Pinkerton2, Salasag Blaskar, RJFs3,6, Joel Lippman, MD, MPH4, 5Columbia Center for Women’s Health Research, Columbia, OH; 6University of Virginia, Division of Midlife Health, Charlottesville, VA; 7Noven Pharmaceuticals, Inc., New York, NY

Objective: Brisdelle (osnepime) 7.5 mg capsules is a non-hormonal agent approved in the US for the treatment of moderate to severe vasomotor symptoms (VMS) associated with menopause. The efficacy of osnepime 7.5 mg was evaluated in two multicenter, double-blind, randomized, placebo-controlled phase 3 trials of 12 and 24 weeks’ duration. Statistically significant reductions in VMS were achieved as early as Week 1 and 2, respectively. Herein we evaluate the onset and durability of response with paroxetine 7.5 mg. Design: Postmenopausal women aged 40-60 years with moderate to severe VMS (>/=7-8 hot flashes [HF]/d; >/=50-60/week) entered a 12-day single-blind placebo-run-in period and received VMS in daily electronic diaries. Compliance participants were randomized 1:1 to receive once-daily paroxetine 7.5 mg or placebo at bedtime. Co-primary endpoints were mean change from baseline (BL) to Weeks 4 and 12 in frequency and severity of moderate to severe VMS. Duringable response, a post hoc exploratory analysis, was defined as patients achieving a50% reduction in frequency of moderate to severe HF’s that continued for a3 or a4 consecutive weeks. Results: Data from 606 women were included in efficacy calculations in the 12-week study (osnepime 7.5 mg, n = 301; placebo, n = 305) and from 568 women in the 24-week study (osnepime 7.5 mg, n = 284; placebo, n = 284). Kaplan-Meier estimates of time to durable response indicate that a greater proportion of women treated with paroxetine 7.5 mg achieved a50% reduction in VMS for a3 weeks compared with placebo (Table). More women in the paroxetine 7.5 mg treatment groups also achieved a50% reduction in VMS for a4 weeks. Median time to durable response using the 3-week definition was ~8 weeks for paroxetine-treated women but was not reached by the placebo groups. Median time to durable response using the 8-week definition was not reached in any group. For most women, responses persisted to the end of the study (12 or 24). Conclusion: A substantial proportion of women were considered responders (using the 3-week definition) ~8 weeks after initiating treatment with paroxetine 7.5 mg, and this response persisted for up to 24 weeks.

S-21. Symptom Clusters Among MS-FLASH Clinical Trial Participants

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Objective: Women experience multiple co-occurring symptoms (symptom clusters) during the menopausal transition and early postmenopause. Although symptom clusters have been identified among community-dwelling populations, to date there have been no studies of participants in clinical trials necessitating inclusion for hot flashes. Our objective was to identify symptom clusters using standardized measures completed by MS-FLASH clinical trial participants at baseline including: hot flashes, sleep disruption, mood, and pain symptoms. Designed for women randomized to interventions and controls from MS-FLASH studies 1-3 (N=800) included. Scores from standardized measures obtained at baseline included: Hot Flash Daily Interference Scale (HFDS), scores, Insomnia Severity Index (ISI) scores, Patient Health Questionnaire (PHQ 9) measure of depressed mood, Generalized Anxiety Disorder (GAD), Pittsburgh Sleep Quality Inventory (PSQI), and Brief Pain Inventory (BPI) scale scores. Latent class analysis was used to identify clusters of symptoms using standardized scale scores and cut points. Results: Using the BIC criterion, three clusters provided the optimal number of clusters. Cluster 1 (n=259) included women with no or moderate pain, little anxiety, no depression, poor sleep quality, sub-threshold or moderate insomnia, and a range of hot flash daily interference. Cluster 2 (n=147) included women with no or moderate pain, mild or sometimes moderate anxiety, mild or moderate depression, poor sleep quality, sub-threshold or moderate insomnia, and higher scores on hot flash interference. Cluster 3 (n=400) included women with no or some moderate pain, little anxiety, no depression, good or fair sleep quality, no insomnia, and low hot flash interference. Conclusion:
Women meeting hot flash frequency criteria for inclusion in clinical trials exhibit multiple co-occurring symptoms that cluster into identifiable groups. Consideration of effects of therapeutic agents on multiple co-occurring symptoms will be important to enhance treatment outcomes and minimize adverse effects on other symptoms.

**S-22.** Relationship between changes in vasomotor symptoms and changes in menopause-specific quality of life and sleep parameters

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**Objective:** Vasomotor Symptoms (VMS) can significantly impact sleep and menopause-specific quality of life (MSQOL). Quantifying the relationship between VMS and patient-centered outcomes can help inform treatment decision-making and guide assessment of outcomes. This study evaluates the relationship of VMS with MSQOL and sleep. **Design:** The dataset was from a 12-week randomized, double-blind, placebo (PBO)-controlled phase 3 clinical trial to evaluate the effect of conjugated estrogens/medroxyprogesterone acetate (CE/BAZ) on VMS. Subjects were postmenopausal women with a uterus (N=318, Mean Age=53.39) experiencing ≥7 moderate-severe hot flashes per day (or ≥50 per week). Regression models were used to determine relationships between frequency and severity of VMS with MSQOL (as assessed by the Menopause-Specific Quality of Life [MENQOL]) questionnaire and sleep parameters (as assessed by the Medical Outcomes Study Sleep Scale [MOS-SS]). Sensitivity analyses were performed to check assumptions of linearity between VMS and outcomes. **Results:** Frequency and severity of VMS showed clear, approximately linear relationships with MSQOL and sleep parameters (see Fig 1), which were statistically significant (P<0.001). Sensitivity analyses supported the assumptions of linearity. Mean differences corresponding to a reduction of 5 hot flashes and a half category decrease in severity found the largest associated changes on the MENQOL were for the VMS functioning domain (0.78 for number of VMS and 0.98 for severity). For the MOS-SS scale, the largest changes were for sleep disturbance (7.38 and 4.66), sleep adequacy (5.60 and 4.66), and the overall sleep problems indices (SFPI: 5.17 and 3.63, SPFII: 5.82 and 3.83). **Conclusion:** VMS have a linear relationship with MSQOL and sleep parameters, such that improvements in bothersome VMS are associated with improvements in MSQOL and sleep. Such relationships allow us to determine changes in sleep and MSQOL that may be expected from VMS treatments.

There is limited evidence about the effect of HF on the sympathetic branch of the ANS. Here we investigate differences in ANS function (sympathetic, parasympathetic) between women who experience either frequent or infrequent subjective and objective VMS. **Design:** Participants included 40 midlife women (M=52.1 years of age) from a parent study investigating the effects of menopausal symptoms on cognition. Two groups of women were recruited: women who reported frequent VMS (>30 per week) and infrequent VMS (<7 per week). VMS were assessed with objective monitors and subjective reporting. Participants wore an ambulatory sternal skin conductance monitor (Biolog Model 3991x/2-HFI) for 72 hours. Parasympathetic activity was assessed with heart rate variability (HRV), which was validated through verifying expected changes with posture (laying, sitting, and standing). Sympathetic activity was measured using salivary alpha-amylase (sAA), which was validated by verification of the expected decrease after awakening. Mixed-effects regressions were used to compare group differences. **Results:** HRV changed across body position (P=0.05) but not between self-reported or objective HF groups (P>0.40). Thirty minutes after wake, women with objective HF had an attenuated awakening response of sAA compared to women without objective HF (β=0.71, SE=0.32, p<0.03, d=0.73). The total number of objective HF was the best predictor of area under the curve (β=0.35, SE=7.97, p<0.03) and awakening response of sAA (β=0.46, SE=2.78, p<0.002). **Conclusion:** Our findings support a state shift in autonomic balance towards increased sympathetic activation with objective, but not self-reported, VMS. We found evidence that objective VMS have a dose-dependent relationship with sympathetic activity. In the context of the broader literature, our findings suggest withdrawal of parasympathetic activity occurs transiently during objective VMS, but not during a validated posture challenge. Overall, our data provide evidence that objective VMS are associated with a shift in the balance between the sympathetic and parasympathetic branches of the ANS; specifically, increased sympathetic tone with increased frequency of objective VMS.

**BASIC SCIENCE POSTER PRESENTATIONS**

**P-1. Identification of Antimullerian Hormone Protein Expression in the Arterial Wall of Premenopausal and Postmenopausal Monkeys**

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**Objective:** Anti-mullerian hormone (AMH) is produced by the ovary and is a marker of ovarian follicle number. AMH concentrations decline during the menopausal transition until follicles are depleted at menopause. AMH is a member of the TGF-β family and, similar to other members of the TGFβ family, it plays a crucial role in cell fate, growth and tissue remodeling. However, potential effects of declining AMH on non-reproductive tissues are not well understood. We have shown that pre-existing low plasma AMH levels predict increased atherosclerosis extent (Appt et al., Menopause, 2012) in pre- and postmenopausal monkeys. Others report that lower AMH is associated with weakening of the aortic wall in men, and AMH receptor mRNA expression has been observed in mouse aorta. The purpose of this study was to determine if AMH protein is present in the artery of female monkeys. **Design:** Midlife pre- and surgically postmenopausal cynomolgus Macaques were used for this observational study. Monkeys (n=14) were fed a Typical American diet for 2 years prior to the collection of carotid, coronary, abdominal and iliac arteries. Anti-AMH mouse monoclonal antibody (AbD Serotec MCA2246T) was used to identify AMH protein expression in arteries and other tissues (ovary, colon, and uterus). **Results:** AMH staining was strong in ovarian granulosa cells. Moderate to strong staining was observed in the smooth muscle cell layer of the carotid, aorta and iliac arteries, while staining in the intimal layer of atherosclerotic plaques was variable. Weaker, more diffuse staining was observed in coronary arteries. Moderate staining was also observed in smooth muscle cells of the uterus and colon. **Conclusion:** In female monkeys, AMH protein is expressed consistently in the arterial smooth muscle cell layer (arterial media) and intermittently within arterial intimal layer plaques. Smooth muscle cells are integral to the response of arteries to stressors (i.e. changes in blood pressure, inflammation and oxidative stress) that are known to increase risk for vascular stiffness and atherosclerosis. Therefore, future prospective studies are needed to determine if AMH has a direct effect on arterial smooth muscle cells.
P-2. Ovarian Metabolomic Profiles Differ Between Monkeys Consuming Prudent and Western Diets

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Objective: The long-term goal of this research is to understand the effects of diet on female reproductive function and aging. Dietary patterns in Western societies have changed remarkably over the past century. Consumption of saturated fatty acids, omega-6 unsaturated fatty acids and refined carbohydrates has risen sharply in the face of declining consumption of fruits, vegetables and omega-3 fatty acids. This dietary pattern is associated with post-prandial oxidative stress and inflammation, both of which could affect reproductive health. Recently, ovarian-metabolomic profiling has been used to characterize oxidative and inflammatory pathways in non-diseased ovaries. We used this methodology to determine whether differences exist in global metabolomic profiles among ovaries derived from subjects of differing nutritional backgrounds. Design: Archived snap-frozen ovarian tissue and serum from midlife Cynomolgus monkeys fed either a Prudent or Western diet were used for this study. Prior to ovary collection, the Prudent diet monkeys (n = 12) were research naïve and had only been exposed to a commercial monkey chow diet (low in cholesterol and saturated fats, high in complex carbohydrates); Western diet monkeys (n = 8) were exposed for 2 years, to a diet high in cholesterol, saturated animal fats and soluble carbohydrates. Metabolomic analysis was done as follows: ovary tissue samples were homogenized and extracted in 50% acetonitrile and serum samples were extracted using methanolic protein precipitation. All data were acquired on a G2-SYNAP-FTOF mass spectrometer equipped with Acquity UPLC system and data were analyzed using Progenesis QI (Waters Corporation, MA) to determine the group differentiating markers. Results: Approximately 3,500 compound ions were detected. Unsupervised PCA analysis show a clear separation of the study groups for both the serum and ovary samples. Orthogonal Projections to Latent Structure-Discriminant Analysis (OPLS-DA) identified group differentiating markers with a VIP (Variable influence on projection) value ≥ 1.0. On average, 64 group differentiating metabolites for serum samples and 47 group differentiating metabolites for ovary samples were identified using in-house standards library and Human Metabolome Database. Conclusion: Dietary exposure has significant effects on the ovaries metabolome. Future investigations are required to determine the impact of diet on specific metabolic markers and subsequent effects on ovarian function.

P-3.

A Quantitative Single Sample Preparation Procedure and a Sensitive and Robust LC-MS/MS Method for the Simultaneous Quantification of Dehydroepiandrosterone (DHEA), Estrone (E1), Estradiol (E2), Testosterone (Testo), Dihydrotestosterone (DHT), Androstenedione (4-dione) and Androst-5-ene-3β,17β-diol (5-diol) in Brain Tissue

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Objective: Menopause is made possible by three concurrent events, namely cessation of estrogen secretion by the ovaries, high circulating dehydroepiandrosterone (DHEA) concentration, and intraincreases enzymes able to convert DHEA into active sex steroids in peripheral tissues. As much as the arrest of estradiol secretion by the ovaries is essential to protect the uterus and possibly other tissues, it is of major importance to keep sex steroids available for most other tissues which need estrogens and/or androgens for their normal functioning. This can be related to the observation that the age-associated decrease in DHEA production is correlated with neurodegeneration while DHEA (prasterone) has been shown to decrease neuroinflammation in many preclinical studies. The peripheral administration of prasterone could potentially restore physiological levels of brain steroids and delay the appearance of neurocognitive impairment and Alzheimer’s disease, a major issue for a large number of women and men in North America and a growing burden for the health care system. It is therefore crucial to develop a highly sensitive and robust method in order to efficiently quantify tissue DHEA and its metabolites by mass spectrometry using as small samples as possible. It would then be possible to measure neurosteroids in all of the brain regions of interest to better assess the contribution of peripheral DHEA in the development of Alzheimer’s disease and potentially other neurodegenerative disorders. Design: Steroid hormones are neutral and do not ionize at a high level, especially E1 and E2, using the electrospray ionization technique. These compounds were usually analysed by gas chromatography coupled to tandem mass spectrometry (GC-MS/MS) with derivatization. GC-MS/MS, however, often encounters robustness issues. With the combination of a sensitive mass spectrometer with an ultra-performance liquid chromatography (UPLC) system, LC-MS/MS should replace GC-MS/MS for the analysis of steroid hormones with only a limited number of compounds needing derivatization. The LC-MS/MS assay of steroids proves to be robust not only for the quantification of serum and plasma samples but also for brain samples. This technology could well pave the way for the analysis of steroids in a series of other less lipid-containing matrices. In fact, high lipid content is notorious for complicating the extraction, chromatography and ionization efficiencies of most compounds quantified by MS. We have therefore developed a highly sensitive method for the simultaneous quantification of estrogenic as well as androgenic free steroid compounds using a standard curve in a 1% BSA/ultrapure water solution. Results: The sample preparation method generates low background with sharp and very specific analyte signals by LC-MS/MS, thus allowing high QC’s and EndoQC’s accuracies. The lower limits of quantification obtained are 4 pg/mL for E1, 1 pg/mL for E2, 250 pg/mL for DHEA, 200 pg/mL for 5-diol, 12.5 pg/mL for 4-dione, 10 pg/mL for DHT and 50 pg/mL for Testo in brain tissue extracts. Conclusion: This method should permit to assess the contribution of circulating DHEA in the formation of steroids in animal models. This should help explain how prasterone administration can optimally improve the health status of menopausal and post-menopausal women, especially by potentially delaying cognition loss, memory loss and Alzheimer’s disease. Furthermore, it opens the way for a wide array of applications for the quantification of steroids in many peripheral tissues during aging and help evaluating the role of sex steroids in regulating the physiological functions of specific tissues.

P-4.

Examining the Estrogenicity of Crinum latifolium L. var. crilae Tram & Khanh, var n. (Amaryllidaceae) Using Cell-based and Receptor-based Assays

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Objective: Although hormone therapy (HT) remains the standard of care for women experiencing vasomotor symptoms related to menopause, multicenter studies such as the Women’s Health Initiative have suggested increased risk of stroke, breast cancer and heart disease in older women taking a combination of estrogen and progesterin. These concerns have led women to reduce their use of HT and seek alternatives for relief of menopausal symptoms such as botanical dietary supplements. Among the botanicals dietary supplements being used by women as alternatives to HT are Actaea racemosa (L.) Nutt., Trifolium pratense L., and Crinum latifolium L. var. crilae Tram & Khanh, var n. Some, like T. pratense, contains estrogenic compounds such isoflavones, others like A. racemosa do not. In this investigation our objective is to determine if C. latifolium contains phytoestrogens. Design: A combination of receptor-based and cell-based assays were used to determine the presence of estrogenic compounds in an extract of C. latifolium which was obtained from Crla Health. For receptor-based screening, recombinant human ER alpha and ER beta was incubated with C. latifolium extract and bound ligands were detected using pulsed ultrafiltration liquid chromatography - mass spectrometry. Positive and negative controls included 4-hydroxymexifen and denaturated receptors, respectively. Ishikawa human endometrial adenocarcinoma cells that expressed estrogen-inducible alkaline phosphatase were used to determine if the extract had estrogenic or anti-estrogenic properties. 17-beta estradiol and 4-hydroxymexifen served as positive controls, and estrogenic activity was determined by percent induction in comparison to estradiol control. Anti-estrogenic activity was determined by the reduction in the percent induction in comparison to DMSO. Results: During mass spectrometry based screening to ligands of the estrogen receptors, positive control 4-hydroxymexifen produced the expected positive result relative to the control. After incubation of the C. latifolium extract with the estrogen receptors, a ligand was bound to ER alpha only. The compound weigh 326 u and had an elemental composition of C13H14N2O8. Determination of the structure of this compound is under investigation. As a functional test for estrogenicity, the C. latifolium extract was evaluated using the Ishikawa cell-based assay. C. latifolium did not show any estrogenic and anti-estrogenic activity in this assay. When estradiol was added to the extract prior to treating Ishikawa cells, the estrogenicity of the extract was enhanced indicating that C. latifolium has synergistic activity with estrogens. Conclusion: Although in vitro ligand to ER alpha was observed, this is no guarantee of in vivo estrogenicity. The fact that the cell-based assay indicated no estrogenic or anti-estrogenic activity for C. latifolium indicates that this botanical is probably not estrogenic in vivo. Therefore, there should be no concern that C. latifolium might have undesirable estrogenic consequences as does HT. This work was supported by NIH grant P50 AT000155 from the Office of Dietary Supplements and the National Center for Complementary and Alternative Medicines.
**P-5. Effects of isoflavones and/or 17β-estradiol in endometrium of diabetic rat models induced by streptozotocin (STZ)**

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**Objective:** To analyze the interactions between estrogen receptors, proliferation and angiogenic parameters of endometrium of diabetic rats treated with isoflavones and/or 17β-estradiol.

**Design:** Fifty-six female rats (Rattus norvegicus albinos) at 3 months of age were divided into six (6) groups: GI (n = 7) Sham control - not ovariectomized animals (estrous phase); GII (n = 7) Sham diabetic control - not ovariectomized animals (estrous phase); GIII (n = 7) 17β-estradiol treated control that received propylene glycol vehicle; GIV (n = 7) ovariectomized diabetic animals, which received vehicle propylene glycol; GV (n = 7). The treatments consisted of isoflavones (150 mg / kg, orally); GVI (n = 7) and/or 17β-estradiol (10μg/Kg subcutaneously). All animals were treated during 180 consecutive days. At the end, they were anesthetized, the tissues were removed and submitted to the appropriate procedures for molecular biology analysis, such as measures of expression of estrogen receptors (ERα, ERβ2), cell proliferation (Ccn1a, ccna2, ccnd1, cdk4, cdk6, cdk2, Ccne1, Ccne2, Mki67) and angiogenesis (Vegf). Another part was immersed in 10% formaldehyde for subsequent histological studies of Ki-67 and VEGF-A.

**Results:** The morphological data showed the groups treated with 17β-estradiol had more developed endometrium than those treated with genistein after ovariectomy (p <0.05). We noticed a higher percentage of cell proliferation (Ki-67) in treatment with 17β-estradiol and no significant difference in Ki-67 in the alternate criterion (p >0.05). Genistein expression of estrogen receptors, vascularization and cell proliferation was also higher when animals were treated with 17β-estradiol. The expression of the same genes in the groups treated with genistein was relatively minor.

**Conclusion:** Genistein offers greater protection in the endometrium of diabetic rats in comparison with those treated with 17β-estradiol.

**P-6. Measuring Hot Flashes: Examination of an Alternate Criterion for Ambulatory Hot Flash Detection in Post-Menopausal Women**

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**Objective:** Hot flashes are a highly prevalent symptom experienced in menopause and in cancer treatment. Physiologic measures of hot flashes can be useful in investigations of the physiology and new treatments for hot flashes. The leading physiologic measure of this current study was to evaluate the in vitro effects of Relizen on the CYP enzyme system.

**Design:** The alternate criterion had greater sensitivity than the standard criterion (77.4%, alternate vs. 56.9%, standard; p <0.01, Cohen’s h = .4). There was a slight deficit in specificity in the alternate criterion (80.1% alternate vs. 86.1%, standard, p<.001). Positive and negative predictive values were broadly comparable. Sensitivity criterion was significantly greater among White versus Non-White participants (83.58% vs. 73.81%, respectively; p<0.05). All other racial/ethnic differences were non-significant. The alternate criterion had a higher area under the curve (AUC) than the standard criterion (77.4% vs. 71.8%, respectively).

**Conclusion:** For the ambulatory SCL-measurement of hot flashes in healthy post-menopausal women, a lower criterion skin conductance change (a 1.2 μmho rise in a 30-s period) performs better than the standard criterion (a 2 μmho rise in a 30-s period). Investigators should also consider racial/ethnic variability in the performance of this measure.

**P-7. Melatonin deficiency may decrease immunoreexpression of estrogen receptors in ovaries of pinealectomized female rats**

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**Objective:** To analyze the immunoreexpression of estrogen receptors in ovaries of pinealectomized female rats. Fourteen (72.9%) rats were randomly divided into three groups of 10 animals each: Group I – Control, Group II - pinealectomized (Pxs), and Group III - Pxs treated with melatonin (10μg/night, per animal). After two months’ treatment, the ovaries were collected, fixed in 10% buffered formaldehyde and processed for paraffin embedding. Sections were subjected to immunostaining by the detection of estrogen receptors. Under 400X of magnification, the analyses were carried out according to the color intensity, which varied from weak to strong immunoreactivity.

**Results:** The Pxs (GI) group showed a higher immunoreactivity of estrogen receptors in the granulosa and interstitial cells, as compared to the control (GII) and melatonin treated (GIII) groups, whereas a similar weak immunostaining was found in the outer and inner theca cells in all groups.**Conclusion:** Melatonin may decrease estrogen receptors immunoreexpression in ovarian follicles of pinealectomized rats.

**P-8. Action of isoflavones on the uterine cervix of ovariecetomized rats**

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**Objective:** To evaluate histomorphometric and immunohistochemical aspects of cell proliferation (Ki-67) and factors endothelial growth factors (VEGF) in the uterine cervix of female rats treated immediately after ovariecetomy (Ovx) with isoflavones (ISO) or estrogens (Design: 20 adult rats, Wistar EPMI (Rattus norvegicus albinos), three months old, were divided into four groups: GI-SHAM (false-operated); GII-Ovx; GIII-Ovx treated with 17beta-estradiol (10μg/Kg/Day); GIV-Ovx treated with 17beta-estradiol (10μg/Kg/Day). At the end of drug administration, the animals were euthanized and the cervix was removed; the tissue fragments were immersed in 10% formalin and after 24 hours processed for paraffin inclusion and subsequent morphometric or immunohistochemical study. Results: We noted atrophy of the uterine cervix in Ovx group, which is less intense in the group Ovx + ISO. We also noticed a marked increase in the thickness of the cervix in the group treated with 17beta-estradiol, especially in the lining epithelium and stroma. The immunoreactivity for Ki-67 and VEGF-A was higher on the cervix of animals treated with 17beta-estradiol, and upper than that found in animals treated with ISO.**Conclusion:** The uterine cervix displays more attenuated proliferative response to isoflavones than to estrogens.

**P-9. Relizen, a non-hormonal treatment for vasomotor symptoms, inhibit the CYP2D6 enzyme system**

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**Objective:** Tamoxifen is used extensively to treat women with invasive breast cancer and for chemoprevention in women at high risk for breast cancer. It is converted to 4-hydroxy-tamoxifen and other metabolites by the cytochrome P450 (CYP) enzymes. Tamoxifen is well known to often initiate or exacerbate vasomotor symptoms (VMS). As systemic drug containment products and diseases, we compared the systemic and concerns exist about the use of phytoestrogen-based products in these women, there are limited options available for the treatment of VMS in this population. Selective serotonin reuptake inhibitors (SSRIs) have been prescribed to alleviate tamoxifen-induced VMS symptoms. However, these SSRIs, including paroxetine, are strong CYP2D6 inhibitors and their labels often contain warnings and precaution that they can reduce the efficacy of tamoxifen. Thus the value of a non-estrogen agent effective against VMS but with no effect on the CYP enzyme system is obvious. Relizen, a non-hormonal purified pollen extract, has shown efficacy vs. placebo in treating VMS in a randomized, double-blind controlled trial. The objective of this current study was to evaluate the in vitro effects of Relizen on the CYP enzyme system.

**Design:** Relizen, as a powder mixture of 75% pollen/pistil extract P182 and 25% pollen extract GC Fern (PE-F), was tested for its potential to inhibit the human CYP isoenzyme, CYP2D6, in pooled human liver microsomes. Quinidine, a known inhibitor of CYP2D6, was used as a reference. The endpoint was conversion of Bufuralol to 1-OH-Bufuralol, analyzed using Liquid chromatography–mass spectrometry (LC-MS/MS). Six concentrations of each compound were tested. All reactions were performed in triplicate. Concentrations of Relizen ranged from 1.65 μg/ml to 400 μg/ml. Quinidine dosing ranged from 2.06 μM to 500 μM. The usual human dose of Relizen is approximately 80 μg/ml, thus the highest test dose corresponds to five times the recommended daily dose.**Results:** Inhibition of CYP2D6 by Relizen was negligible at all concentrations and ranged from 1.23% to +7.16%. Inhibition of CYP2D6 enzyme with Quinidine increased in a linear dose related fashion from -7.07% at 2.06 μM to 84.05% at 500 μM.**Conclusion:** Relizen is a non-hormonal treatment of VMS that does not show inhibition of the CYP enzyme system. Clinical utility for Relizen in women using tamoxifen for breast cancer treatment or chemoprevention who experience VMS is obvious.
Menopausal transition, body adiposity, lean mass and hormonal levels in black urban African women in the Study of Women Entering and in Endocrine Transition (SWEET)

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Objective: The menopause transition (MT) is closely associated with changes in body fat distribution (BFD), particularly increased visceral adiposity, which is a principal risk factor for metabolic disease. There is debate as to whether changes in visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT) and lean mass during the MT are related to either chronological or reproductive aging, or both. Sarcopenia is associated with increased risk for metabolic disease. Obesity and associated disorders are widely prevalent amongst mid-life, black South African women. Causes of this are not known. Previous data from SWEET show a high rate of obesity at menopause (68%). Central adiposity and its strong association with metabolic disease and reproductive hormones across the MT have been widely described in Western literature, but no such data are available on sub-Saharan African women. Therefore, the aim of our study was to determine whether body adiposity and lean mass change during the MT, and if these changes are due to changes related to serum concentrations of sex hormones. Design: The women, 40 - 60 years, in this cross-sectional study, are participants in SWEET. STRAW+10 criteria were used to ascertain menopause stage. The number of participants in each STRAW+10 stage was as follows: late reproductive (-3b, -3b), 195; early and late menopausal transition (-1, -1), 123; early postmenopause (+1a, +1b, +1c), 154 and late postmenopause (+2), 133. Serum levels of follicle stimulating hormone (FSH), estradiol (E2), dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate (DHEAS), testosterone, and sex hormone binding globulin (SHBG) were obtained from fasting samples. A voluntary HIV rapid test was offered to all women. Simple anthropometry measures were obtained. VAT, SAT and total body lean and fat mass were measured by ultrasound and DEXA, respectively. Differences in anthropometric and hormone measurements across the MT were analysed using ANOVA, and multivariate linear regression used to identify the strongest correlates of the anthropometric and hormone data. All hormone data were log transformed to normality before use. Data were adjusted for HIV status. Results: The study population contained 702 women; mean age (±SD) was 49.2 ± 5.29 years and 21.3% of participants were HIV positive, of whom 55.3% were receiving antiretroviral therapy (ART). Whole body lean mass fell significantly across MT (p=0.002), but this trend was nullified (p=0.98) after adjustment for FSH levels in an ANCOVA. There was a tendency for BMI to fall with progression across MT (p=0.06), as did SAT (p=0.05). No other significant MT-related anthropometric changes were noted. FSH levels rose across the MT (p=0.0005) whilst E2 and DHEAS (p=0.007) and SHBG and E2 fell (p=0.0005 for both). The serum levels of other hormones did not change across the MT. Both BMI (p=0.49, p=0.02) and total body fat mass (p=0.38, p=0.005) were lower in women using ART than women not using it and SHBG levels correlated negatively with BMI (β=−1.71, p=0.04) and body fat mass (β=−3.46, p=0.02). The major hormonal correlates of lean mass were FSH (β=−2.06, p=0.0005), SHBG (β=−2.47, p=0.01) and DHEAS (β=−1.06, p=0.005). Conclusion: The principal anthropometric change observed in this study was a fall in lean mass across the MT, which was independent of age. There is a strong negative correlation between total lean mass and FSH levels, a relationship that has been observed in previous studies. Measures of total body fat correlated negatively with SHBG levels, confirming data from previous studies. Antiretroviral treatment was also associated with lower body adiposity. Future research is needed to determine whether this trend of sarcopenia is related to changes in cardiometabolic disease risk factors.

Efficacy of Rheum rhaponticum ERr 731® extract in alleviating vasomotor menopausal symptoms in an ovariectomized rat model

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Objective: Hot flashes are one of the most common and debilitating symptoms of menopause. Even though hormone therapy (HT) with estrogen is considered the most effective and reliable treatment of moderate to severe vasomotor symptoms, it is not recommended as a long-term solution due to the increased risk of hormone-related cancers by estrogen receptor (ER)-α. Nutraceutical interventions targeting the ER-β receptor are considered a safer option. ERr 731® (Chemisch-Pharmazeutische Fabrik Göppingen, Carl Müller, Apotheker, GmbH u. Co. KG, 73033 Göppingen, Germany) is a standardized extract containing rhapontin and deoxyrhapontin from Siberian rhubarb (Rheum rhaponticum) was shown to improve vasomotor symptoms in humans. In this study, we evaluated ERr 731® for thermoregulation and novel biology in ovariecetomized (OVX) rats. Design: Similar to humans, elevated ovarian steroids in rats activates heat loss mechanisms and this increase is reversed by estrogen replacement. Cutaneous vasodilatation of the tail is a primary mechanism of thermoregulation that functions to increase skin temperature (Tskin) and heat loss. In this study, we examined the relationship between oral administration of ERr 731® and several underlying components of skin vasomotion in OVX rats. Sham or bilaterally OVX female Sprague Dawley rats (n=6/group) were gavaged daily with vehicle (10% DMSO in saline), 0.5, 1, or 3 mg/kg ERr 731® suspension in vehicle, or 0.3 mg/kg/d clomiphene citrate (as a positive control). Tskin recordings were obtained with Cuco Mini dataloggers inserted into a protective covering and attached on the ventral surface of the tail during the 12 h active phase of the light cycle on day 2, 7, and 14 of administration. Statistical comparisons were made using one-way or two-way ANOVA (as appropriate) and Tukey’s post hoc test with p<0.05 was considered significant. Results: We evaluated the specificity of ERr 731® for ER-α and ER-β agonistic activity using cell based reporter assays and ER-α/ER-β dependent genes in tissues. Results: All groups displayed circadian rhythms of Tskin and E2 treatment of OVX rats resulted in decreased Tskin during the dark (active) phase as early as day 2 of oral administration. Oral administration of ERr 731® dose dependently reduced Tskin values by an average value of 1°C. The rapid onset of this effect was observed in 1 and 3 mg/kg ERr 731® groups as early as day 2 of administration and remained in place for the duration of the treatment (2 weeks). OVX surgery resulted in a significant body weight gain as compared to Shams (average body weight 301+/-31 vs 225+/-15 g); this effect was partially reversed by E2 treatment (279+/-19 g) and the higher dose of ERr 731® (275+/-24 g). Body composition measurements showed that the observed decrease in total body mass was due to equal reduction of lean, fat mass and total body water. Reporter assays confirmed that ERr 731® is specific to ER-β and had no ER-α activity. These observations were further substantiated by expression pattern of genes related to ER-α/β signaling in the corresponding tissues. Conclusion: Tskin was increased by OVX and reduced by administration of exogenous estrogen and ERr 731® in rats. Our experimental findings provide further evidence for efficacy of the ER-β selective modulator, ERr 731® towards alleviating vasomotor menopausal symptoms. Furthermore, this data validates the OVX/Tskin rat model as a suitable screening platform to evaluate the mechanisms and treatments of menopause.

Effect of melatonin, metformin and clomiphene citrate in ovary of rats in the permanent estrus

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Objective: To evaluate and compare the effects of melatonin, metformin and clomiphene citrate in ovaries of rats in permanent estrus. Design: Thirty female rats were divided into five groups of 6 animals each, as follows: SHAM - in physiological estrus; Ctr – in permanent estrus; MEL - treated with melatonin; MET - treated with metformin and CT – treated with clomiphene citrate. The animals of the SHAM group remained under a normal light/dark cycle period, whereas the other groups remained under continuous illumination (400 Watts), for a period of 60 days. During the period of light exposure, the MEL group received daily administration of melatonin (0.4 mg / ml), diluted in drinking water, whereas the animals of the MET group received daily treatment of metformin (50 mg / kg) by gavage. The animals of the CC group received daily administration clomiphene citrate (1.6 mg / kg) by peritoneal injection during the last five days of light exposure. Afterwards, the animals were anesthetized and euthanized by transcardiac perfusion, the ovaries were collected, immersed in 10% phosphate buffered formalin and processed for paraffin embedding. Sections were stained with hematoxylin for histomorphometric analysis, in which the amount of cysts, corpora lutea and the relative area occupied by interstitial cells were analyzed, while were statistically analyzed by ANOVA and Tukey test (p<0.05). Results: The Ctr group showed a high percentage of ovarian cysts, absence of corpora lutea and larger concentration of interstitial cells, as compared to the SHAM group. The MEL, MET and CC groups showed the presence of corpora lutea, which was found in greater quantity in the MET group followed by the CC group. There was also a slight reduction of cysts in the MEL group compared to the Ctr group.
P.13. Immunompression of CYP17 and CYP19 in ovaries of rats in the permanent estrus treated melatonin, metformin and clomiphene citrate
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Objective: To evaluate the immunompression of CYP17 and CYP19 in ovaries of rats in the permanent estrus under melatonin, metformin and clomiphene citrate treatments.

Design: Twenty four rats were divided into four groups of 6 animals each: Ctr – in permanent estrus; MEL - treated with melatonin; MET - treated with metformin and CC - treated with clomiphene citrate. The animals remained under continuous illumination (400 Watts), for a period of 60 days. During the period of light exposure, the MEL group received daily administration of melatonin (0.4 mg / ml), diluted in drinking water, whereas the animals of the MET group received daily treatment of metformin (50 mg / kg) by gavage. The animals of the CC group received daily administration of clomiphene citrate (1.6 mg / kg) by peritoneal injection during the last five days of light exposure. Afterwards, the animals were anesthetized and euthanized by transcardiac perfusion, the ovaries were collected, immersed in 10% phosphate buffered formalin and processed for paraffin embedding. Sections were subjected to immunohistochemistry for the detection of CYP17, CYP19, 17alpha hydroxylase/17, 20 lease (CYP17) and cytochrome P450 aromatase (Cyp19). Under a light microscopy at 400X of magnification, the immunoreactivity pattern of CYP17 and CYP19 in ovarian follicles and interstitial cells was evaluated.

Results: The MEL and CC groups showed a higher immunoreactivity to CYP17 and CYP19 in the theca interna and interstitial cells, as compared to the Ctr and MET groups.

Conclusion: Melatonin and clomiphene citrate treatments may increase the immunompression of CYP17 and CYP19 in ovaries of rats in the permanent estrus.

P.14. Follistatin and Inhibin-βA: expression and influence ovarian function by the upregulation and downregulation of steroidogenesis related genes in ovary of pinealectomized rats in proestrous phase
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Objective: To analyze the expression of genes related to steroidogenesis in ovary of pinealectomized rats.

Design: 32 adult female virgin rats, with regular estrous cycle, were pinealectomized (Px) and equally divided into two groups, as follows: GI (Px) that received vehicle solution and GII (Px+Mel) treated with melatonin, 10μg/night, per animal, during 60 consecutive days. After treatment, the animals were euthanized by overdose of ketamine and xilazine, some ovaries were collected, kept in liquid nitrogen and stored at -80°C for posterior expression analyses by cDNA microarray (Kit GeneChip® Rat Genome 230 2.0 Array, Affymetrix) of genes related to ovarian functions. The microarray assay was carried out in triplicate for each group. Data were normalized and subjected to the GeneChip® Operating Software and later confirmed by the DNA-Chip Analyzer (dChip) software of secondar analyses. Gene expressions were considered significantly different when they were 1.5x over or low expressed, when compared to the group in which the assay was performed.

Results: 101 overexpressed genes and 72 low expressed genes were compared to Px group. The genes related to ovarian steroidogenesis were statistically significant upregulation (Inhibin-βA, Follistatin and Abl-Interactor1) and low expressed (prostaglandin D2 synthase, LIM Homebox 9 and Glutathione S-transferase Mu1), in the Px+Mel compared to Px group. Among the upregulated Ctr genes (p < 0.05), mainly in the MET group, followed by the higher expression. Based on these data, we later confirmed the upregulation of the following genes by RT-PCR (Px+Mel > Px, p<0.01) and by immunohistochemistry, which showed higher immunoreactivity in Px+Mel (INHBA=74.43±2.89 ; FST=48.53±3.51 in the follicular and interstitial cells, as compared to Px (INHBA=54.32±4.32; FST=51.4±2.3). Conclusion: Our results suggested that melatonin replacement interfered with the ovarian gene expression of pinealectomized rats, especially inhibin-βA and follistatin upregulation.

P.15. Expression of Bcl-2 and Bax in ovaries of pinealectomized or melatonin-treated pinealectomized rats
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Objective: To evaluate the expression of Bcl-2 and Bax in ovaries of pinealectomized or melatonin-treated pinealectomized rats.

Design: Thirty adult rats were randomly divided into three groups of 10 animals: Group I – Control; Group II - pinealectomized (Px), and Group III - Px treated with melatonin (10μg/night, per animal). After two months treatment, on the night of proestrus, the animals were placed in metabolic cages for night urine collection and subsequent measurement of 6-sulatoxymelatonin (6-SMT). The rats were anesthetized, blood samples were taken for estrogen and progesterone determinations, and they were then euthanized. The ovaries were collected, fixed in 10% buffered formaldehyde and processed for paraffin embedding. From the paraffin blocks, 5μm thick sections were collected to silanized slides and submitted immunohistochemical methods for the detection of Bcl2 (Spring Bioscience Corp. US) and Bax (Spring Bioscience Corp. US). Images were obtained using a light microscope (AxioLab Standard 2.0 - Carl Zeiss) attached to a high definition camera (Axiocam MRC - Carl Zeiss) and by the image analyzing software (AxioVision Rel. 4.8.2 - Carl Zeiss). Reaction expression was analyzed and quantified according with the color intensity with the aid of the Image J Pro Plus, having photographed 5 fields each slide, with the 40x objective. Obtained data was submitted to statistical analysis using ANOVA test complemented by the Tukey-Kramer test (p<0.05). Results: The urinary levels of 6-SMT and serum progesterone were lower in the Px group (GI), Exogenous melatonin treatment restored both blood melatonin and 6-SMT urinary levels. The Bax/Bcl-2 ratio was highly immunompressed in the GI - Px treated with melatonin (GI = 60.9±3.9) when compared with the Control (GI = 40.9±3.5) and GI - Pinealectomized (Px) (GI = 51.0±2.85) (p<0.05). Conclusion: Our data showed that melatonin enhances apoptosis in the ovary of pinealectomized rats.

P.16. Steroidogenesis-related gene expression in rat ovary exposed to melatonin supplementation
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Objective: To analyze steroidogenesis-related gene expression in rat ovary exposed to melatonin supplementation

Design: Thirty-two virgin adult female rats were randomized to two groups as follows: GI – Control, received vehicle and GII – Experimental, received melatonin supplementation (10μg/night, each animal) for 60 consecutive days. After the treatment, the animals were anesthetized and the collected ovaries were immediately placed in liquid nitrogen and then frozen at -80°C for further DNA microarray analyses.

To determine the expression of various genes, a GeneChip® Rat Genome 230 2.0 Affymetrix Array was used, according to the supplier’s specifications; the experiment was repeated three times for each group. The results were normalized with the GeneChip® Operating Software program and confirmed through analysis with the secondary DNA-Chip Analyzer (dChip) software. Upregulation and downregulation of genes were considered significant when they were 2.0 times higher or lower, respectively, than the control group. The data were further confirmed by RT-PCR analyses.

Conclusion: Our data suggest that melatonin supplementation decreases expression of the gene in cyclic AMP changing ovarian steroidogenesis
P-17. Immunoexpression of vascular endothelial growth factor (VEGF-A) in the endometrium of rats treated with melatonin in the permanent estrus phase

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Objective: to analyze the expression of VEGF-A, in the endometrium of rats treated with melatonin in the permanent estrus phase

Design: Twenty adult, virgin female rats in the permanent estrus phase (by light exposure) were divided into two groups (10 animals each): GI - Control, which received vehicle; GII - Experimental, that received melatonin reposition (10μg/night, each animal) for 60 consecutive days. After treatment, the animals were anesthetized in the permanent estrus phase and the ovaries were collected, fixed in 10% formaldehyde and processed for paraffin embedding. Sections with 5μm thick were collected in silanized slides and submitted to immunohistochemistry for the detection of VEGF-A. Sections were collected, fixed in 10% formaldehyde and embedded for paraffin embedding. Sections with 5μm thick were collected and submitted to immunohistochemistry for the detection of VEGF-A (AxioLab Standard 2.0 - Carl Zeiss) attached to a high definition camera (AxioCam MSC - Carl Zeiss) and by an image analyzing software (AxioVision Rel. 4.8.2 - Carl Zeiss).

At the objective of 40x, five fields in each slide were captured. The immunoexpression reaction was analyzed and quantified according to the color intensity using the Image J Pro Plus Program. Data was submitted to statistical analysis using the Student’s t-test (P<0.05).

Results: Immunoexpression of VEGF-A was expressed at a higher percentage in the Control, in both superficial (GI = 85.2 ± 3.4; GII = 5.7 ± 2.7; P<0.001) and glandular epithelia (GI = 82.4 ± 6.3; GII = 7.9 ± 5.8; P<0.001). However, these immunoexpression were observed in a lower percentage of the melatonin treated animals (GI = 54.8 ± 44.8 ± 2.5; P<0.05). Conclusion: Our data suggest that melatonin may influence the vasculization of the endometrium of rats in the permanent estrus phase.

P-18. Melatonin treatment influences the immunoexpression of Ki-67 in the endometrium of female rats in the permanent estrus phase

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Objective: to evaluate the immunoexpression of Ki-67 in the endometrium of female rats treated with melatonin in the permanent estrus phase

Design: Twenty adult, virgin female rats in the permanent estrus phase (continuous light), were divided into two groups (10 animals each): GI - Control, which received vehicle; GII - Experimental, that received melatonin reposition (10μg/night, each animal) for 60 consecutive days. After treatment, the animals were anesthetized and the ovaries were collected, fixed in 10% formaldehyde and processed for paraffin embedding. Sections with 5μm thick were collected and submitted to immunohistochemistry for the detection of Ki-67. Images were obtained using a light microscope (Axioskop Standard 2.0 - Carl Zeiss) attached to a high definition camera (AxioCam MRC - Carl Zeiss) and by an image analyzing software (AxioVision Rel. 4.8.2 - Carl Zeiss). At the objective of 40x, five fields in each slide were captured. The immunoexpression reaction was analyzed and quantified according to the color intensity using the Image J Pro Plus Program. Data was submitted to statistical analysis using the Student’s t-test (P<0.05).

Results: Melatonin treatment showed the lower percentages of Ki-67 immunoreactivity, in both superficial (GI = 65.2 ± 2.3; GII = 33.7 ± 2.7; P<0.001) and glandular (GI = 74.5 ± 4.2; GII = 66.5 ± 5.8; P<0.05) epithelium, as well as in the lamina propria (GI = 43.5 ± 8.5; GII = 33.5 ± 2.7; P<0.05). Conclusion: Our data suggest that melatonin reduces the proliferation in epithelial tissue and connective tissue in the endometrium of rats in the permanent estrus phase.

P-19. Angiogenesis gene expression across different life stages in non-human primates (Macaca fascicularis) in normal and cancerous mammary gland - an exploratory study

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Objective: To investigate the impact of reproductive life stages on the angiogenesis gene expression profiles of the mammary gland in a primate model, in comparison to the hormone treated postmenopausal mammary gland and breast cancer.

Design: Comparative transcriptomic analyses were carried out using breast tissues obtained from rhesus macaques at different life stages, that is: prepuberal (n=4), adolescent (n=4), adults in the preluteal phase of the menstrual cycle (n=5), pregnancy (n=6), lactation (n=3) and postmenopause (n=5), compared to treatment with tamoxifen (G1) (n=3), treatment with conjugated combined estrogens combined with medroxyprogesterone acetate (CEE/MPA) (n=3) and breast cancer (BC) (n=5).

Mammary gland RNA was isolated, purified, and hybridized to a rhesus macaque genome microarray (Affymetrix GeneChip® Rhesus Macaque Genome Array). Differential gene expression was analyzed using MAS 5.0 (Affymetrix® Microarray Suite) for ANOVA with adjusted p-values (Benjamini & Hochberg) and DAVID 6.7 (Database for Annotation, Visualization and Integrated Discovery) for cluster analysis. Angiogenesis markers ADAM12, HGF, HIF-1α, KDR, Ki-67, MMP-9, PDGF, PECAM-1, TGF-β, THBS1 and VEGFA were measured by qRT-PCR and analyzed using nonparametric ANOVA with adjusted p-values (Benjamini & Hochberg) and DAVID 6.7 (Database for Annotation, Visualization and Integrated Discovery) for cluster analysis. Angiogenesis markers ADAM12, HGF, HIF-1α, KDR, Ki-67, MMP-9, PDGF, PECAM-1, TGF-β and VEGFA was localized and quantitatively evaluated by immunohistochemistry (IHC). Results: Gene Expression Arrays - Hierarchical cluster analysis revealed distinct sequences of angiogenesis gene life stages and life groups, BC, TAM+ and CEE/MPA treated mammary gland, respectively. Principal component analysis revealed 3 main clusters, one consisting of prepuberal+adolescent+adult +postmenopausal animals; another of pregnant+lactating animals; and a third including BC+CEE/MPA; the TAM treated animals were separate from all others. PCR - ADAM12 mRNA was highest in juveniles and postmenopausal animals, in contrast VEGFA mRNA was highest in pregnant animals. Ki-67, HIF-1α, PECAM-1 gene expression was lowest in the adolescents. IHC - Each marker had different protein expression patterns and localizations. In general VEGFA was localized primarily to vascular endothelium. ADAM12, TGF-β and PDGF stained positively both lobular endothelium and vascular endothelium; HIF stained primarily ductal epithelium positive; and KDR was localized to periglandular and perivascular extracellular matrix. These findings suggest paracrine cross-talk between glandular and vascular structures. Conclusion: Our data demonstrate distinct patterns of angiogenesis gene expression during breast development, (anti-) estrogenic treatment and in BC. Furthermore microanatomical relationships indicate paracrine signaling may be important.

P-20. Estrogens act to rapidly increase excitatory synaptic transmission in the hippocampus and basal forebrain of male and female rodents

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Objective: Traditional actions of estrogens are thought to regulate normal physiology through ligand-activated transcription factors mediating long-term genomic effects over the course of days, months and years. Detailed knowledge of estrogen receptor function is critical because decreasing estrogen levels during menopause may contribute to the increased incidence of stroke, cognitive impairment and inflammatory responses. Recently, rapid (non-genomic) signaling effects of estrogens have been described that occur within minutes and are postulated to contribute to neuronal excitability, neuroprotection, homeostasis, synaptic plasticity and cognition (Woolley, Rev Pharmacol Toxicol, 47:657-680, 2007). It is unknown whether these rapid, non-genomic actions of estrogens continue to play a role during menopause. The purpose of this study is to begin to delineate estrogen receptor mechanism(s) that modulate excitatory synaptic transmission in a female rodent model of reproductive senescence. Design: Both male and female Sprague-Dawley rats were used. Young rats, both males and females, were between 1-5 months of age, and acyclic middle-aged females were 9-12 months of age. These later rats are considered reproducively senescent and represent a rodent model of human postmenopause. We utilized in vitro brain slice preparations to evaluate the effects of estrogen reposition (100 nM) was applied for 5-10 minutes and a second I/O curve recorded. The G-protein estrogen receptor agonist G1 (100 nM) was also tested. Results: Estrogen receptor agonists (both 17E and G1) rapidly and reversibly increased excitatory synaptic transmission in both the hippocampus and basal forebrain. In the hippocampus, 17E 100nM increased I/O curves both female (7/11, 64% responding) and male (6/13, 40% responding). Cells responding both sexes increased the paired-pulse ratio using a double-pulse paradigm. These later data suggest that estrogens may influence the proliferation in epithelial tissue and connective tissue in the endometrium of rats in the permanent estrus phase.
P-21. Effects of metformin on the immunoeexpression of Cyp17a1 and Cyp19a1 of human granulosa cells in ovariates of estrus-permanent rats
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Objective: To evaluate the effects of soy isoflavones and/or 17β-estradiol on bone tissue of ovariectomized rats
Gisela R. Sasso1, Clelia R. Bertoncini2, Cristiane D. Teixeira, Dr1, Rinaldo Florencio-Silva1, Carla C. Maganhin, post doctoral1, Katia de Vasconcelos1, Ricardo S. Simões, Dr1, Ekman J. Simões, PhD1, José M. Soares-Jr, MD, PhD1, 1Gynecology, Paulista School of Medicine at Federal University of São Paulo, EPM/UNIFESP, São Paulo, Brazil; 2Obstetrics and Gynecology, School of Medicine at University São Paulo, São Paulo, Brazil
Objective: To evaluate the effects of metformin on immunoexpression of Cy17a1 and Cyp19a1 in the ovaries of metformin-treated female rats at permanent estrus phase. Design: Thirty-six newly born female EPM1-rats were randomized on their third day of life into 3 groups of 12 animals each, as follows: control group (CG), androgenized group (AG), and androgenized plus metformin group (AGmet). The AG and AGmet groups received a single dose of 0.1 ml of testosterone propionate (1.25 mg /animal) diluted in castor oil (vehicle), whereas the control group received only vehicle by subcutaneous injection in the dorsum. After 90 days, the CG and AG groups received distilled water, while the AGmet group was treated with metformin (50mg/Kg), by gavage for 90 consecutive days. Afterwards, the animals were anesthetized, blood was collected for glucose and fasting glucose serum measurements, and the ovaries were removed and processed for immunohistochemical detections of Cyp17a1 and Cyp19a1. Results: The glucose and the HOMA-IR were higher in the AGmet group when compared to AG and CG groups. The AGmet group showed the 17β-estradiol expression in the theca interna and in the interstitial cells, and the Cyp19a1 only in the granulosa cells, as compared to the other groups. Conclusion: Metformin may influence the ovarian Cyp17a1 and Cyp19a1 expression and steroidogenesis.

P-22. Immunohistochemical and histological analysis of the effects of metformin ovaries of rats in estrus-permanent
Gisela R. Sasso1, Roberta R. Antonini1, Carla C. Maganhin, post doctoral2, Rinaldo Florencio-Silva1, Paula C. Franco, Dr1, Ricardo S. Simões, Dr1, Manuel J. Simões, PhD1, Edmund C. Baracat1, José M. Soares-Jr, MD, PhD1, 1Gynecology, Paulista School of Medicine at Federal University of São Paulo, São Paulo, Brazil; 2Obstetrics and Gynecology, School of Medicine at University São Paulo, São Paulo, Brazil
Objective: To analyze the immunoeexpression of vascular endothelial growth factor (VEGF-A) and cell proliferation (Ki-67) in the ovaries of metformin-treated female rats at permanent estrus phase. Design: Thirty-six newly born female EPM1-rats were randomized on their third day of life into 3 groups of 12 animals each, as follows: control group (CG), androgenized group (AG), and androgenized plus metformin group (AGmet). The AG and AGmet groups received a single dose of 0.1 ml of testosterone propionate (1.25 mg /animal) diluted in castor oil (vehicle), whereas the control group received only vehicle by subcutaneous injection in the dorsum. After 90 days, the CG and AG groups received distilled water, while the AGmet group was treated with metformin (50mg/Kg), by gavage for 90 consecutive days. Afterwards, the animals were anesthetized, blood was collected for glucose and fasting glucose serum measurements, and the ovaries were removed and processed for immunohistochemical detections of Cyp17a1 and Cyp19a1. Results: The glucose and the HOMA-IR values were higher in the AG rats (P<0.01). Histomorphometric analysis of the ovaries showed a reduction in the area of degenerating follicles and in the number of interstitial cells and the emergence of corpora lutea in AGmet as against AG (P<0.01). Proliferation decreased in the theca interna and in the interstitial cells as evidenced by Ki-67, and VEGF-A expression diminished in the theca interna, the granulosa, and the interstitial cells in AGmet. Conclusion: Metformin led to improvement in glucose and in the HOMA-IR index, to a partial reversion of histomorphometric characteristics, and to reduction in ovarian cell proliferation in previously androgenized rat ovaries as shown by Ki-67 and VEGF-A.

P-23. Effects of early and late treatments of low intensity, high frequency mechanical vibration on bone parameters in estrogen deficient rats
Gisela R. Sasso1, Rinaldo Florencio-Silva1, Carla C. Maganhin, Miriam A. Santos, Paula C. Franco, Dr1, Ekman J. Simões, PhD1, 1Gynecology, Paulista School of Medicine at Federal University of São Paulo, EPM/UNIFESP, São Paulo, Brazil
Objective: To evaluate the effects of soy isoflavones and/or 17β-estradiol on bone tissue of ovariectomized rats in the permanent estrus phase
Gisela R. Sasso1, Rinaldo Florencio-Silva1, Carla C. Maganhin, post doctoral1, Katia de Vasconcelos1, Ricardo S. Simões, Dr1, Ekman J. Simões, PhD1, José M. Soares-Jr, MD, PhD1, 1Gynecology, Paulista School of Medicine at Federal University of São Paulo, EPM/UNIFESP, São Paulo, Brazil; 2Obstetrics and Gynecology, School of Medicine at University São Paulo, São Paulo, Brazil
Objective: To evaluate the effects of soy isoflavones and/or 17β-estradiol on bone tissue of ovariectomized rats
Gisela R. Sasso1, Clelia R. Bertoncini2, Cristiane D. Teixeira, Dr1, Rinaldo Florencio-Silva1, Carla C. Maganhin, post doctoral1, Katia de Vasconcelos1, Ricardo S. Simões, Dr1, Ekman J. Simões, PhD1, José M. Soares-Jr, MD, PhD1, 1Gynecology, Paulista School of Medicine at Federal University of São Paulo, EPM/UNIFESP, São Paulo, Brazil; 2Obstetrics and Gynecology, School of Medicine at University São Paulo, São Paulo, Brazil
Objective: To evaluate and process histomorphometric and polarized light microscopy for collagen fibers analysis or subjected to immunohistochemistry of cleaved caspase-3 in osteocytes. Statistical analysis was done by ANOVA followed by the Bonferroni post hoc test (P<0.05). Results: BMD was similar among the groups before Ovx, but after treatments, it was significantly higher in GI and GIV compared with their control groups (P<0.05). Femur length and cortical bone thickness was similar among the groups, but the diaphysis diameter of GI was higher compared to GI. Trabecular bone area was higher in the vibrated groups, but was greater in GII (P<0.05). Also, GII showed the higher presence of mature collagen fibers and lower percentage of apoptotic osteocytes (positive caspase-3 immunoreactivity) when compared to the other groups.

Conclusion: These results suggest that both early- and late-treatments with LHMV counteract bone loss and improve bone parameters in Ovx rats, being the early treatment more effective than the late treatment.

P-25. Effect of associated or isolated melatonin and melatonin in bone tissue of rats in the permanent estrus phase
Gisela R. Sasso1, Rinaldo Florencio-Silva2,1, Ekman J. Simões, PhD2, Paulo C. Franco, Dr1, Maria A. Santos, Dr1, Joao S. Mattos, Dr1, Ricardo S. Simões, PhD1, José M. Soares-Jr, MD, PhD2, Carla C. Maganhin1, 1Gynecology and Obstetrics, School of Medicine at Federal University of São Paulo, EPM/UNIFESP, São Paulo, Brazil; 2Obstetrics and Gynecology, School of Medicine at University São Paulo, São Paulo, Brazil
Objectives: To evaluate and compare the effects of melatonin and metformin in the alveolar process and periodontal ligament of rats in the permanent estrus. Design: 35 adults, albinos and virgins female rats, at the age of 3 months of were kept in cages with food and water ad libitum. Seven of these animals were maintained on 12 hours light-dark cycle and was considered the Sham Group (Sham). The others 28 animals were kept in continuous light for four weeks, to induce a state of permanent estrus, which was confirmed after daily collection of vaginal swabs for 21 consecutive days. The animals were then equally divided into the following groups: Control Group (CE); Group treated with Melatonin (0.4 mg / ml) diluted in drinking water (MEL); Group treated with Metformin (50 mg / kg) by gavage (MET) and Group treated with Melatonin and Metformin associated (MELA+MET). After 60 days of treatment, the animals were anesthetized and euthanized by transcardiac perfusion and fragments containing the maxillary alveolar process and periodontal ligament of the first molar were removed, fixed, decalcified in EDTA and processed for paraffin embedding. Some sections were stained with hematoxylin and eosin for histomorphometric analysis and others for picrorosius Red method and immunohistochemistry method for detection of osteocalcin and Hyaluronic Acid. Results: The bone area of the alveolar process and thickness of the periodontal ligament as well as birefringence of the group treated with Isoflavone (ISO) were higher (p<0.05), when compared to control group (CRT), and these results were similar to the Sham and treated with Estradiol (17β) groups. The immunostaining for osteocalcin showed higher positivity in osteoblasts of the alveolar process in the Sham and treated with estradiol (17β) compared to CRT and ISO groups. The periodontal ligament showed higher positivity in 17β-treated group compared to the other groups, in which data was similar. The immunostaining for hyaluronic acid showed no difference between groups in both the alveolar process bone as the periodontal ligament. Conclusion: Soy isoflavones protects the periodontal ligament and alveolar bone without compromising bone loss, and these results were similar to that found in rats treated with 17β-estradiol.
P-26. Neurophysiology assessment in simulated pelvic pain

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Objective: Evaluate and compare cortical activity at medium to low frequencies at rest and in a state of physiologic pelvic pain. Design: Five healthy volunteers underwent 64 channel dipole EEG using an EGI Net Amps 300 system. Subjects first underwent default mode session consisting of 6 minutes with eyes closed, resting quietly. They were then presented images of facial expressions for 8 minutes. Then, the default mode session was repeated for another 6 minutes. These were done once with a full bladder and repeated after voiding. Data analysis was done using EGI Lab where data was average referenced and filtered from 1 to 50 Hz. Artifact rejection was performed. Individual recordings for subjects were appended according to condition and then channel measures were computed. Results: Power - frequency analysis demonstrated divergence of the full and empty conditions in the delta band (0.7 Hz), the low alpha (9-11 Hz) and beta (13 Hz and higher) (Fig 1). This divergence is well illustrated with an overlaying average reference (Fig 2). Scalp lead power spectrum differed between the two conditions (Fig 3, left) with different levels of statistical significance (Fig 3, right). Significant differences (p<0.05) between full and empty conditions are shown in figure 4. Individual scalp power frequency analysis between the two conditions at each frequency, along with significantly different electrode locations is seen in figure 5 for the frequencies of 19 Hz - 21 Hz. Conclusion: By simulating a physiologic painful state with a full bladder, this study begins to describe the difference in neurophysiology between those who suffer from pain syndromes compared to those who are pain free. Group differences in scalp power are evident at different frequencies in healthy controls between bladder empty and full states. This represents an initial step in the evaluation of bladder pain. Next steps include discrete dipole source modeling, followed by distributed cortical source estimation. Once cortical location and frequencies of normal bladder pain in healthy controls are known, investigation of pathologic states, such as interstitial cystitis can begin. We can begin to determine if a central cortical dysfunction is present in patients with chronic pelvic pain. If this difference is proven, EEG evaluation can be used as an objective measure to direct clinicians toward more effective therapeutic options i.e.. noninvasive neuro-stimulation techniques and pharmacotherapy. Neurophysiological assessment may provide a framework by which clinicians can approach some of the most challenging patients in medicine.

P-27. Prevalence and determinants of urinary stress incontinence in the city of Campeche, Mexico

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Objective: Urinary incontinence affects women of all ages, but is particularly prevalent at midlife. In the Nurses’ Health Study II, 43% of women aged 37 to 54 reported leaking urine at least once/month. Determinants of urinary incontinence include age, ethnicity, parity, age at first birth, hysterectomy, menopausal status, hormone therapy, obesity, and smoking. The purpose of this study was to examine the prevalence and determinants of urinary stress incontinence among women at midlife in the city of Campeche, Mexico. Design: To date, a structured survey has been administered to 1288 women aged 36 to 67 in the city of Campeche. Women also participated in anthropometric, strength, and balance measures. Women were categorized as Mayan (n=71), non-Mayan (n=49), or not clearly definable (n=18) on the basis of their two last names, place of birth, and language, and the two last names, place of birth, and language of their parents and grandparents. Menopausal status was classified as pre-menopausal (regular menses or small changes), peri-menopausal (cycles changed in frequency by at least 6 days or more, or missed a period), or post-menopausal (no menses in the past 12 months). Women were asked if they had experienced a list of symptoms during the past two months, including “se orina con el esfuerzo o la risa?” (have you urinated with exertion or laughter?); Chi-square analyses and t-tests were used to examine urinary stress incontinence in relation to variables noted from the literature, as well as history of tubal ligation, a range of daily activities, and measures of strength and balance. Based on a review of the literature and data collected from a focus group following were emplaced into the logistic regression model, and examined by backwards stepwise analysis: age (<45, 45-50, 50+), menopausal status (pre, peri, post), ethnicity (Mayan, not Mayan, not defined), smoking, history of hysterectomy, history of tubal ligation, days per week that women swept floors (0-7), BMI (<25, 25-29.9, 30+), parity (0, 1,2,3+), and ability to stand with one foot in front of the other for 30 seconds. Results: To date, participants have a mean age of 47.5 years (s.d. 5.8), a mean parity of 2.0 children (s.d. 1.3), and a mean BMI of 30.8 kg/m2 (s.d. 5.9). Fifteen percent of women reported a history of hysterectomy, 46% a history of tubal ligation, 35% were pre-menopausal, 32% peri-menopausal, and 34% post-menopausal. The frequency of urinary stress incontinence was 50%. Stress incontinence was more frequently reported by women who were overweight or obese compared to women of normal/under-weight (52% and 58% vs. 20%, p<0.05). Stress incontinence was also more frequently reported by women with a history of tubal ligation compared to women without a history of tubal ligation (61% vs. 40%, p<0.05). Other significant determinants in univariate analyses included not being able to stand with one foot in front of the other for 30 seconds, and more days per week a woman swept the floor. Four variables were included in the final logistic regression model: BMI, history of tubal ligation, number of days a woman swept the floor, and the inability to balance with one foot in front of the other. All increased the likelihood of stress incontinence. Conclusion: Data collection continues in the city of Campeche. To date, one half of participants aged 36 to 67 reported stress incontinence during the two weeks prior to in-person interview. Association of an elevated BMI and stress incontinence is consistent with other studies. It appears that tubal ligation, rather than history of hysterectomy, is associated with stress incontinence in this population. Women in this urban community are not highly active, so it is interesting to see that one of the few vigorous activities, sweeping the floor, is associated with stress incontinence. A measure of balance, standing with one foot in front of the other for 30 seconds is also related to stress incontinence and requires further investigation.

P-28. Effects of black cohosh on estrogen biosynthesis in hippocampus of non-human primates ex vivo in vitro and in human neuroblastoma cells in vitro

Petra Stute, MD1,2, Gunnar Habermann2, Hans-Henrin Heinheke-von Zepelin, Ph.D.1,2, Hans-Alexis de Arribas1, Obstetrics and Gynecology, University Hospital, University of Bern, Berne, Switzerland; 1Covance Laboratories GmbH, Muenster, Germany; 2Schaper & Bruegger GmbH & Co. KG, Salzgitter, Germany

Objective: Preclinical data indicate a positive impact of steroid sulfatase (STS) inhibitors on menopausal symptoms. The aim of the study was to investigate the impact of an isoflavone extract of Cimicifuga racemosa (iCR, black cohosh), 17b-estra-diol (E2) and testosterone (T) on local estrogen formation in hippocampus of non-human primates ex vivo in vitro and human neuroblastoma cells (SH-SY5Y) in vitro. Design: Neuroblastoma cells were incubated in RPMI 1640 medium containing 5% steroid depleted fetal calf serum for 3 d, and subsequently incubated in absence or presence of iCR at 10 μg/ml (n=5) and 1 μg/ml (n=5), E2 at 10-8 M (n=5), and 10-6 M (n=5), and T at 10-8 M (n=5), and 10-6 M (n=5) at 37°C for 24 h directly in cell culture wells (iCR). Hippocampus tissue from healthy female cynomolgus macaques (n=14) was homogenized and treated accordingly. STS activity was evaluated by incubating homogenized brain tissues and separating the products estrone (E1) and E2 by thin layer chromatography. Results: Basal STS activity was detected in both, untreated hippocampus tissue and SH-SY5Y cells in vitro. In both systems, local E2 formation was significantly higher than E1 formation. In hippocampus, STS activity was significantly diminished by iCR in a dose-related manner (n=14; control: 37.8± 3.6 vs. iCR (10 μg/ml): 11.5 ± 1.2 and E2 (1 μg/ml): 28.8 ± 2.9 fold). In contrast, testosterone (T) was reduced by E2 at 10-6 M (n=3) and 10-8 M (n=3) by 5.7% only (p=0.1). In SH-SY5Y cells, direct incubation with both, iCR and T significantly reduced STS activity (n=5; control: 1416.4± 114.7 vs. iCR (10 μg/ml): 295.4 ± 12.3 and 10-6 M (n=5) at 37°C for 24 h directly in cell culture wells (iCR). Equol producing bacteria can make -equol alone or other bioactive components of SE5-OH such as isoflavones (daidzein, genistein, and equol) (Fig 3, right). Significant differences in univariate analyses included not being able to stand with one foot in front of the other for 30 seconds.

P-29. S-equol and the Fermented Soy Food Containing S-equol (SE5-OH) effect on Bone Loss, Blood Flow, and Mammary Estradiol Levels in Overiectomized Rats

Tomomi Ueno1, Yuko Touser1, Shigeto Uchiyama, MS1, Soh Iwashita2, Belinda H. Jenkins2, Yoshikio Ishimi2. 1Saga Nutraceutical Research Institute, Otsuka Pharmaceutical Co., Ltd., Saga, Japan; 2Food Function and Labeling, National Institute of Health and Nutrition, Tokyo, Japan; 3Scientific Affairs, Pharmacvet LLC, Northridge, CA

Objective: Past research has evaluated isoflavone supplements for menopausal management with mixed efficacy results. The discrepancy of the results could be attributed to whether women had equal producing capacity. Only people who host equol producing bacteria can make S-equol after soy consumption. Therefore, we have developed a fermented soygirm food containing S-equol (SE5-OH) using equol producing lactobacillus bacteria (Lactobacillus acidophilus strain 20-92). In a previous study, it has been reported that SE5-OH improved menopausal symptoms (especially, hot flushes and shoulder stiffness), lipid profile, glycemic control, bone and skin health for postmenopausal women. S-equol is believed to be the primary biologically active metabolite of SE5-OH but it is not fully understood how the S-equol alone or other bioactive components of SE5-OH such as isoflavones (daidzein,

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genistin, and genistein analog) contribute to the observed clinical effects. This study used ovarioctomized rats to compare the effects of SE5-OH and S-equol on vascular function. The rats were exposed to SE5-OH, estradiol (E2), or no treatment. The body tissues after ingestion of SE5-OH and S-equol were assessed.

Table 1. Severity of Symptoms Ranked 0-4 in Hispanic Women Differentiated by Level of Acculturation

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<th>2</th>
<th>3</th>
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Table 2. Regression Results of Reported Moderate-Severe Menopausal Symptoms in Hispanic Women

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<td>0.94</td>
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<td>0.94</td>
<td>0.78</td>
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<td>0.27</td>
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<td>Night sweats with night sweats with night sweats with night sweats with night sweats with night sweats with hot flashes</td>
<td>0.78</td>
<td>0.66</td>
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P-30. Comparison of the quality of life in Afro-descendant and indigenous Colombian women in climacteric who present hypoactive sexual desire disorder

Cindy Arteta-Acosta, Katherin Portela, Alvaro Monterrosa-Castro. Universidad de Cartagena, Cartagena, Colombia

Objective: To compare the results of the assessment of quality of life in afrodescendant women with hypoactive sexual desire disorder (HSDD) with those obtained in indigenous women with HSDD.

Methods: Design: A convenience sample of 204 Afro-descendants and 216 indigenous women with HSDD was studied (49.9±5.4 and 51.5±5.6, respectively). There were not significant differences in marital status, menopausal status and activity as housewife. Indigenous women had more years in postmenopause. Major prevalence of heart discomfort and dryness of vagina was observed in indigenous women (p<0.001) without differences in other manifestations. Indigenous women had more impairment of Somatic and urogenital domain and QoL than Afro descendants with HSDD, but it was not Statistically significant. Conclusion: 36% Indigenous women had severe deterioration of QoL, mainly by severe impairment of Urogenital Domain 40% (p<0.05). Indigenous had two times more risk than Afrodescendants with HSDD to present severe deterioration of QoL (OR:2.2 [1.4-3.5]) and Urogenital Domain (OR:1.9 [1.3-2.9])

P-32. Central obesity as risk factor for sleep quality and insomnia in climacteric Afro-descendant women

Cindy Arteta-Acosta, Sally Parra-Almeida, Alvaro Monterrosa-Castro. Universidad de Cartagena, Cartagena, Colombia

Objective: to establish if the central obesity (CO) is risk factor for the general sleep quality, the impact of sleep in the daily activities and insomnia (Definition: Cross-sectional study, part of the CAVIMEC (Calidad de Vida en Menopausia y Etnias Colombianas) research project, carried out in afro-descendant women, natives and residents in communities from Cartagena, Cartagena, Colombia and indigenous women from the west region of Colombia.

Methods: A convenience sample of 204 afro-descendant women of peri-menopausal status were included. The average of the abdominal circumference was: 83.0 cm. 50.5% had overweight and 23.9% had obesity. The average of age was 55.4 years. The average of Body Mass Index was: 27.6±4.5. 50.5% had overweight and 23.9% had obesity. The average of the abdominal circumference was: 83.0±10.4. 35.5% were in premenopause, 15.4% in perimenopause and 49.1% were postmenopausal women. There were not significant differences in relation to menopausal status, hypothyroidism, diabetes mellitus, hypertension and use of hormonal therapy, according to the presence of CO.

The prevalence of insomnia in all the population was 39.0%, being 42.8% in women with CO and 37.0% in women without it. Women with CO had lower total duration of sleep, worse well-being and functioning during the day (p<0.05). There were not observe differences in relation to daytime sleepiness, quantitative assessment and sleep quality (p=0.1). Women with CO presented worse impact of insomnia on the activities of the day (p=0.03). In a model of univariate logistic regression, the CO was not risk factor for sleep induction, awakenings during the night, final awakening earlier than desired, total sleep duration, overall quality of sleep, sense of well-being during the day, functioning (physical and mental) during the day, somnolence, quantitative assessment of sleep, impact of sleep on the daily activities and Insomnia (p<0.005). CO was not risk factor for subjective characteristics of sleep in afro-descendant women from the west region of Colombia.

CLINICAL POSTER PRESENTATIONS (continued)
Objective: Numerous studies of acupuncture for hot flashes (HF) have reported end of treatment data, but few studies provide results following treatment completion. This presentation provides end of treatment results of a randomized trial of acupuncture treatment for menopausal HF and post-treatment follow-up data. Design: Peri or postmenopausal women reporting an average of at least 4 HF per day based on daily diary completion for 2 weeks were recruited from the community and randomized to an acupuncture or wait-list control group. The study was conducted at 2 sites: Winston-Salem and Chapel Hill, North Carolina. Women in the acupuncture group were allowed to receive up to 20 acupuncture treatments in the community (2 acupuncturists at each site) over a 6-month period and were then followed for 6 additional months. In this crossover design, control group women were followed for 6 months with no treatment and then allowed to receive up to 20 treatments over 6 months. For both groups, the number of treatments received was allowed to vary and determined by the participant and her acupuncturist in order to ultimately examine patterns of treatments (e.g. frequency and dose) to achieve treatment effectiveness. All women kept daily diaries of their HF (frequency and severity) throughout the first 6 months and completed one weekly diary per month thereafter. Results: 209 women were randomized to the study and 184 completed the 6-month follow-up. Women in the acupuncture arm received a median number of 19 acupuncture treatments. At 6 months, frequency of daily HF decreased by 34.5% in the acupuncture group and increased by 2.4% in the control arm (p = 0.0001) (see figure). At 9 months (3 months following end of treatment) the decrease in frequency of HF (from baseline) was 28.4% in the acupuncture arm, for an increase of 6.1% from 6 months (p = 0.02). The control arm showed a decrease in frequency of 21.3% from baseline. Similar results were found for the HF index (frequency X severity). Conclusion: Results show a clear benefit of acupuncture for reducing menopausal HF. Although this benefit begins to decline 3 months following the end of treatment, there is still an improvement over baseline. All follow-up data will be completed by July 2014 and additional results will be presented for 6 months following the end of treatment. Acknowledgement: Supported by Grant R01AT005854 from NCCAM, NIH.

P-35.
Quality of life in women with cervical cancer
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Objective: Cancer of the cervix is the second most common gynecological tumor. Pelvic radiation therapy is one of the most used forms of treatment and it is associated with substantial side effects that may lead to quality of life loss. Studies have evaluated the effects of radiation therapy but there are few data about quality of life before initiating the treatment. Our objectives were to evaluate quality of life and its associated factors in women with cervical cancer before the initiation of radiotherapy. Design: A cross-sectional study was conducted with 80 women with cervical cancer, aged 18-75 years, referred for radiotherapy at the Women’s Hospital of the State University of Campinas – Brazil, from January 2013 to March 2014. The outcome variable was quality of life, assessed using the abbreviated version of the World Health Organization (WHOQOL-BREF) questionnaire. The independent variables were sociodemographic data, health related habits and the characteristics of the neoplasm. Statistical analysis was carried out using frequency distribution, Mann-Whitney test and multiple linear regression using the stepwise selection criteria. Results: The mean age of the women was 48.1 (± 13.5) years. Thirty-four women (42.5%) were postmenopausal, 57.5% were white and 55% had clinical stage IIIb. In the final statistical model, having a more advanced clinical stage (p = 0.04) and lower family income (p = 0.01) were associated with worse quality of life in the physical domain of the questionnaire. In the psychological domain, use of any medication (p = 0.02) was associated with worse quality of life. Regarding the environment domain, having a more advanced clinical stage (p = 0.04) and lower family income (p<0.01) were associated with worse quality of life. Having higher schooling (p = 0.03) and no smoking (p<0.01) were associated with better general quality of life. Not having undergone surgery before radiotherapy (p = 0.01) and having higher schooling (p<0.01) were associated with worse general health. No smoking (p = 0.01) was associated with better general health. Conclusion: Quality of life before the initiation of radiotherapy treatment was better for women with less advanced clinical stage, lower family income, and smoking are some of the factors associated with poorer quality of life before radiotherapy. This information is useful to identify women who need more support and attention during the course of therapy for cervical cancer.
Acknowledgments: Funding by Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) number 2012/09215-7

P-36.
Quantitative Analysis of Internet Searches on Menopausal Issues
Gloria Bachmann, Dr., Nicole M. Scaramella. Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ
Objective: Menopause is generally viewed as a negative life event needing intervention. This viewpoint appears to be reinforced by the Internet with a plethora of sites unilaterally directed to distressing menopausal sequelae, such as vasomotor symptoms, sexual dysfunction, atrophic skin and body changes, unwanted weight gain and suggested management options. Quantifying the number of internet searches directed to female aging issues, especially in the area of weight gain, can be a starting point for understanding the depth of menopausal education accessibility by the Internet and for focusing on ways clinicians can proactively address these issues with balanced information. The Internet releases articles and websites that relay divergent messages to the general population, especially in the area of menopause. One aspect of menopause that has garnered significant attention is unwanted midlife weight gain. Societal changes and advancements in food production means that even slight weight gain leads to poor health and loss of sexual allure. The concept of an unflattering body image due to menopause often stems from the media, with the Internet becoming an important source of this information. This research evaluated the extent that Internet users are performing searches on menopause, with specific attention to searches on menopausal weight. Design: This abstract reviewed mainstream website articles for both quantity and quality through Google using search terms such as: “menopause,” “menopause symptoms,” “menopause weight gain,” and more. Google
P-37. Associations between supplement information sources and menopausal women’s consumption of herbal supplements
Natalie Crousella, MPH candidate,1 Elizabeth J. Roemer, M.S.2, David A. Baker.2
1Program in Public Health, Stony Brook University, Stony Brook, NY; 2Department of Obstetrics, Gynecology and Reproductive Medicine, Stony Brook University, Stony Brook, NY
Objective: For menopausal women who may be interested in using supplements to support their health and manage their climacteric symptoms, there are many potential sources that may be consulted to inform herbal supplement consumption; it is unclear whether the source of supplement information is ultimately associated with supplement consumption. Furthermore, the role of consumer perception of supplement regulation within this association is unknown. We investigated the potential associations between five information sources, which included: (1) friends, family members, co-workers, or self; (2) healthcare provider (including doctors, pharmacists, drugstore); (3) the Internet; (4) books, newspapers, newsletters, radio, magazines, television shows or commercials; 5) a health store—and one-time herbal supplement consumption. Design: Using data from Stony Brook University’s Dietary Supplements in Menopause survey of postmenopausal women, ages 55 to 75, the association between the five information source categories and any herbal supplement consumption were evaluated using a bivariate chi-square analysis and multivariate logistic regression. Covariates included age, race, income, education, marital/partnership status, the severity of mental symptoms of menopause, the severity of physical symptoms of menopause, self-perceived health status and perception of the Food and Drug Administration’s role in supplement regulation. The sample was then stratified, or divided, based on whether respondents knew the FDA does not regulate supplements and, the multivariate regression was performed in each of these subpopulations. Results: Menopausal women who received supplement information from a healthcare professional had a 54 percent reduced odds (OR = 0.46, CI = 0.27–0.78) of having consumed an herbal supplement at least once relative to those who did not consult this information source. Those who experienced severe physical symptoms of menopause had an 84 percent increased odds (OR = 1.84, CI = 1.01–3.34), relative to those with mild symptoms, of having consumed an herbal supplement at least once. Those respondents who were unsure of whether the FDA regulates supplements had 60 percent reduced odds (OR = 0.40, CI = 0.17–0.92) of having consumed an herbal supplement at least once compared with those who believed the FDA does not regulate supplements. After dividing the population based on knowledge of whether the FDA does not regulate supplements, among respondents who believed the FDA does not regulate supplements, those who used healthcare providers as a supplement information source had 73 percent reduced odds (OR = 0.27, CI = 0.12–0.62) of having consumed an herbal supplement at least once compared to those who did not consult this information source. Within this subpopulation, those who consulted health stores for supplement information had 5.23 times the odds (OR = 5.23, CI = 1.57–17.36) of having consumed an herbal supplement at least once compared to those who did not consult this information source. Conclusion: The perception of the FDA’s role in supplement regulation, as well as the information sources consulted, enrich our understanding of supplement information sources and consumption behavior. Furthermore, by using this variable to divide the population, we were able to examine the association between having a positive outcome within a new subsample. We found a specific perception of supplement regulation—associations between the supplement information sources consulted and the one-time herbal supplement consumption altered after this division of the population. This research demonstrates a need for healthcare providers to communicate with all their menopausal patients about supplement regulation.

P-38. The Effect of Conjugated Estrogens/Bazedoxifene on Body Weight in Postmenopausal Women
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Objective: The Effect of Conjugated Estrogens/Bazedoxifene (CE/BZA) on body weight and body mass index (BMI) in postmenopausal women in the Selective estrogens, Menopause, And Response to Therapy (SMART) trials. Design: Data were pooled from 5 randomized, double-blind, placebo (PBO)- and active-controlled studies in non-hysterectomized postmenopausal women aged 40–75 given CE 0.45 mg/BZA 20 mg (n=1067), CE 0.625 mg/BZA 20 mg (n=1598), or PBO (n=1256) for 12 weeks to 2 years to examine body weight changes and shifts from baseline BMI (kg/m2) category (underweight <18.5, normal 18.5 to <25, overweight 25 to >30, obese ≥30). Treatment effect modification by baseline weight/BMI was tested (interaction alpha=0.15). Results: Changes from baseline body weight and incidence of BMI category shifts were not significantly different with CE/BZA vs PBO. Mean body weight change was <1.0 kg with CE 0.45 mg/BZA 20 mg, CE 0.625 mg/BZA 20 mg, and PBO. The percentage who gained weight, shifting to overweight (14.7%, 14.3%, 14.7% respectively) or obese (10.5%, 12.8%, 15.1% respectively) was similar in all 3 groups, as was the percentage who lost weight, shifting to underweight (1.0%, 1.2%, 0.7% respectively), normal (13.0%, 15.9%, 17.5% respectively), or overweight (22.3%, 22.3, 18.3% respectively). Most BMI category shifts were within ±7%. Efficacy of CE/BZA on change from baseline hot flush frequency was not significantly modified by baseline weight/BMI; a significant interaction between baseline BMI and hot flush severity was seen (P=0.112). Conclusion: CE/BZA effects on body weight and BMI were minimal and similar to placebo. Weight and BMI influenced efficacy for hot flush severity, but not frequency.

P-39. The Association of Breast Aberrant Califications (BACs) and Cardiovascular Diseases: Preliminary Results of a 10-Year Prospective Study
Ragad Asmaro, MD, Elizabeth Budnik, BS,1,2 Xuezh Ji, MD, LA,2 Lauren Good4, Peter F. Schatz, D.O.3, 1ObGyn & Int. Medicine, Reading Hospital, Reading, PA; 2ObGyn, PCOM, Philadelphia, PA; 3ObGyn & Int. Medicine, Jefferson Medical College, Philadelphia, PA
Objective: BACs are califications 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 califications differ from that of internal califications. Whereas a benign nature of BACs have been suggested, internal califications are strongly associated with Cardiovascular Disease (CVD) related morbidity and mortality. The true clinical significance of BAC presence is not yet known, however. Thus, the primary objective of this 10-year 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 cardiovascular disease (CVD), specifically stroke and Coronary Heart Disease (CHD), 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 experienced by the patient over the 10 years of follow-up. Ten-year follow-up data is currently being collected for the patient-complication time to date were collected (angina, abnormal angiography, MI, stenting, CABG, stroke, CHD). Mammograms, which screened for BACs along with baseline demographics and CVD risk factors. Results: Of 1,995 patients enrolled in the study, 1,725 (87%) were BAC- negative and 270 (13%) were BAC positive at baseline. Included in the current statistical analyses are the preliminary 10-year follow-up data from 612 patients with 533 (87%) BAC-negative and 79 (13%) BAC-positive patients. A multiple logistic regression model was used with CHD and stroke as outcome variables. All of the risk factors were taken into account in the model (BAC, age, HTN, smoking, diabetes, hypercholesterolemia, family history of CVD, and menopausal status). Out of the 612 patients, 599 were negative for stroke at baseline, of which 13 developed a stroke over the 10 year follow-up. Five out of 74 who were BAC-positive at baseline developed a stroke, while only 8 out of 525 BAC-negative patients developed a stroke (6.8% vs 1.5%, p<0.015). While BAC was not a significant risk factor for stroke (OR 4.67, 95% CI 1.48-14.66). As for CHD (angina, abnormal angiography, MI, or CABG), 601 patients were CHD-negative at baseline, of which 25 developed CHD over the 10 year follow-up. Six out of 74 who were BAC-positive at baseline developed CHD and 19 out of 527 BAC-negative patients developed CHD (8.1% vs 3.6%, p<0.1). While BAC was not a significant risk factor for CHD (OR 2.36, [CI 0.91-6.11), logistic regression only identified HTN as a significant risk factor (OR 3.85, 95%CI 1.69-8.74). Conclusion: The presence of BACs on routine mammography indicates a significantly increased 10-year risk of stroke. We were not able to demonstrate a significant association (p<0.1) between BAC and CHD. Since data collection is still ongoing, we cannot rule out the possibility that this finding may change upon final analysis. Interestingly, HTN was found to be a significant single risk factor for CHD. While completion of this study along with additional large prospective studies may be needed to confirm our preliminary findings. The development of cardiovascular diseases, the evidence that BACs are benign is waning.
P-40. Sexually Risky Behavior in College-Aged Students and Correlation to finds in Older Women
Carol Caico, PHD, N.P., Nursing, NYIT, Safford, NY
Objective: To examine college-aged students sexual risky behavior taking risk and determine their knowledge of STIs. Look at risky behavior in older women to determine if same risks. Design: Design: Exploratory Descriptive Design utilizing a monkey-survey. Participants/Setting: A convenience sample of college-aged students between the ages of 18-24 in a private suburban college in the Mid-Atlantic Region.
Results: Seven hundred and seventy students responded to the survey. Findings revealed that 33% had sexual intercourse with two to five individuals, and 15.5% between eleven and twenty sexual partners. 50.9% had unprotected sexual intercourse, not using condoms. 22.1% did not insist on using condoms for sexual intercourse and 24.7% responded that they sometimes insist on condom use. 47.2% are not worried about getting AIDS. 41.3% never examine partners for genital sores or abrasions, and only 22.3% do so sometimes. 55.9% disagree with sexual abstinence to avoid STIs. 68-86% answered questions about specific STI’s, correctly, 42.4% would rate themselves as not being very knowledgeable about sexually transmitted infections. 12.4% of the females had unintended pregnancies and overall 74.9% would not feel comfortable discussing their sexual activity with their mothers. 58.1% use alcohol prior to or during sexual intercourse. In applying research to older women it is found that they are practicing same risks and acquiring sexually transmitted infections. Conclusion: Findings of the study indicated that sexual risky behavior is practiced by this population. In addition there is a lack of adequate knowledge about STIs, the lack of concern demonstrates a disregard in this young population for transmitting or contracting Results are correlated with literature and clinical findings in older women.

P-41. A Randomized, Double-Blind, Controlled Trial on the Effects of a Soy-Based Dietary Supplement Compared to Low-Dose Hormone Therapy on Quality of Life in Postmenopausal Women
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Objective: To compare the effects of a soy-based dietary supplement, low-dose hormone therapy (HT) and placebo on climacteric symptoms and on quality of life (QOL) of postmenopausal women, and to evaluate the impact of the type of treatment for menopausal symptoms and their correlation with QOL. Design: Sixty participants were recruited from gynecologic outpatient clinics at the Center for Women’s Integrative Healthcare of the University of Campinas and at the Leonor Mendes de Barros Hospital in São Paulo, Brazil to participate in a 16-week double-blind, randomized, placebo-controlled trial. The women were randomized into three groups: Hormone therapy: one tablet containing 1mg of estradiol and 0.5mg of norethisterone acetate, in addition to 2 portions/day of placebo powder. Soy group: one placebo tablet plus 2 portions/day of dietary soy supplementation powder containing a total of 90 mg of isoflavone/day. Placebo group: one placebo tablet and 2 portions/day of placebo powder. Menopausal symptoms were evaluated through Menopause Rating Scale (MRS). QOL was measured by the abbreviated version of the World Health Organization’s Quality of Life instrument (WHOQOL-BREF) at baseline and at 16 weeks of treatment. Statistical analysis: MRS and QOL scores were assessed over time by the Wilcoxon signed rank test and Kruskal-Wallis test. Correlation analysis was performed using the Correlation Spearman Coefficient. Results: The mean age of the patients was 52.4 years (SD 3.9) and mean age at menopause was 48 ± 3.7 years. Comparison between groups revealed a statistically significant improvement in somatic and urogenital symptoms in the users of HT and dietary soy supplementation. QOL scores increased significantly in the following domains: physical health, psychological health and urogenital symptoms in the users of HT and dietary soy supplementation. Comparison between groups revealed a statistically significant improvement in somatic and psychological domains and also in general health assessment. Conclusion: Only the HT group showed a significant correlation between the improvement of climacteric symptoms and the improvement in QOL. Our findings suggest that HT may improve climacteric symptoms and QOL to a greater extent than soy therapy and placebo.

P-42. Postmenopausal weight change and fracture incidence in the Women’s Health Initiative Study
Carla J. Crawford-Stein, MS1, Vedat Yildiz2, Jean Waechtlin-Wende1, Karen C. Johnson, MD3, Zhao Chen1, Scott Grogg4, Nicole Wright5, Jane Caley6.1. University of California, Los Angeles, Los Angeles, CA; 2. Ohio State University, Columbus, OH; 3. State University of New York at Buffalo, Buffalo, NY; 4. University of Tennessee Health Science Center, Memphis, Memphis, TN; 5. University of Arizona, Tucson, AZ; 6. University of Alabama at Birmingham, Birmingham, AL; 7. University of Pittsburgh, Pittsburgh, PA
Objective: To determine associations of change in body weight and subsequent fracture incidence among postmenopausal women, classified by anatomical region. Design: Prospective cohort study from the Women’s Health Initiative Observational Study and Clinical Trials. The cohort included 120,566 postmenopausal women, aged 50-79 years at baseline, followed from 1995-2013 (mean follow-up duration 11 years). Predictors were: 1. percentage change in measured body weight (i.e. weightvisit 3 - weightbaseline / weightbaseline * 100), classified as: 0, 5-15% change, >15% loss (i.e. weightvisit 3 < weightbaseline * 0.85); 2. self-reported intentional and unintentional weight loss. Outcomes were: incident self-reported fractures of the upper limbs, lower limbs, and central body, medical record-confirmed hip fractures. Results: Mean participant age was 63 years; 16% were nonwhite. Average weight change (year 3 - baseline) was -10.0 kg (SD 15.0 kg) in the weight loss group and 8.7 kg (SD 13.4 kg) in the weight gain group. Compared with stable weight, weight loss was associated with 62% higher hip fracture incidence (adjusted hazard ratio [aHR] 1.62, 95% CI 1.45-1.81) and higher incidence of upper limb (aHR 1.11, 95% confidence interval [CI] 1.04-1.19) and central body fracture (aHR 1.29, 95% CI 1.20-1.39) and lower hip fracture incidence (aHR 1.16, 95% CI 1.09-1.22) fracture incidence (Table). Conclusion: Weight gain and weight loss are associated with increased fracture incidence, but associations differ by fracture location.

Table: Association between body weight change (follow-up visit 3 minus baseline) and fracture incidence according to anatomical location, before and after adjustment for falls1

<table>
<thead>
<tr>
<th>Weight change</th>
<th>Hip fracture (65% CI)</th>
<th>Lower limb fracture (65% CI)</th>
<th>Central body fracture (65% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stable</td>
<td>1.00 (0.97, 1.03)</td>
<td>1.00 (0.97, 1.03)</td>
<td>1.00 (0.97, 1.03)</td>
</tr>
<tr>
<td>Weight loss</td>
<td>1.16 (1.13, 1.20)</td>
<td>1.07 (1.04, 1.10)</td>
<td>1.17 (1.13, 1.21)</td>
</tr>
<tr>
<td>Weight gain</td>
<td>0.84 (0.81, 0.88)</td>
<td>0.88 (0.85, 0.91)</td>
<td>0.98 (0.95, 1.01)</td>
</tr>
</tbody>
</table>

1. Adjustment for falls refers to adjustment for the number of falls in the past 12 months
2. Includes fractures of the upper arm/humerus, shoulder, lower extremity, and elbow
3. Includes fractures of the hip, pelvis, and spine
4. Includes fractures of the hip, pelvis, and spine
5. Includes fractures of the hip, pelvis, and spine

P-43. Management of Postmenopausal Chronic Uterine inversion
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Objective: To highlight a unique technique of subtotal vaginal hysterectomy for postmenopausal chronic uterine inversion Design: Case details- 55 year old postmenopausal woman seen with something coming out of the introitus, severe pain & bleeding p/v since 4 months, had menopause 6 yrs back. After obtaining informed consent the patient was operated on. On examination the cervix was not palpable, the uterus was not felt. Only the fundus of the uterus was felt coming out of the introitus. On P/v uterus was not palpable. A decision for Examination under Anaesthesia was taken then identified to be a case of inversion with a small benign submucous fibroid 4x3x2.5cm. There was profuse bleeding, the fibroid was clamped & removed. The constriction ring was very tight & flushed with vagina,vagina was atrophic & friable.She was not fit for prolonged anaesthesia.We could not perform the routine surgeries for inversion so the decision for this unique approach was taken. Results: Steps of Operation-After catheterization of bladder, the mass which was coming out of the introitus was the fundus of the uterus surrounding the constriction ring. A vertical incision was given on whole of this prolapsed fundus extending anteroposteriorly from 12 o'clock position to 6 o'clock position, the fundus was bisected into two halves & opened. On examination the subcutaneous pedicles & round ligaments of both sides were then visualized, they were then clamped cut & ligated on both sides one by one and were then pushed into the perineal cavity. The prolapsed part of uterus was cut flush to the constriction ring step by step .Cut edges were sutured by continuous interlocking stitches. Thus whole of the body of the uterus was removed & cervix remained in situ with its blood supply. Inversion was corrected in a short span of time - 8 minutes.Postoperative recovery was uneventful, discharged on the 3rd postoperative day. She came for regular follow ups & was perfectly alright. Conclusion: This is a safe, effective, time saving procedure . As this case was postmenopausal, the tissues were friable & atrophic there was a danger of trauma to the pedicles and extension of tear up to the uterine vessels if reposition would have been done by the routine techniques,so this unique technique proved useful.
incision anteroposteriorly on the prolapsed fundus

P-44. Efficacy and safety of odanacatib in postmenopausal women with osteoporosis: overall results and age subgroup analysis from the Phase III Long-Term Odanacatib Fracture Trial

Michael R McClung1, Bente Langdahl2, Socrates Papapoulos3, Kenneth G Saag4, Tobias III Long-Term Odanacatib Fracture Trial Objective: Odanacatib (ODN), a selective oral inhibitor of cathepsin K, is in development for the treatment of osteoporosis. The Phase III Long-Term Odanacatib Fracture Trial (LOFT; NCT00529373) and its planned blinded extension in which patients continue on their originally assigned treatment, evaluated the efficacy and safety of ODN in reducing the risk of fractures in postmenopausal women with osteoporosis. Subgroup analyses were conducted to investigate the efficacy of ODN as a function of patients’ baseline characteristics. Design: This randomized, double-blind, placebo-controlled, event-driven study enrolled women ≥65 years of age with a bone mineral density (BMD) T-score ≤−2.5 at the total hip or femoral neck or with a radiographic vertebral fracture and a T-score ≤−1.5 at the total hip or femoral neck. Participants were randomized to either ODN 50 mg once-weekly or placebo (1:1) and also received weekly vitamin D3 (50,000 IU) and daily calcium supplements as needed to ensure a total daily calcium intake of ≥1200 mg. Primary efficacy endpoints were new morphometric vertebral, clinical vertebral, hip, and clinical non-vertebral fractures. Secondary endpoints included safety and tolerability, clinical vertebral fractures, lumbar spine and hip BMD, and bone turnover markers. Treatment effects on the primary fracture endpoints as well as BMD and safety were investigated for subgroups of patients classified according to age (<70 years, ≥70 years, 70 to <80 years, and ≥80 years). Results: A total of 16,713 participants were randomized at 387 centers in 40 countries, with 16,071 included in the analyses, and 642 were used for statistical analyses. Duplicate randomization (n=483), failure to take any study drug (n=156), at baseline, mean (SD) age was 72.8 (3.5) years, 57% were Caucasian, 46.5% had a vertebral fracture prior to study entry, and mean BMD T-scores were: lumbar spine -2.7, total hip -2.4, and femoral neck -2.7. This event-driven study was planned to be completed when 237 patients had experienced a hip fracture. A prespecified interim analysis was performed when ≥70% of targeted events had accrued. An external Data Monitoring Committee (DMC) reviewed these data and recommended that the base study be closed early due to robust efficacy and a favorable benefit-risk profile. The DMC noted that safety issues remained in certain selected areas and recommended that safety and efficacy continue to be monitored in the planned blinded extension trial. Data from an average follow-up of 40.8 months have been accrued from the base and extension studies, with 7,081 patients completing at least 4 years of follow-up. Age subgroup populations were: <70 years, n=5,067 (31.5%); 70 to <80 years, n=9,077 (56.5%); and ≥80 years, n=1,927 (12.0%). At the time this abstract was written, final data analyses were not complete. Fracture incidence rates, BMD and safety data will be presented for each age subgroup of patients treated with ODN or placebo. Conclusion: The blinded, placebo-controlled base plus extension study periods of LOFT will provide information on the efficacy and tolerability of ODN in different patient age subpopulations. Acknowledgments: This study was sponsored by Merck Sharp & Dohme Corp.

P-45. The association of vulvovaginal atrophy (VVA) symptoms with health-related quality of life among post-menopausal women in the United States and Europe

Marcia Dtronventura, PhD1, Xuemei Luo, PhD2, Margaret Moffatt, MPH1, Andrew Bushmakin1, Maya Kumar, MPH1, Joel Bobula, MA1, 1Kantar Health, New York, NY; 2Pfizer Inc., Groton, CT; 3Pfizer Inc., New York, NY; 4Pfizer Inc., Collegeville, PA Objective: Vulvovaginal atrophy (VVA) represents vaginal and urogenital atrophy due to an estrogen deficiency and can occur in women of all ages. Although past research has examined the effect of menopausal symptoms broadly, and vasomotor symptoms in particular, few studies have focused exclusively on VVA symptoms and their relationship with health outcomes. The aim of this study is to address this gap by quantifying the burden of VVA symptoms on health-related quality of life (HRQoL) in the United States and Europe. Design: Data were used from the International Women’s Health Study, a cross-sectional Internet survey of women aged 40-75 in the United States, Europe (France, Germany, Italy, Spain, and UK), and Japan (N=12,200). Only post-menopausal women in the United States and Europe were included in the analyses (N=7,068). VVA symptoms were assessed using the Menopause Rating Scale. HR-QoL was assessed using health utility values from the EQ-5D-3L, a generic measure of HR-QoL. VVA symptom severity (no VVA, mild, moderate, severe) was used to predict HR-QoL, in a series of regression models controlling for demographic and health history variables. HR-QoL values for women with moderate-to-severe VVA symptoms were also compared to 10 common chronic conditions (identified as a priori) using regression modeling. Results: Between 39.90% (Germany) and 54.42% (Spain) of respondents reported VVA symptoms; with roughly half of these women also reporting their symptoms as moderate-to-severe. Controlling for demographics and health history variables, HR-QoL decreased with increasing VVA symptom severity in each country (France: EQ-5D health utilities = 0.83 vs. 0.73 for none and severe VVA symptoms, respectively; Spain: 0.88 vs. 0.81; Italy: 0.88 vs. 0.81; and Germany: 0.82 vs. 0.69; UK: 0.80 vs. 0.68; US: 0.86 vs. 0.77; all p<0.05). Pooling data from all countries together and controlling for chronic conditions, the adjusted HR-QoL for women with moderate-to-severe VVA was 0.63, a value comparable to most other chronic conditions assessed in the study (e.g., arthritis = 0.62, asthma = 0.63, COPD = 0.63, though higher than depression (0.59) and fibromyalgia (0.61). Conclusion: The results suggest a high prevalence of VVA symptoms among post-menopausal women in the United States and Europe. There was a consistent effect of VVA symptom severity on worsening health status, increasing level of severity was often associated with a significant and clinically relevant decrement in health utilities. The health utility burden of moderate-to-severe VVA symptoms was similar to other chronic conditions that are present in post-menopausal women such as arthritis, COPD, OAB, and IBS, among others. Although VVA symptoms may be not traditionally viewed as burdensome as other medical conditions, these results suggest the effect on the patient may be similarly dramatic and warrants attention from the clinical community.

P-46. Endogenous Sex Hormones at Midlife are Associated with a More Athrogenic Lipoprotein Profile: The Study of Women’s Health Across the Nation (SWAN)

Samar R. El Khoudary, PhD, MPH, Maria M. Brooks, Rebecca C. Thurston, PhD, Karen A. Matthews. University of Pittsburgh, Pittsburgh, PA Objective: Lipoprotein sub-classes (lower levels of large high-density lipoprotein particles (HDL-P) and a shift in low-density lipoprotein particle (LDL-P) size toward a smaller, denser phenotype) has been reported in postmenopausal women. This suggests a possible hormonal influence on lipoproteins. Whether sex hormone levels in midlife women are associated with lipoprotein profiles may render women more vulnerable to coronary heart disease after menopause. Acknowledgments: The Study of Women’s Health Across the Nation (SWAN) has grant support from the National Institutes of Health (NIH), DHHS, through the National Institute on Aging (NIA), the National Institute of Nursing Research (NINR) and the NIH Office of Research on Women’s Health (ORWH) (Grants U01NR004061; 2Pfizer Inc., Groton, CT; 3Pfizer Inc., New York, NY; 4Pfizer Inc., Collegeville, PA

Design: Data were...
Women with Higher Estradiol Levels After Menopause are at Greater Risk of Atherosclerosis: The Study of Women’s Health Across the Nation (SWAN)

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Objective: The menopause-related reduction in estradiol (E2) levels has been hypothesized to put midlife women at a greater risk of cardiovascular disease. However, the pattern of E2 reduction across the final menstrual period (FMP) varies among women. Four distinct patterns of E2 changes over the menopausal transition were recently identified. The aim of this study was to assess the associations between the identified E2 trajectories over the menopausal transition and early markers of atherosclerosis after menopause. Design: Early markers of atherosclerosis (mean carotid intima-media thickness (cIMT) and presence of carotid plaque (cPlaque)) were measured at visit 12 (after 13.7±0.5 years of follow-up) for 856 naturally postmenopausal women (age 59±5±7 years; White:46±7%, Black:30±7%, Chinese:16±5% and Hispanic:6±1%), who never reported a stroke or a heart attack during follow-up. Linear and logistic regression were used to assess the associations between the identified E2 trajectory groups (Figure 1) and early markers of atherosclerosis. Final models were adjusted for covariates listed under table 1.

Results: cIMT varied significantly by E2 trajectory groups. Women with the medium E2 trajectory had the highest cIMT (cIMT for medium E2 =0.82mm, low E2 =0.77mm, high E2-early decline =0.78mm, and for high E2-late decline cIMT varied significantly by E2 trajectory groups. Compared to women with lower levels of E2 before and after FMP, the levels began to decrease and were lower after 65. IGF rose as well, which was a novel finding. Estrogen reached its lowest points after 50-65+ and a second transition (Geripause) appeared after the age of 65. Symptom complexes were evaluated and reviewed. The second transition is the result of the following factors: 1) Elevated FSH 2) Diminishing IGF-1 3) Estradiol reaching lowest levels 4) Dominance of aging as shown by both questionnaire and laboratory values 5) Occurs at age 65+±2.4 years as shown in figure 1.

Conclusion: These results define two transitions, one at the onset of menopause, and the other after maximal estrogen hormone reductions (geripause). The value of this separation is in the determination of therapy needed to treat viable symptoms. Further study of these transitions should provide both proper therapies and time-line testing opportunities for making better decisions in patient care. This will be particularly useful in the older geripause (very elderly) cases, which are now becoming more prominent.

The Menopause and the Geripause represent two separate stages in female aging

P.47.

How can hot flashes be managed for breast cancer patients and survivors without risk?

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Objective: For patients with breast cancer, the return to a normal quality of life is a key element in their wellbeing. The onset of hot flashes, whether natural or induced by anti-cancer therapy, can make it difficult to achieve this goal. As hormone replacement therapy is contraindicated in these women, other therapeutic methods must be considered. After a comprehensive review of the physiopathology of hot flashes and of the factors aggravating their frequency and severity in patients with breast cancer or in remission, this article takes stock of relevant scientific literature in order to evaluate the efficacy and safety of the various pharmacological and non-pharmacological methods for treating hot flashes. It clarifies the place of a product consisting of purified pollen cytoplasm extracts (Relizen™) as part of the therapeutic arsenal available to postmenopausal women with breast cancer or with a history of breast cancer. Design: A review of the literature shows that the use of antidepressants (venlafaxine, paroxetine, citalopram and fluoxetine), antihypertensives (clonidine) or anticonvulsants (gabapentin and pregabalin), significantly reduces the frequency and severity of hot flashes. The superiority of any of these methods has not, however, been demonstrated. However, the interaction of these products with anti-cancer therapy taken by the patient (usually tamoxifen) and the many side effects induced must be taken into consideration before proposing one of these therapies. The available data do not support the use of “natural” health products such as phytoestrogens, black cohosh and St. John’s wort in the treatment of hot flashes. Few studies have been conducted and none have demonstrated a significant impact on the frequency or severity of hot flashes. Moreover, the use of some of these products, including St. John’s wort and black cohosh, could be harmful for patients treated with tamoxifen because they interfere with its metabolism. Also, they are known for their estrogenic activity, which renders their use inadvisable in women with breast cancer or in remission. All these data emphasize the need for a safe and effective alternative treatment for the management of menopause symptoms in these patients. Results:
P-50. Low Testosterone Levels in Menopausal Women Presenting with Alopecia

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Objective: Female pattern hair loss (FPHL) is most common in postmenopausal women and is further subdivided into patients with androgen excess, often referred to as “androgenic alopecia,” and normal androgen levels. Low testosterone levels have not been reported in the setting of FPHL. We hypothesize that menopausal women with low testosterone levels are not as uncommon an association as the lack of reports suggests. Design: We reviewed 1,294 consecutive charts in a reproductive endocrine practice. Information regarding age, body mass index (BMI), hormonal values, menopausal status, and alopecia was gathered retrospectively. Of the 450 menopausal women, 35 women presented with alopecia. Because measuring testosterone is not included in a routine evaluation of asymptomatic women, we used historic controls (1, 2). In addition, we also compared these women to a group of premenopausal women with hypothalamic amenorrhea and low testosterone levels (3).

Results: The average age (years) was 52.6 ± 5.7, weight (pounds) 137.3 ± 20.8, and BMI (kg/m2) 23.5 ± 4.7. Six of the 35 women had premature menopause and their total and free testosterone levels were not different compared to the women with a normal menopause. Menopausal women with alopecia had mean total testosterone levels of 15.5 ± 10.8 ng/dl compared with historic controls with mean total testosterone levels of 43.2 ± 28.8 ng/dl (P<.001) (1). Free testosterone levels in menopausal women with alopecia, 0.85 ± 0.91 pg/ml, compared to the historical control free testosterone, 0.79 ± 0.41 pg/ml, showed no statistically significant differences (2). Additionally, the menopausal women with alopecia had mean total testosterone levels (15.5 ± 10.8 ng/dl) lower than previously reported in premenopausal women with hypothalamic amenorrhea (32.2 ± 14.2 ng/dl) (P<.001) (3). Conclusion: Low testosterone levels have not been previously reported in menopausal women with FPHL. Our findings challenge current treatment regimens for these patients that often include antiandrogen medications. References for Historical Controls 1. Cauley JA, Gutai JP, Kuller LH, LeDonne D, Powell JG. The epidemiology of serum sex hormones in postmenopausal women. American Journal of Epidemiology. 1989;129(4):312-31. 2. Berrino F, Muti P, Micheli A, Bolelli G, Krogh V, Sciajno R, et al. Serum levels of total and free testosterone, estradiol, and dihydrotestosterone in perimenopausal female monkeys. Journal of the National Cancer Institute. 1996;88(5):291-6. 3. Sum M, Warren MP. Hypothalamic amenorrhea and low testosterone levels (3).

P-51. Improving IUD counseling among Internal Medicine Residents for the perimenopausal female

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Objective: Contraception counseling in the perimenopausal female is an important and often overlooked issue by both generalists and gynecologists. Pregnancy and its associated risks still exist for the perimenopausal female, and each patient should be adequately advised on all forms of birth control. Long acting contraceptive methods, such as the intrauterine device (IUD) are becoming increasingly popular as their utilization is rising and their efficacy has been found to be superior to almost all other forms of birth control methods, and is known to have less surgical risk to patients than invasive sterilization procedures. A pilot study utilizing responses from Internal Medicine (IM) residents at Case Western Reserve University (CWRU) showed a lack of guidance specific to IUDs, including their efficacy, infection risk, and their role in perimenopause and associated positive menstrual-related side effects. IM residents also noted a distinct lack of confidence in their self-reported ability to counsel and refer patients for IUDs. Major barriers included a lack of expert knowledge and experience in counseling IM residents about primary care educational intervention. The intervention included a one hour lecture on the topic of contraception with special attention made for IUDs. A pre-test was administered before the lecture and consisted of two parts: 1) A knowledge assessment which included fifteen evidence based questions based on the principals of IUDs. Seven questions used to assess the residents attitudes, behaviors, and practice patterns surrounding IUD usage, including referral patterns for placement of IUDs. Three months later, each of the 37 residents received post-tests which included copies of the same two forms as mentioned above. Results: Of the 37 residents who completed the pre-test, 20 participants submitted post- tests. IM resident knowledge improved on each individual question (P<.001), and the final pre-test was significantly higher than the post-test (P<.001). IM residents noted a distinct lack of confidence in their self-reported ability to counsel and refer patients for IUDs. The proposed RTC may address this gap in knowledge and improve residents comfort level counseling patients about IUDs, which includes knowledge of benefits, side effects, and side effects of IUDs did not change significantly. Conclusion: There was an increase in provide knowledge on IUDs, however, self- reported confidence in counseling and referral patterns did not change. Future plans include a multi-centered randomized control trial to address this knowledge gap and enhance confidence in counseling patients about IUDs.

P-52. Estradiol Variability, Stress Sensitivity and Depressed Mood in the Menopause Transition

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Objective: The menopause transition is associated with a two to four fold increased risk for major depression. While predictors of depression in the menopause transition have been identified, including stressful life events proximate to the transition, the pathophysiological mechanisms underlying this increased risk are unclear. It has been hypothesized that ovarian hormone variability, characteristic of the menopause transition, may trigger dysmorphic mood in a subset of vulnerable women. In line with this hypothesis, the current study examined the relationship between ovarian hormone deficiency and the onset of depressive symptoms over 14 months in perimenopausal women, and whether recent stressful life events moderated that relationship. Design: In our ongoing RCT, designed to examine beneficial effects of transdermal estradiol (E2) on mood and cardiovascular risk, we recruit medically healthy women (age 45-55) meeting STRAW•10 criteria for the early or late menopause transition (stages -2 and -1), not taking psychotropic medications and free of current psychiatric disorders. Analyses for this report are based only on those women randomized to placebo and were conducted by the first author, who remains blinded and has no interaction with the research subjects and no access to identifiable data. Plasma E2 and progesterone (P4) are measured at two pre-randomization points (study enrollment and again one month later) and also 6 and 12 months post-randomization (study months 8 and 14). The standard deviation of E2 and P4 was calculated and used as an index of hormone variability over the entire 14 months. At enrollment, participants completed the Life Experiences Scale and the Center for Epidemiologic Studies Depression Scale (CES-D), providing measures of overall life stress in the previous 6 months (a composite of number and severity of stressors) and current depressive symptoms, respectively. At study months 8 and 14, the CES-D was re-administered and participants underwent a stressor battery involving a speech and mental arithmetic task. Participants rated their feelings of anger and rejection on a ten-point scale in response to the tasks. Data were analyzed with general linear models, using CES-D score at enrollment as a covariate. Results: To date, 43 women have completed testing. Neither mean E2 nor mean P4 concentrations were associated with CES-D score at study months 8 or 14. However, greater E2 variability across the 14-month interval predicted greater depressive symptoms at month 14 (F=9.4, p=.005). Furthermore, a significant interaction effect revealed that E2 variability was only predictive of depressive symptoms at month 14 in women reporting elevated life stress at baseline (F=4.3, p=.046). E2 variability was also associated with greater anger (F’s=8.2, 4.4; p’s=.047 , .044) and feelings of rejection (F’s=8.8, 5.4; p’s=.006, .003) in response to the speech task at both months 8 and 14, regardless of life stress. P4 variability did not predict depressive mood or emotional responses to the stress tasks. Conclusion: The current study found E2 variability to be predictive of the development of depressive symptoms across a 14-month window of the menopause transition in women who had a recent history of stressful life events. Furthermore, even prior to the onset of the depressive symptoms at month 14, greater E2 variability was associated with an exaggerated negative emotional response to a psychosocial laboratory stressor at month 8 as well as month 14. These preliminary data suggest the possibility that E2 variability enhances emotional sensitivity.
to psychosocial stress, which, in combination with increased stressful life events proximal to the menopause transition, may contribute to the development of depressed mood. Future research ought on the degree of symptomatology (versus placebo) is associated with beneficial effects on depressive symptoms via its ability to stabilize the ovarian hormone environment during the menopause transition.

P-53. Hormone levels and chronic vulvar pain symptoms in a cohort of postmenopausal women

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Objective: To assess prevalence of chronic vulvar pain and its association with serum hormone levels, hormone use, and self-reported symptoms of vaginal dryness in Black and Hispanic postmenopausal women. We used data from 380 participants from the Michigan site of the Study of Women’s Health Across the Nation (SWAN), who participated in the 13th follow-up visit. Women had a median age of 61.3 years. Women completed a screening questionnaire regarding chronic vulvar pain and provided demographic information as well as a blood sample to assess hormone levels. We compared women with current chronic vulvar pain to women with past or short-duration vulvar pain symptoms and women without vulvar pain symptoms, using chi-squared and Fisher’s Exact tests. Relative odds ratios and 95% confidence intervals were calculated using multinomial logistic regression models adjusted for age, body mass index, and race/ethnicity.

Results: In total, 4.0% (95% CI: 2.5%, 6.6%) of women reported current chronic vulvar pain symptoms while 13.7% (95% CI: 10.6%, 17.6%) reported past or short-duration vulvar pain. Women with current vulvar pain symptoms had lower E2, lower DHEA-S, and lower T levels in the prior year, were associated with elevated odds of current chronic vulvar pain. Some women experience chronic vulvar pain symptoms independent of current estrogen levels, and even while taking hormone replacement. This evidence substantiates that post-menopausal vulvar pain is not a single disorder, that atrophy and estrogen deprivation is not always the cause, and that careful assessment and treatment specific to the disorder identified is needed to achieve optimal clinical response. Acknowledgements: The Study of Women’s Health Across the Nation (SWAN) has grant support from the National Institutes of Health (NIH), DHHS, through the National Institute on Aging (NIA), the National Institute of Nursing Research (NINR) and the NIH Office of Research on Women’s Health (ORWH) (Grants U01NR004061; U01AG012505, U01AG012531, U01AG012539, U01AG012546; U01AG012553, U01AG012554, U01AG012495).

P-54. Low-dose isoflavone aglycone supplement alleviates menopausal symptoms: a randomized, double-blind, placebo-controlled study

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Objective: To examine whether lower doses of soy isoflavone aglycones on menopausal symptoms had been conducted using higher doses than this recommendation, we examined whether lower doses of soy isoflavone aglycone supplement on menopausal symptoms: a randomized, double-blind, placebo-controlled study. We used data from 380 postmenopausal Italian women revealed that 5 years of treatment with 150 mg/day of soy isoflavones significantly increased the occurrence of endometrial hyperplasia (3.4 % vs. 0 %, P < 0.05) (Unfer V, et al. Fertil Steril 82(1):145-8). Based on this report and the fact that estrogenic dietary isoflavones are generally not of total current chronic vulvar pain. Some women experience chronic vulvar pain symptoms independent of current estrogen levels, and even while taking hormone replacement. This evidence substantiates that post-menopausal vulvar pain is not a single disorder, that atrophy and estrogen deprivation is not always the cause, and that careful assessment and treatment specific to the disorder identified is needed to achieve optimal clinical response. Acknowledgements: The Study of Women’s Health Across the Nation (SWAN) has grant support from the National Institutes of Health (NIH), DHHS, through the National Institute on Aging (NIA), the National Institute of Nursing Research (NINR) and the NIH Office of Research on Women’s Health (ORWH) (Grants U01NR004061; U01AG012505, U01AG012531, U01AG012539, U01AG012546; U01AG012553, U01AG012554, U01AG012495).

P-55. Tomato juice intake lowers serum triglycerides and blood pressure in midlife women

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Objective: Tomato juice contains variety of bioactive ingredients, such as gamma-aminobutyric acid (GABA), lycopene, dietary fiber, and 13-oxo-9,11-octadecadienoic acid (13-oxo-OXA), which may be effective for health problems in midlife women: 13-oxo-OXA lowers plasma cholesterol levels, 13-oxo-OXA lowers triglycerides; and dietary fiber improves intestinal environment. We investigated the net effect of tomato juice intake on a variety of health parameters in midlife women. Design: We conducted an open-label single-arm study in 93 women who had at least one menopausal symptom. The study was approved by the Ethics Committee of Tokyo Medical and Dental University. For the first 2 weeks (week -2 – -1), the participants were instructed to restrict foods and drinks rich in tomato and tomato products. After the run-in period, the participants started to consume 200 ml of unaltered tomato juice twice a day (right before breakfast and dinner) for 8 weeks (week 0 – 8). The tomato juice used in this study is a product of Nippon Del Monte Corporation (Gunma, Japan). Their menopausal symptoms were evaluated using Menopausal Symptom Scale (MSS), Hospital Anxiety and Depression Scale (HADS), and Athens Insomnia Scale at weeks 0, 4, and 8. Serum levels of triglycerides, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, glucose and hemoglobin A1c, and body composition and cardiovascular parameters were also measured. Results: 91 women (98%) completed the study. The women with high level 8-OHdG had lower body weight (51.0 vs. 53.5, P < 0.01 and < 0.01). Background factors that were associated with high levels of urinary 8-OHdG included BMI > 25 kg/m2 (P < 0.01) and increased physical activity (P < 0.01). The women who consumed high level serum 8-OHdG also had lower serum HDL-C levels (4.7 ± 0.8 vs. 5.1 ± 0.8, P < 0.05) and lower serum total cholesterol levels (210 ± 40 vs. 221 ± 40, P < 0.05) than the other group.

P-56. Oxidative stress is associated with depression in midlife women

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Objective: Oxygen is metabolized into reactive oxygen species that can chemically change the structures of proteins, lipids and nucleic acids, causing damages to cells and tissues. The oxidative stress is known to be associated with various conditions, such as aging, inflammation, arterial sclerosis, and carcinogenesis. In the present study, we investigated if the psychological and physiological symptoms of menopause and lifestyle factors are associated with oxidative stress in midlife women. Design: 96 women aged 40 to 60 years who had at least one menopausal symptom were enrolled into the study. The participants were assessed for their age, menopausal status, body composition, blood pressure, physical and psychological symptoms of menopause, and lifestyle factors. Statistical analysis was conducted using multiple logistic regression analysis. Results: The women with high level 8-OHdG had lower body weight (51.0 ± 8.3 vs. 53.5 ± 6.5 kg, meansE, P = 0.111) and body mass index (20.6 ± 3.4 vs. 21.9 ± 2.5 kg/m2, P = 0.05), had higher systolic blood pressure (136 ± 40 vs. 136 ± 40, P = 0.123), scored higher for anxiety (6.0 ± 3.4 vs. 4.9 ± 2.6, P = 0.010) and depression (5.3 ± 2.0 vs. 3.5 ± 2.3, P = 0.015) in Hospital Anxiety and Depression Scale, and drank more (the proportion of women who drank daily, 22.2 % vs. 11.9 %, P = 0.196). Multiple logistic regression analysis revealed
POSTER PRESENTATIONS (continued)

P-57.

Breast-feeding lowers the risk of later-life obesity: a population-based study in Chinese premenopausal women
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Objective: Obesity is an increasing public health problem associated with many adverse health outcomes such as hypertension, diabetes, dyslipidemia, cardiovascular disease, musculoskeletal pain, etc. About half of Hong Kong Chinese early postmenopausal women are overweight or obese. The effect of breast feeding on maternal weight retention has been equivocal. Data on the long-term relationship between breast-feeding and later-life obesity, particularly in women approaching mid-life, are scarce. This study aimed to investigate the relationship between breast-feeding and obesity in women approaching mid-life.

Design: This study was based on the baseline cross-sectional analysis of a population-based cohort study on dietary intake and breast density in Chinese premenopausal women. Chinese women aged 35 to 45 years were recruited through stratified cluster sampling according to the housing type ratios in Shatin District in Hong Kong. Women within the specific age range were screened for eligibility (defined as Chinese women aged 35-45 years, premenopausal, and without any of these conditions: history of breast cancer, chronic hypertension, on estrogenic hormones in recent use, on long-term antibiotics, on special diet or with a previous history of mal-absorption disorders, surgical removal of the stomach or intestines). All eligible women were invited to the University Centre for face-to-face interviews and anthropometric measurements. 817 women were recruited into the study. Age, socioeconomic status, level of education, reproductive history, physical activity, alcohol drinking and smoking, were obtained based on interviewer-administered standardized questionnaire. Dietary intake of past year was obtained based on food frequency questionnaire. Height and weight were measured using the beam balance scale (Tanita TBF-40) with only light clothing and without shoes. Only 640 women with at least one life birth were included in the analysis. Obesity was defined based on body mass index (weight (kg)/height (m)^2) ≥ 28, a cut-off used for the Asian population. Results: The mean age of the study sample (N=640) was 41.1 ± 2.6 years, mean age of first birth 27.2 ± 4.2 years, mean number of live births 2.4 ± 1.7, BMI 23.0 ± 2.8. 58.9% of all women were breast-fed ≥ 18 months, 92% had breast-fed, 4.9% of the ever breast-fed women was obese while that among the never breast-fed women was 10.9%. Compared with never breast-fed women, the ever breast-fed women had about 60% lower risk of being obese (crude OR 0.42; 95% CI 0.23-0.77). Based on univariate logistic regression analysis on the association of potential confounding factors with obesity, variables with p<0.1 were included in the adjusted logistic regression model. After adjusting for education level, smoking status, sleep duration, family income, frequency of TV watching, and frequency of playing mahjong, ever breast-fed remained to be significantly associated with a lower risk of obesity (OR 0.48; 95% CI 0.25-0.92). Multivariable logistic regression analysis showed that besides breastfeeding, women with at least secondary level of education had also a lower risk of obesity (OR 0.63; 95% CI 0.42-0.92), whereas those who breast-fed ≥ 18 months had the double risk than those compared with never smokers (OR 2.34; 95% CI 1.04-5.26).

Conclusion: Our results suggest that ever breast-fed has a protective effect against later-life obesity in postmenopausal women approaching mid-life. Higher level of education also had a protective effect on later-life obesity, while ever-smoking doubled the risk.

P-58.

Whole-plant food intake pattern was associated with fewer menopausal related symptoms in Chinese postmenopausal women with prehypertension
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Objective: intake has been suggested to be related to the presentation of symptoms around menopause, and fewer menopausal symptoms have been noted in the Asian population.

Methods: 726 premenopausal and postmenopausal women aged 35-45 years, premenopausal, and without any of these conditions: history of benign breast disease, diabetes, dyslipidemia, cardiovascular disease, musculoskeletal pain, etc. About half of Hong Kong Chinese early postmenopausal women are overweight or obese. The effect of breast feeding on maternal weight retention has been equivocal. Data on the long-term relationship between breast-feeding and later-life obesity, particularly in women approaching mid-life, are scarce. This study aimed to investigate the relationship between breast-feeding and obesity in women approaching mid-life.

Design: This study was based on the baseline cross-sectional analysis of a population-based cohort study on dietary intake and breast density in Chinese premenopausal women. Chinese women aged 35 to 45 years were recruited through stratified cluster sampling according to the housing type ratios in Shatin District in Hong Kong. Women within the specific age range were screened for eligibility (defined as Chinese women aged 35-45 years, premenopausal, and without any of these conditions: history of breast cancer, chronic hypertension, on estrogenic hormones in recent use, on long-term antibiotics, on special diet or with a previous history of mal-absorption disorders, surgical removal of the stomach or intestines). All eligible women were invited to the University Centre for face-to-face interviews and anthropometric measurements. 817 women were recruited into the study. Age, socioeconomic status, level of education, reproductive history, physical activity, alcohol drinking and smoking, were obtained based on interviewer-administered standardized questionnaire. Dietary intake of past year was obtained based on food frequency questionnaire. Height and weight were measured using the beam balance scale (Tanita TBF-40) with only light clothing and without shoes. Only 640 women with at least one life birth were included in the analysis. Obesity was defined based on body mass index (weight (kg)/height (m)^2) ≥ 28, a cut-off used for the Asian population. Results: The mean age of the study sample (N=640) was 41.1 ± 2.6 years, mean age of first birth 27.2 ± 4.2 years, mean number of live births 2.4 ± 1.7, BMI 23.0 ± 2.8. 58.9% of all women were breast-fed ≥ 18 months, 92% had breast-fed, 4.9% of the ever breast-fed women was obese while that among the never breast-fed women was 10.9%. Compared with never breast-fed women, the ever breast-fed women had about 60% lower risk of being obese (crude OR 0.42; 95% CI 0.23-0.77). Based on univariate logistic regression analysis on the association of potential confounding factors with obesity, variables with p<0.1 were included in the adjusted logistic regression model. After adjusting for education level, smoking status, sleep duration, family income, frequency of TV watching, and frequency of playing mahjong, ever breast-fed remained to be significantly associated with a lower risk of obesity (OR 0.48; 95% CI 0.25-0.92). Multivariable logistic regression analysis showed that besides breastfeeding, women with at least secondary level of education had also a lower risk of obesity (OR 0.63; 95% CI 0.42-0.92), whereas those who breast-fed ≥ 18 months had the double risk than those compared with never smokers (OR 2.34; 95% CI 1.04-5.26).

Conclusion: Our results suggest that ever breast-fed has a protective effect against later-life obesity in postmenopausal women approaching mid-life. Higher level of education also had a protective effect on later-life obesity, while ever-smoking doubled the risk.

P-59.

Device-Guided Slow-Paced Respiration for Treatment of Menopausal Hot Flashes: A Randomized Controlled Trial
Alison Huang, MD, MAS, Sara Phillips, Michael Schermbr, Eric Viettinghoff, Deborah Gluckl1,1, University of California San Francisco, San Francisco, CA
Objective: Paced respiration has been recommended as a non-pharmacologic treatment for menopausal hot flashes, but the data supporting its efficacy are limited, and some prior studies have used methods of teaching paced respiration that are not generalizable. We evaluated the efficacy of slow-paced respiration using a portable, commercially-available, guided-breathing device for treatment of hot flashes in pre- and postmenopausal women.

Design: The Menopausal symptom Treatment Using Relaxation Exercises (MaTURE) trial was an NIH-funded, parallel-group, randomized trial of slow-paced respiration using a portable, commercially-available, guided-breathing device manufactured by Intercure, Ltd and approved by the Food and Drug Association for adjunctive treatment of hypertension. Peri- or postmenopausal women aged 40 to 59 years who reported at least 4 hot flashes/day and were not using other pharmacotherapy for their symptoms were recruited from the San Francisco Bay area from 2012 to 2014. Women were randomly assigned in equal ratios to use either a standard guided-breathing device to practice slowing their breathing rate to <10 breaths/minute (N=62), or use an identical-controlling device reprogrammed to play relaxing non-rhythmic music rather than pacing respiration (N=61). Women in both groups were instructed to practice their assigned intervention for at least 15 minutes/day for 12 weeks. Participants were aware of treatment assignment, but investigators and staff responsible for abstracting outcomes data were blinded to treatment allocation. Changes in hot flash frequency and severity were assessed using validated symptom diaries in which women documented all hot flashes over a 7-day period and rated their severity as mild (scored as 1), moderate (2), or severe (3). Repeated measures analyses using linear mixed models assessed treatment effects on frequency of hot flashes as well as moderate-to-severe hot flashes per day and were confirmed to have completed at least 6 practice sessions/week (P=98). Women in the paced respiration group reported an average decrease of 1.8 (95%CI:0.9-2.7) hot flashes/day (21%) after 12 weeks, compared to a decrease of 3.0 (95%CI:2.1-3.9) hot flashes/day (35%) in the music control group (P=0.08). The paced respiration intervention was also associated with an average decrease of 1.0 (95%CI:0.2-1.8) moderate-to-severe hot flashes/day (19%), compared to an average decrease of 2.4 (95%CI:1.6-3.2) moderate-to-severe hot flashes/day (44%) associated with the music control (P=0.02). Conclusion: In this randomized trial of a device-guided slow-paced respiration intervention, paced respiration appeared less effective than a music-listening intervention in reducing the frequency and severity of hot flashes in peri- and postmenopausal women. These findings suggest that paced respiration should not be recommended as a treatment for menopausal hot flashes, at least when taught using a portable guided-breathing device.

P-60.

Age-Related Changes in Ovarian Antral Follicular Dynamics: Associations with Endometrial Hyperplasia
Kailey Turner1, Caitlin Hunter1, Heidi Vanden Brink1, Donna Chizen1, David Robertson2, Kailey Turner1, Caitlin Hunter1, Heidi Vanden Brink1, Donna Chizen1, David Robertson2, 1Institute of Medical Research, Monash Medical Centre, Clayton, VIC, Australia
Objective: To test the hypothesis that transient elevations in estradiol, associated with the dominant follicle during ovulation, relate to endometrial hyperplasia as women age. Design: Changes in endometrial growth, antral follicle development, and hormone production were characterized in ovariul women of Reproductive Age

that among these factors, only the HADS-depression score independently contributed to the presence of high-level 8-OHdG (adjusted odds ratio, 1.24; 95% confidence interval, 1.06-1.45). The score for depression was shown to be independently associated with high level of urinary 8-OHdG in midlife women, suggesting the link between oxidative stress and mood in this population.
The correlations between sex hormonal levels and brain morphologic changes in menopausal women

Gwang-Woo Jeong, PhD, MPH1, Taehoon Kim2 (Radiology, Chonnam National University Medical School and Hospital, Gwang-Ju, Republic of Korea; 3Radiology, Chonnam National University Medical School, Gwang-Ju, Republic of Korea)

Objective: This study assessed the brain morphologic changes in menopausal women using voxel-based morphometry (VBM), but also to reveal the correlation between the brain volume variation (VC) and sex hormone (SH) levels. Design: Twenty-four premenopausal (mean 40 years) and 24 menopausal women (mean 56 years) were participated. Both groups have no history of hormone therapy and neurological illness. The measured SH included total estrogen, estradiol, estranol, free testosterone (free-TS), follicle-stimulating hormone (FSH), luteinizing hormone (LH), and sexual hormone-binding globulin (SHBG). The subjects underwent on MR imaging at a 3 T. The variation of brain volume between the premenopausal and menopausal women was analyzed by ANCOVA for controlling aging (FWE at p < 0.05). The correlation between the levels of SH and the VC was analyzed by simple regression on SPM and Spearman’s correlation on SPSS (ver. 19).

Results: The total estrogen and estradiol in menopausal showed lower levels than those in premenopausal women, whereas the levels of FSH and LH are higher in menopause. The menopausal showed significantly reduced gray matter (GM) volumes in the regions of the globus pallidus, gyrus rectus, hypothalamus, fusiform gyrus and superior temporal gyrus as contrasted with premenopausal (Fig. 1). The premenopausal showed the positive correlations between the total estrogen levels and the VC of the superior temporal gyrus (Spearman’s rho, 0.467; p < 0.021) and the LH levels and the VC of the gyrus rectus (r = 0.409, p < 0.047). Conclusion: This study revealed the correlation between the levels of sex hormones and the brain VC in menopausal women. These findings would be helpful for understanding the morphometric changes in association with the levels of sex hormones following menopause.

Fig. 1. The brain areas showing significantly reduced volumes in menopausal women.

P-62. Timing and Persistence of Effect of CE/BZA in Postmenopausal Women

Risa Kagan, MD1, Barry Komr2, Kelly Ryan2, Joanne Lavenberg3, Ching-Ray Yu3

1University of California, San Francisco, San Francisco, CA; 2University of California, San Francisco East Bay Physicians Medical Group, Berkeley, CA; 3Pfizer Inc., Collegeville, PA; 4Pfizer Inc., New York, NY; 5University of Virginia Health System, Charlottesville, VA

Objective: Conjugated estrogens/bazedoxifene (CE/BZA), a new treatment for moderate-severe vasomotor symptoms associated with menopause and prevention of postmenopausal bone loss, demonstrated efficacy/safety in healthy postmenopausal women with a uterus in phase 3 Selective estrogens, Menopause, And Response to Therapy (SMART) trials. Determine the time course (onsset, persistence) of CE/BZA’s effects. Methods: We identified women in CE/BZA ≥ 0.45 mg BZA 0.2 mg CE group where BZA ≥ 0.45 mg BZA 0.2 mg CE at mo 12 first achieved a statistically significant difference (P = 0.05) vs placebo (PBO) in the 5 individual SMART trials and the duration the difference persisted for pre-specified efficacy end points. Outcomes included hot flush (HF) frequency/severity collected in daily diaries and reported weekly through wk 12 (SMART-1 and -2), then monthly (SMART-1); bone mineral density (BMD) at the lumbar spine, total hip, and femoral neck and trochanter at baseline (BL) and mo 6, 12, 18, and 24 (SMART-1), mo 12 and 24 (SMART-4), or mo 6 and 12 (SMART-5); vulvar-vaginal atrophy (VVA); % superficial and % parabasal cells at BL and mo 6, 12, 18, and 24 (SMART-1) or wk 4 and 12 (SMART-3); menopause-specific quality of life (MENQOL) at BL and mo 3, 6, 12, 18, and 24 (SMART-1) or mo 3 and 12 (SMART-5); and sleep assessed by daily diary in wk 1-3 then mo 6, 12, 18, and 24 (SMART-1) or MOS sleep scale at BL and mo 3 and 12 (SMART-5). We performed a similar analysis when possible for CE/medroxyprogesterone acetate (CE/MPA), an active comparator in SMART-4 and -5, vs PBO. Results: In SMART-1 and -2, CE/BZA in first produced significant reductions vs PBO in HF at wk 6 (CF 0.625 mg BZA 20 mg, 3-4 CE 0.45 mg BZA 20 mg, BZA 0.2 mg CE 0.45 mg BZA 20 mg, and HF severity at wk 6 (both doses), which were maintained through mo 24. Significant changes were seen at wk 1 in treatment of lumbar spine, total hip, and trochanter BMD (mo 6 and 12), and BMD at lumbar spine with mo 3 or 6; effects were similar with the CE 0.45 mg BZA 20 mg at wk 24. Significant changes in femoral neck BMD were evident at first assessment (mo 6 or 12) in all studies except SMART-1, in which this difference was significant at mo 12-24 (but not at mo 6) for CE 0.45 mg BZA 20 mg in substudy 1 (>5 postmenopausal, osteopenia, a risk osteoporosis risk factor) and both doses in substudy 2 (<5 postmenopausal, osteopenia 1 osteoporosis risk factor). In women with VVA at BL, mean proportion of vaginal superficial cells was significantly increased vs PBO at wk 4 for both doses and wk 12 for CE 0.625 mg BZA 20 mg in SMART-3, at only mo 12 for CE 0.45 mg BZA 20 mg; at mo 12 for CE 0.45 mg BZA 20 mg. In SMART-1, at mo 12 for CE 0.625 mg BZA 20 mg. In SMART-1 at only mo 12-24 for CE 0.45 mg BZA 20 mg in SMART-1. In SMART-1 for CE 0.45 mg BZA 20 mg and CE 0.625 mg BZA 20 mg respectively, sleep quality was improved at wk 4 and 5, minutes to fall asleep at wk 4 and 6, and minutes slept at wk 8 and 7; significance was achieved in a majority of weeks thereafter. In SMART-5, time to fall asleep was significantly reduced vs PBO at mo 3 with CE 0.45 mg BZA 20 mg; at mo 12, there were significant differences vs PBO in time to fall asleep (both doses), sleep disturbance (both doses), sleep adequacy (CE 0.625 mg BZA 20 mg), and sleep problem index 1 and 2 (CE 0.625 mg BZA 20 mg). These findings support continued use of CE/BZA for menopausal bone outcomes, MENQOL, and VVA and were similar to those with CE/MPA. CE/BZA HF data are available. Conclusion: For most efficacy end points, both doses of CE/BZA achieved significance vs PBO at early assessments, and benefits were well maintained. Time course of benefit was similar to CE/MPA for available end points.

P-63. Association of Hot Flash with Adipokines and Ghrelin in Early vs. Late Postmenopausal Women

Roksana Karim, MBBS, PhD1, Ha Dong, MS1, Howard Hodis, MD1, Frank Z. Stanczyk, PhD1, Roberta D. Brinton, PhD2, Wendy J. Mack, PhD2 (Pediatrics and Preventive Medicine, University of Southern California, Los Angeles, CA; 2Preventive Medicine, University of Southern California, Los Angeles, CA; 3Obstetrics and Gynecology, University of Southern California, Los Angeles, CA; 4Pharmacology and Pharmaceutical Science, University of Southern California, Los Angeles, CA; 5Atherosclerosis Research Unit, Medicine, University of Southern California, Los Angeles, CA)

Objective: Hot flash is a common menopausal symptom experienced by most women going through menopausal transition. In addition, a considerable proportion of women continue to experience hot flashes through late menopause (1). Yet, the exact physiologic mechanism of hot flash is not well understood. Increased adiposity has been identified as a risk factor for hot flash. Adipose tissue derived cytokine-like substances collectively known as adipokines, have been linked with hot flash in women going through menopausal transition and midlife women. The association of adipokines with hot flash has not been evaluated in older postmenopausal women who are likely to gain weight further into menopause. Ghrelin, a peptide hormone released from the stomach, stimulates appetite and plays an important role in energy homeostasis. Role of ghrelin in hot flashes has not been evaluated to date. Design: This is a cross-sectional study including baseline data on hot flash, adipokines, ghrelin, and other demographic and clinical factors from two clinical trials, Women’s Isoflavon Sway Health (WISH) and Early vs. Late Intervention Trial of Estrogen (ELITE), were used in this study. Both WISH and ELITE has similar study design, includes demography and data collection process. Study participants of both trials were healthy, currently non-smoking.
non-HT in postmenopausal women, free of cardiovascular disease or any other chronic disease conditions. Both trials used the same hot flash diary in which participants recorded the number of daily hot flashes, which was categorized as hot flash or no hot flash in this analysis. Leptin, adiponectin, resistin and ghrelin concentrations were assayed using highly sensitive radioimmunoassay in eight hour fasting blood sample collected at baseline of both the trials. Logistic regression model was used to evaluate the association of adipokines and ghrelin with hot flash. Multivariate models were not adjusted for BMI because BMI is essentially in the pathway for the adipokine, ghrelin and hot flash associations. Results: A total of 896 postmenopausal women, 645 from the ELITE and 251 from the WISH trial, contributed to this analysis. Participants mean (SD), age was 60.4 (6.7) years, BMI 27 (5.3) kg/m2, 67% Caucasians, 52% were within 10 years of menopause. Hot flash experience was associated with age, BMI, education and years since menopause. Adjusted for the factors associated with hot flash other than BMI, women in the highest quintile of ghrelin had significantly greater risk of experiencing hot flash (OR (95% CI) 1.13 – 2.63) compared with the lowest quintile. The association was more pronounced among the overweight and obese women compared to the women with normal BMI (OR (95% CI) 2.03 (1.10 – 3.76) vs. 1.20 (0.52 – 2.76)). The ghrelin and hot flash associations were similar between women taking menopausal hormone and those without. Leptin, adiponectin, and resistin were not associated with hot flash. Conclusion: Increased concentration of ghrelin is a significant risk factor for hot flash in postmenopausal women, both among early (within 10 years) and late (over 10 years) menopausal women. The effect of ghrelin is even stronger in overweight and obese postmenopausal women.

Multivariate association between ghrelin and Hot flash

<table>
<thead>
<tr>
<th>Total Sample</th>
<th>Stratified by BMI</th>
<th>Stratified by years since menopause</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;25 kg/m²</td>
<td>&gt;25 kg/m²</td>
<td>&lt;10 years</td>
</tr>
<tr>
<td>Hot Flash</td>
<td>Hot Flash</td>
<td>Hot Flash</td>
</tr>
<tr>
<td>Ghrelin (pg/mL)</td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>&lt;99</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>100-147</td>
<td>1.10 (0.73 – 1.66)</td>
<td>0.91 (0.57 – 1.43)</td>
</tr>
<tr>
<td>148-200</td>
<td>1.35 (0.86 – 2.13)</td>
<td>1.03 (0.61 – 1.76)</td>
</tr>
<tr>
<td>&gt;200</td>
<td>1.72 (1.16 – 2.52)</td>
<td>1.23 (0.75 – 2.01)</td>
</tr>
</tbody>
</table>

Total p-value

P = 0.05

P-64. Simultaneously Sensitive and Accurate Measurements of Androgens and Estrogens in Post-Menopausal Women Serum by a Robust LC-MS/MS Method

Yoyong Ke, PhD, Renaud Gonthier, Fernand Labrie. BioLab, EndoCeutics Inc, Québec, QC, Canada

Objective: To develop a sensitive and robust LC-MS/MS for the simultaneous measurement of seven androgens and estrogens in post-menopausal women serum, i.e. the simultaneously sensitive and accurate measurement of estrone (E1), estradiol (E2), dehydroepiandrosterone (DHEA), androstenedione (4-dione), testosterone (Testo) and dihydrotestosterone (DHT). Design: Accurate and sensitive measurement (pg/mL) of androgen and estrogen steroidal compounds, especially estradiol in post-menopausal serum or plasma, usually uses derivatization to increase sensitivity. The low sensitivity of estrogens and androgens is due to their low concentrations, these metabolites were derivatized using a ketone reagent. The system chosen for method development assay was an UPLC (Nexera P-64). Method

Conclusions: Increased concentration of ghrelin is a significant risk factor for hot flash in postmenopausal women, both among early (within 10 years) and late (over 10 years) menopausal women. The effect of ghrelin is even stronger in overweight and obese postmenopausal women.

Multivariate association between ghrelin and Hot flash

P-66. 25-Hydroxyvitamin D levels and body mass index in healthy postmenopausal women

Heung-Yeol Kim, MD, PH.D,¹ Hoon Chol.² Dept of OB & GYN, Kosin University, College of Medicine, Busan, Republic of Korea; 2Dept of OB & GYN, Kosin University, College of Medicine, Busan, Republic of Korea

Objective: Obesity is associated with alterations in vitamin D (Vd) system. We evaluated the correlation between Vd level and body mass index (BMI), for the evaluation of obesity in postmenopausal women. Design: To study the relationship between Vd levels and obesity, We recruited 310 healthy postmenopausal women between January 2005 and March 2011 and analyzed the correlation between BMI and 25-hydroxyvitamin D (25(OH)VD) level. We also analyzed the relationship between serum Vd level and bone health status such as bone mineral density measured by DXA, bone turnover marker, and parathyroid hormone (PTH). Results: With a cut-off level for Vd deficiency at 30 ng/mL, 98.9% patients showed a Vd deficiency, while 87.8% patients showed a vitamin D deficiency with a 20-ng/mL cut-off level. Vd levels had no significant correlation with age, weight, height, BMI, or bone turnover markers. PTH level and serum 25(OH)-VD level showed a negative correlation. Vd level showed negative correlation with BMI, but statistically not significant. Conclusion: In this study, most of postmenopausal women (more than 87.8%) had a Vd deficiency, and Vd level showed negative correlation with BMI, but was not statistically significant.

P-67. Bone Mineral Density of Lumbar Spine and Femur in Patients with Gynaecologic Cancer

Ik-Soo Kim, MD, PH.D,¹,³ Ari Kim.¹ Dept of OB & GYN, Kosin University, Busan, Republic of Korea; 2WonKwang University, Iksan, Republic of Korea

Objective: Patients with cervical cancer have lower bone mass than women without cancer, whereas women with endometrial cancer have higher bone mineral density (BMD) than control subjects, possibly due to the prevalence of high body-fat mass. The aim of this study was to compare BMD in patients with cervical cancer, endometrial cancer, and controls. Design: We analysed and compared spinal and femoral BMD in 130 patients with cervical cancer, 68 with endometrial cancer, and 140 age-matched menopausal female control subjects. We also compared serum calcium, phosphorus, total alkaline phosphatase, osteocalcin, and urinary deoxyypyridinoline levels. Results: Compared with the control group, T-scores for some lumbar vertebrae (L4), the femoral neck, and Ward’s triangle were lower in patients with cervical cancer, whereas only L4 T-scores in patients with cervical cancer were significantly lower than those in women with endometrial cancer. The BMD levels were significantly lower in women with endometrial cancer (P < 0.002) than in women with cervical cancer, but no other biochemical variable differed among groups. Conclusion: Cervical cancer was associated with lower BMD and may be a risk factor for secondary osteoporosis. However, endometrial cancer generally seemed to have no damaging effect on bone. A larger follow-up study is required to clarify these findings.

P-68. Primary ovarian insufficiency as drug adverse reaction – signal detection

Tak Kim, MD,Ph.D,¹ Sun Kyoung Yam, MD,² Hyung Moo Park, Ph.D.³ OB/GYN, Korea University College of Medicine, Seoul, Republic of Korea

Objective: Primary ovarian insufficiency (POI) is reported to occur in about 1% of women. In the absence of autoimmune disorders, genetic disorders, smoking, and cancer treatment, premature menopause is considered idiopathic. Systemically administered drugs have the potential to affect normal women’s physiology in various ways, most of
which are unknown. Epidemiological approaches using large databases can generate new hypotheses on etiopathogenesis. The objective of this study is to examine the risks of POI associated with environmentally exposed estrogen. Design: We used the FDA adverse event reporting system as the data source. The relevant MedDRA PT term for POI, “premature menopause,” was used for event extraction. Using frequentist method of proportional reporting ratio (PRR), disproportionality was calculated for the twenty drugs with the most frequent events for premature menopause. A disproportion is considered on the basis of three pieces of information: PRRp2, χ2p2 and at least 3 cases. Results: Out of a total of 13,067,819 reports of drug-event pairs in the database, 283 reports of premature menopause were found. Contraceptives Mirena and Depo-provera had PRRs of 11.84 and 33.10 respectively, both of which are positive safety signals. Fosamax had a PRR of 7.65. Statins, Lecisol and Lipitor, had PRRs 44.9 and 0.85 respectively, the former being a signal and latter not. For Antihypertensives, Micardex, Co-Apiproved, and Zanidip had positive signals whereas, Lasix did not. For antidepressants, Elavil had a positive signal, but Effexor and Lexapro did not. Conclusion: In conclusion, many drugs demonstrated positive risk associations with premature menopause. Given the health implications of early deprivation of ovarian hormones, these signals warrant further in depth evaluation.

Disproportionality assessments of twenty drugs with highest frequencies of premature menopause reported to the FDA as adverse events

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>PRRp2</th>
<th>χ2p2</th>
<th>Number of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actavis</td>
<td>3.60</td>
<td>7.71</td>
<td>32</td>
</tr>
<tr>
<td>Mirena</td>
<td>11.84</td>
<td>28.72</td>
<td>111</td>
</tr>
<tr>
<td>Aweek</td>
<td>33.39</td>
<td>68.47</td>
<td>34</td>
</tr>
<tr>
<td>Statins</td>
<td>3.55</td>
<td>67.61</td>
<td>30</td>
</tr>
<tr>
<td>Lipitor</td>
<td>0.85</td>
<td>0.12</td>
<td>21</td>
</tr>
<tr>
<td>Neogyn</td>
<td>12.75</td>
<td>22.14</td>
<td>12</td>
</tr>
<tr>
<td>Depo-Provera</td>
<td>3.55</td>
<td>67.61</td>
<td>30</td>
</tr>
<tr>
<td>Tramadol</td>
<td>3.55</td>
<td>67.61</td>
<td>30</td>
</tr>
</tbody>
</table>

According to European Medicines Agency (EMEA, EMA), when all of the following criteria are met, it is considered a safety signal: 1) Proportional reporting ratio (PRR), disproportionality was calculated for the twenty drugs with the most frequent events for premature menopause. A disproportion is considered on the basis of three pieces of information: PRRp2, χ2p2 and at least 3 cases. Results: Out of a total of 13,067,819 reports of drug-event pairs in the database, 283 reports of premature menopause were found. Contraceptives Mirena and Depo-provera had PRRs of 11.84 and 33.10 respectively, both of which are positive safety signals. Fosamax had a PRR of 7.65. Statins, Lecisol and Lipitor, had PRRs 44.9 and 0.85 respectively, the former being a signal and latter not. For Antihypertensives, Micardex, Co-Apiproved, and Zanidip had positive signals whereas, Lasix did not. For antidepressants, Elavil had a positive signal, but Effexor and Lexapro did not. Conclusion: In conclusion, many drugs demonstrated positive risk associations with premature menopause. Given the health implications of early deprivation of ovarian hormones, these signals warrant further in depth evaluation.

The three co-primary efficacy assessments were the mean change in subjects’ self-assessed severity of dyspareunia, mean change in vaginal pH, and the mean change in the percentage of parabasal and superficial cells in vaginal cytology. Additionally, the investigator assessed vaginal health by visual inspection of the vagina for signs of atrophy, pallor, dryness, friability, and petechiae. Subjects’ self-assessed severity of other symptoms of VVA of vaginal dryness and vaginal bleeding associated with sexual activity was also assessed. Results: After 12 weeks, the estradiol vaginal group vs the vehicle group. Vaginal pH and the percentage of parabasal and superficial cells all improved significantly in the estradiol cream group from baseline to Week 12 and Week 12/Final Assessment compared with vehicle (p<0.0001). The investigator’s assessment of vaginal health also showed significant improvements for the estradiol vaginal cream group vs vehicle from baseline to Week 12 and Week 12/Final Assessment (p<0.0001). Subjects’ self-assessed severity of vaginal dryness improved significantly from baseline to Week 12/Final Assessment (p=0.004). Additionally, the percentage of subjects with vaginal bleeding associated with sexual activity was significantly less with estradiol vaginal cream compared to vehicle (p=0.0058). Among the subjects who experienced adverse events (52.3% estradiol vaginal cream, 49.8% vehicle) almost all were mild or moderate in severity. Most frequently reported adverse events were vulvovaginal mycotic infection (6.9%) and urinary tract infection (3.6%) for estradiol vaginal cream, and urinary tract infection (7.7%) and application site pain (5.5%) for vehicle. Treatment-emergent SAEs were reported in 3 subjects in the estradiol vaginal cream group and 1 subject in the vehicle group, and all except one were unlikely related to study drug. Eight (2.9%) subjects treated with estradiol vaginal cream and 6 (2.2%) subjects treated with vehicle experienced AEIs that led to withdrawal from the study. Conclusion: The new low-dose estradiol vaginal cream significantly improved the severity of dyspareunia in sexually active postmenopausal women and was well tolerated.

P-70. Evaluation of NEOGYN® Feminine Soothing Cream in Treating Female Sexual Function in Postmenopausal Women with Chronic Vulvar Pain and Discomfort

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Objective: Objective: The menopausal process is a natural progression for women. In addition to exacerbation of vasomotor symptoms, vaginal and vulvar dryness, pruritis, and atrophy of the vulvar skin, postmenopausal women often experience painful intercourse (dyspareunia) and gradual decline of sexual interest. The aim of this study was to evaluate the effect of Neogyn®, a feminine vulvar soothing cream, in eleving chronic mild-to-moderate outer genital discomfort or pain in otherwise healthy, postmenopausal women. Neogyn is a cellular lysate cream that is hormone, fragrance and paraben free. It is a proprietary blend of proteins and interleukins specifically formulated by Swiss scientists. The test was also designed to evaluate the effect of Neogyn® on vulvar pain and discomfort are highly associated with patient reported sexual dysfunction and dissatisfaction. Design: Design: Convenience sampling was used at two geographically diverse clinical institutions to enroll 24 postmenopausal women in this single-group, open label, pre-post-test study design. At the time of screening, all subjects reported vulvar and intercourse related pain and discomfort. The patients were consented, examined and screened to ensure qualification. The subjects were not on any other treatments for vulvar pain or discomfort. Subjects were educated with anatomical pictures on where to and how to apply 0.25–0.30g of the study product to their outer genital areas once daily or as much as clinically indicated for 12 weeks. Assessments at baseline and 12 weeks consisted of an 11-point numeric rating scale of discomfort, the Female Sexual Function Index (FSFI), and the McGill Genital Pain Questionnaire. Global assessments of the treatment were also made at 4 and 8 weeks. Results: Results: Twenty-four predominantly (93.8%) white postmenopausal women ages ranging from 53-80 (average 62.4 ± 7.7) were enrolled between June and November 2013. With a response range of 0 for no discomfort and 10 the worst possible discomfort; the average vulvar discomfort score was 6.2 ± 1.8 at baseline and 2.7 ± 2.5 at 12 weeks representing a 56% improvement in outer genital discomfort (p < 0.0001). Utilizing the McGill Genital Pain Questionnaire, 3 (12.5%) subjects reported none-mild pain at baseline in contrast to 13 (56%) subjects reporting none-mild pain at 12 weeks (p = 0.008). The total FSFI score improved from 7.6 at baseline to 21.4 ± 8.2 at 12 weeks (p = 0.006). When comparing the baseline and 12-week FSFI domain average scores, there was also a 77% improvement in the Pain domain (p = 0.029), a 46% improvement in the Arousal domain (p = 0.016), and a 30% improvement in the Clitoral domain (p = 0.082). Based on the global assessments of the study cream, can relieve vulvar pain and discomfort.
and henceforth improve sexual wellbeing in many postmenopausal women. Neogyn® is a novel non-hormonal vulvar product that should be added to the treatment paradigm options for outer genital discomfort.

P-71. Longitudinal Assessment of Menopause Symptoms in Perimenopausal Women with HIV

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Objective: We have previously shown in a cross-sectional evaluation that perimenopausal women with HIV experience greater hot flash severity and related distress, insomnia, anxiety and depressive symptoms compared to perimenopausal non-HIV-infected women of similar age, race and menstrual patterns. We now present findings from a one year longitudinal evaluation of menopause symptoms among this study cohort. Design: Perimenopausal HIV-infected and non-HIV-infected women completed questionnaires at baseline and twelve months including the Menopause Rating Scale (MRS), Hot Flash Related Daily Interference Scale (HFREDIS), Insomnia Severity Index (ISI), Generalized Anxiety Disorder Assessment (GAD-7) and Center for Epidemiologic Studies Depression Scale (CES-D). Student’s t-tests (and Wilcoxon rank sum for non-normally distributed data) were used to evaluate differences between the HIV-infected and non-infected women at baseline and at twelve months. Change over 1 year was compared within groups using paired t-tests. Results: Of 33 HIV-infected and 33 non-HIV-infected women, 31 (94%) and 32 (97%) completed the twelve month visit. Menstrual patterns during follow-up remained similar in the two groups (number of periods in past 6 months HIV-infected 2 (IQR 1.4) vs 2 (IQR 1.4) p=0.6). Menopausal symptom scores were relatively stable among all study subjects from baseline to 12 months and no significant within group differences were observed. However, at 12 months greater symptom burden persisted among the HIV-infected women compared to the non-HIV-infected women. Between group differences in questionnaire scores at 12 months: MRS (p=0.002), HFREDIS (p<0.001), ISI (p=0.002), GAD-7 (p<0.001), CES-D (p=0.005). Hot flash severity was similar between the groups at 12 months (MRS item 1; p=0.99). Conclusion: This study is among the first to report longitudinal data on menopause symptoms in perimenopausal HIV-infected women. Over one year of follow up, menopause symptoms were relatively stable, though the HIV-infected women continued to experience greater hot flash related distress, insomnia, anxiety and depressive symptoms compared to non-HIV-infected women at twelve months. These longitudinal data extend the findings of our baseline survey

Primary Outcome Results

P-72. Factors associated with menopausal symptoms in women from metropolitan region of Campinas, Brazil: a population-based household survey

Jeffrey F. Lui, MSc, Luiz F. Baccaro, Tatiane Fernandes, Lucia S. Costa-Paiva, MD, PhD, Aarao M. Pinto-Neto, MD, PhD. Department of Obstetrics and Gynecology, School of Medical Sciences, University of Campinas (UNICAMP), Campinas, Brazil.

Objective: To evaluate factors associated with menopausal symptoms in women from the Metropolitan region of Campinas – Brazil. Design: A cross-sectional study was conducted with 749 women of 45-60 years of age, at 19 cities of the metropolitan region of Campinas - Brazil, in the form of a population-based household survey. The dependent variable was the intensity of menopausal symptoms assessed using the Menopause Rating Scale (MRS). The independent variables were sociodemographic data, health related habits and problems, self-perception of health, and gynecological background. Statistical analysis was carried out by Chi-square test and Poisson regression using the backward selection criteria. Results: The mean age of the women was 52.5 (±4.4) years. With regard to menopausal status, 16% were premenopausal, 16% perimenopausal and 68% postmenopausal. The intensity of menopausal symptoms was defined according to the median of the total score of MRS and was considered severe for values above eight. In the final statistical model, depression/anxiety (PR 1.82, 95% CI 1.49-2.21, p<0.01), rheumatic diseases (PR 1.46, 95% CI 1.23-1.73, p<0.01), self-perception of health as fair/poor/very poor (PR 1.44, 95% CI 1.21-1.72, p=0.01), history of abortion (PR 1.26, 95% CI 1.09-1.47, p=0.01), current or previous treatment for menopausal symptoms (PR 1.23, 95% CI 1.06-1.43, p=0.01), perimenopausal or postmenopausal status (PR 1.38, 95% CI 1.08-1.76, p=0.01), number of normal deliveries (PR 2 (IQR 1.99, 95% CI 1.02-1.39, p=0.01) and asthma (PR 1.21, 95% CI 1.01-1.45, p=0.01) were associated with more severe menopausal symptoms. Older age (PR 0.96, 95% CI 0.96-0.97, p<0.01) was associated with less severe symptoms. Conclusion: The severity of menopausal symptoms are associated with a great number of risk factors. Understanding and controlling these factors can help to improve health care and provide data to define groups that require greater attention from health services.

P-73. Can a portable handheld device that provides instantaneous cooling attenuate menopausal vasomotor symptoms (VMS)? - a randomized trial

Bryden Magee, Jill Trueman, Philip M. Hahn, Robert Reid, MD. Division of Reproductive Endocrinology and Infertility, Queen’s University, Kingston, ON, Canada.

Objective: Anecdotes suggest that some women find a cold drink can, when applied to the back of the neck, may attenuate the severity of menopausal VMS. Though a variety of cooling devices are sold via the internet for this purpose there is currently no published research on the effects of external cooling devices for menopausal VMS. This Queen’s University REB approved RCT evaluated the efficacy of a novel handheld cooling device (Menopod®) applied to the back of the neck at onset of each VMS. The click of a button on the device elicits a brief vibration followed by instantaneous cooling to a temperature of 6°C. These findings are among the first to report longitudinal data on menopause symptoms in perimenopausal women worldwide, in the form of a population-based household survey. The dependent variable was the intensity of menopausal symptoms assessed using the Menopause Rating Scale (MRS). The independent variables were sociodemographic data, health related habits and problems, self-perception of health, and gynecological background. Statistical analysis was carried out by Chi-square test and Poisson regression using the backward selection criteria. Results: The mean age of the women was 52.5 (±4.4) years. With regard to menopausal status, 16% were premenopausal, 16% perimenopausal and 68% postmenopausal. The intensity of menopausal symptoms was defined according to the median of the total score of MRS and was considered severe for values above eight. In the final statistical model, depression/anxiety (PR 1.82, 95% CI 1.49-2.21, p<0.01), rheumatic diseases (PR 1.46, 95% CI 1.23-1.73, p<0.01), self-perception of health as fair/poor/very poor (PR 1.44, 95% CI 1.21-1.72, p=0.01), history of abortion (PR 1.26, 95% CI 1.09-1.47, p=0.01), current or previous treatment for menopausal symptoms (PR 1.23, 95% CI 1.06-1.43, p=0.01), perimenopausal or postmenopausal status (PR 1.38, 95% CI 1.08-1.76, p=0.01), number of normal deliveries (PR 2 (IQR 1.99, 95% CI 1.02-1.39, p=0.01) and asthma (PR 1.21, 95% CI 1.01-1.45, p=0.01) were associated with more severe menopausal symptoms. Older age (PR 0.96, 95% CI 0.96-0.97, p<0.01) was associated with less severe symptoms. Conclusion: The severity of menopausal symptoms are associated with a great number of risk factors. Understanding and controlling these factors can help to improve health care and provide data to define groups that require greater attention from health services.

Conclusion: This study failed to demonstrate a statistically significant difference in the “Sloan” hot flash scores in those randomized to the use of a handheld cooling device compared to women receiving a sham device. However comments from many of those receiving the active device suggested that it did afford relief from VMS. A handheld cooling device may afford improvement to quality of life for some women seeking an alternative to hormone therapy for distressing vasomotor symptoms.

Primary Outcome Results

Delta = (Active Device Baseline value - Week 4 Value) - (Sham Baseline value - Week 4 value)

P-74. Conservative Management of Stress Urinary Incontinence in Women - A Scoping Review of the Literature

Louise McIntosh, MSN. University of British Columbia Okanagan, Kelowna, BC, Canada.

Objective: Stress urinary incontinence is a serious threat to the wellbeing of millions of women worldwide. It is still considered to be a taboo topic by many, and as a result many women do not discuss it with their primary care provider, making it difficult to source the actual numbers of women who suffer from this condition. This research involved conducting a scoping study of the literature to answer the primary question: What conservative treatment options are currently available to treat stress urinary incontinence in women? Three secondary questions that arose from the review of the literature, which were also addressed, included: The benefits, complications and adverse effects of the conservative treatment options identified in the literature. What further research could be undertaken to advance the knowledge and conservative treatment for urinary incontinence in women? And, What role can nurses play in the education and treatment of stress urinary incontinence in women? In addition to the primary and secondary research questions, three themes arose from the review: the taboo nature of discussing urinary incontinence; how underreporting leads to underestimating the cost of managing it; and the need for education of the public and health care professionals around the topic and strategies for its management. Design: A scoping review of the literature was the chosen method for this research. A scoping study is utilized to understand the breadth of literature available on the topic of interest rather than to critique findings, structure, quality and validity of empirical studies. A scoping study examines a wide range of evidence and provides a summative narrative account of interventions. This scoping study was undertaken with the intent of identifying a collection of relevant literature on the topic of conservative management of stress urinary incontinence in women, and possibly directing further research on the role of the nurse in the management and treatment of this condition. Results: Various conservative treatment options were identified: strengthening pelvic floor muscles, the use of intravaginal and intrarectal device, electrical biofeedback and lifestyle modifications, products, and alternative therapies. All forms of conservative treatment have benefits, but they also have some degree of negative implications, complications or adverse effects. In addition to describing the different
modalities for treatment, other areas were identified where nurses could make a major contribution to the knowledge base on this topic: by enhancing public awareness to remove the taboos associated with discussing this condition with health care providers; by ensuring that primary health care providers can correctly assess and treat stress urinary incontinence in women; and by offering education on the conservative treatment options by ensuring that primary health care providers can correctly assess and treat stress urinary incontinence in different countries, based on the socially acceptable treatment modalities used in different cultures, and this may guide future research into areas of treatment that have not been considered traditional in our Western culture. Finally, in order to influence policymakers that the problems associated with stress incontinence are worth investment, more accurate statistics on the incidence of incontinence are needed. In order to get better statistics the taboo and social stigma associated with incontinence must be removed. In order to remove the social stigma and taboo, more education of the public and health care providers is needed.

P.75. Validation of a New Menopause Survey, the wScore and Comparison to the Utian MQOL and the Greene Climacteric, Part III

David C. Miller, M.D.1,2, Lovera W. Miller, M.D.2,3, Sasha F. Franger, MA2, Brienna G. Miller, MBA1,3. 1Pain Management, Indiana University Health, La Porte, IN; 2Women’s Care, Indiana University Health, La Porte, IN; 3School of Medicine, University of Queensland, Brisbane, QLD, Australia

Objective: Surveys performed to screen for risk factors, diagnose a disease, or follow response to treatment constitute an important information source in medical care. A survey of high validity may effect clinical decisions and outcomes. Menopause is a natural change in ovarian function that may alter a myriad of physical, emotional, and social functions; rendering validation of medical menopause surveys, attempting to track these changes, problematic. The source of menopause transition symptoms and related problems is the age-related change in ovarian hormone production. The most accepted method for categorizing a woman’s reproductive hormone status is through the STRAW classification. This study proposes applying the STRAW framework as a means to classify women and measuring how well a new menopause survey, the wScore, performs in estimating the presence of perimenopause and early postmenopause related problems. This method of statistical validation is appropriate for tests or surveys where there is an accepted criterion standard (also known as a gold standard) by which to compare the results. Similar comparison to the Utian Menopause Quality of Life and the Greene Climacteric are performed. Design: 720 consecutive women consented to a prospective cross-sectional study by successfully completing three menopause surveys. Patients were contemporaneously categorized according to STRAW criteria. Results: 349 were naturally cycling or menopausal women. STRAW stages were assigned in the same manner as in Parts I & II. The Greene Climacteric and the wScore were scored according to their 0-3 Likert scale and the Utian Menopause Quality of Life was adjusted and inverted, as previously described. To minimize overfitting, cut points were predetermined to be the numerical average between means of adjacent STRAW categories (see data from Part I). The validation tests were performed after generation of a 2 X 2 contingency table and the determination of the numbers of each cell: true positive, false positive, false negative, and true negative. Conclusion: Validity is determined by measuring how well a test or survey performs against a criterion or gold standard, providing one exists. If a medical survey is used to evaluate, diagnose, or follow response to interventions for menopause related problems; it may be expected to have a meaningful relationship to the designated stages of menopause formalized through the consensus structure of the STRAW. In this population of women, the wScore does well in distinguishing perimenopausal and early postmenopausal (STRAW -2, -1, +1) related problems from reproductive and late menopausal women (STRAW -5, -4, -3, -2). A test or survey with a kappa value above 0.6 is considered to be in “good” agreement with the criterion. The Greene Climacteric is in “slight” agreement, and the Utian MQOL is in “poor” agreement under these circumstances. Two of these surveys have been validated in the past through other methods.

Validation Statistics Menopause Surveys vs. STRAW

<table>
<thead>
<tr>
<th>Survey</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Likelihood Ratio</th>
<th>kappa</th>
</tr>
</thead>
<tbody>
<tr>
<td>wScore</td>
<td>0.78</td>
<td>0.33</td>
<td>4.6</td>
<td>0.62</td>
</tr>
<tr>
<td>Greene</td>
<td>0.67</td>
<td>0.72</td>
<td>2.4</td>
<td>0.38</td>
</tr>
<tr>
<td>Utian</td>
<td>0.69</td>
<td>0.63</td>
<td>1.4</td>
<td>0.20</td>
</tr>
</tbody>
</table>

P.76. Comparison of Menopause Surveys to the STRAW Timeline, Part I: Utian MQOL, Greene Climacteric, wScore In Women Not Taking Hormone Therapy

Lovera W. Miller, M.D.1, David C. Miller, M.D.1, Sasha F. Franger, MA1, Brienna G. Miller, MBA1,3. 1Women’s Care, Indiana University Health, La Porte, IN; 3University Queensland, Brisbane, QLD, Australia

Objective: A medical survey is a type of test that looks for the presence or absence of a condition or disease, and may be used to track response to therapy. Two validated surveys for menopause are commonly utilized to evaluate menopausal problems: Utian Menopause Quality of Life with an emphasis on global sense of wellbeing and Greene Climacteric intended as a standardized measure of core menopausal symptoms. An additional “hybrid” survey, wScore, was developed to evaluate and track menopausal problems and response to therapy. These three surveys are presently compared to each other with respect to the STRAW. Design: 720 consecutive women consented to a prospective cross-sectional study by completing three menopause surveys. Patients were contemporaneously categorized according to STRAW criteria. Results: 349 women were not current users of hormone therapy. Greene Climacteric (range 0-63) and the wScore (range 0-99) are structured with a higher value representing a greater problem. The Utian is oriented oppositely with a lower score indicating a greater problem. For analysis and visual purposes the Utian score was adjusted to zero and reoriented leaving the Utian (range 0-92) with a higher score indicating a greater problem. Significant differences (p < 0.05) between all STRAW categories were found for wScore and Greene. There is a significant difference between STRAW categories of reproductive and perimenopause for Utian, but no significant difference seen for Utian between peri and postmenopause. Conclusion: No single survey adequately captures the essence of problems attributed to the menopausal transition. The wScore accurately functions as a surrogate to both the Utian MQOL and Greene Climacteric by virtue of its menopausal symptom list, as well as, its evaluation of mood, sleep, cognition, and sexual function.

Comparison of Utian QOL, Greene Climacteric, and wScore across STRAW timeline

P.77. Comparison of Three Menopause Surveys Across the STRAW Timeline, Part II: Utian MQOL, Greene Climacteric, wScore In Women Taking Systemic HT

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Objective: A medical survey is a type of test that looks for the presence or absence of a condition or disease, and may be used to track response to therapy. Two validated surveys for menopause are commonly utilized to evaluate menopausal problems: Utian Menopause Quality of Life with an emphasis on global sense of wellbeing and Greene Climacteric intended as a standardized measure of core menopausal symptoms. In Part I, a new hybrid menopause survey, wScore, was compared to these two surveys in naturally cycling or postmenopausal women across the STRAW Timeline. In this study, Part II, the three surveys are compared across surveys in postmenopausal women across the STRAW Timeline. Design: 720 consecutive women from a single private practice consented to a prospective cross-sectional observational study by completing three menopause surveys (Utian, Greene, wScore). Patients were contemporaneously...
P-79.
Usage of FDA-approved and compounded menopausal hormone therapy in the USA following the WHI study
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Objective: To quantify trends of use of FDA approved and non-FDA approved compounded menopausal hormone therapy (MHT) in the US during the period from the publication of the WHI study through 2013. Design: Although it has been previously reported that the use of FDA approved MHT decreased significantly following the publication of the WHI study, the usage of compounded non-FDA approved MHT has largely been unrecognized. A contributing factor is that compounded prescriptions are not captured in a database as are FDA approved prescriptions. To quantify the overall market of FDA approved MHT and non-FDA approved compounded MHT, three separate data sources were utilized: 1) Prescription data for 1998 through 2013 from Source Healthcare Analytics. 2) A 2014 internet survey of women conducted by Rose Research (Rose). Rose surveyed 90,210 women age 40 and greater; 17,897 responded and 2,044 were identified as current or former users of MHT. 3) US Census data 2013. These three sources of data were used to calculate the number of MHT users, including FDA approved and compounding non-FDA approved MHT in US women 40 to 84 years of age. The FDA approved MHT use was compared to the total current MHT users to calculate the numbers of users of non-FDA approved compounded MHT. Results: Overall, approximately 5% of US women 40 to 84 years of age were reported to use MHT (FDA-approved or non-FDA approved compounded). The percentage of current use of MHT varied by age: 6.5% ages 40 to 54, 4% in those ages 60 to 84 and 2.5% of those ages 55 to 59. Ever use of MHT was greatest (24%) in those aged 75-84 with the lowest use (7.7%) in those ages 55 to 59 and 13.5% use in ages 40 to 54. FDA approved MHT use decreased in the US after the 2002 publication of WHI study from approximately 11% of women to a current usage level in approximately 3% of US postmenopausal women. This decrease was most dramatic from 2002 to 2005 and plateaued from 2010 through 2013. Based upon the three data sources, it is estimated that at least 2% of women age 40-84 currently take non-FDA approved compounded MHT. The growth of non-FDA approved compounded MHT has occurred almost exclusively following WHI. Conclusion: FDA approved MHT usage decreased significantly in postmenopausal US women from 2002 through 2013. However, currently compounded non-FDA approved MHT is utilized by approximately 2% of women, which comprises approximately 40% of the overall MHT usage in the US.

P-80.
Hormonal therapy and sexual dysfunction in postmenopausal women from the Colombian Caribbean
Alvaro Montesroura-Castro, Katherine Portela, Liczel Ulloque-Caamaño, Angel Paternina-Caicedo, Ginecología, Universidad de Cartagena, Cartagena, Colombia
Objective: To compare the prevalence of sexual dysfunction (SD) in postmenopausal women according to the use of hormonal therapy Design: Comparative study that is part of CAIVIMEC (Calidad de Vida en la Menopausia y Enanas Colombianas) project, carried out in women from the Colombian Caribbean of different ethnic groups (Mestizo, indigenous and Afro-descendant), aged between 40-59 years, in postmenopause, who expressed had sexual partner and regular sexual activity. They were assessed in their 111 of women with a general questionnaire and the brief FSFI of 6 questions (FSFI-6). To lower score, higher sexual deterioration and SD is a score ≤9. Data analysis was performed using the EPI-INF0-7. A p<0.05 was considered significant Results: 1280 Colombian women from the Caribbean Coast were assessed. They were distributed in two groups: 241 (18.8%) who used any form of hormonal therapy and 1039 (81.1%) who do not use it. Significant differences were not observed in desire, arousal, lubrication, orgasm and sexual satisfaction. Users of hormonal therapy presented better score when discomfort or pain during intercourse was evaluate (p=0.01); however, they presented worse total score of the scale (p=0.04). There was not observed significant difference in the presence of SD between users of hormonal therapy: 49.5 % [44.3-54.8] and nonusers of hormonal therapy: 42.2% [40.2-44.2]. Conclusion: There was not observed significant difference in the presence of SD between users or non-users of hormonal therapy. Women who take hormones had significantly lower presence of pain or discomfort during intercourse.
P-84. Hormone therapy is associated with lower coronary artery calcification: a population-based study
Karen Oppermann1, Verónica Colpani1, Gabriela Ambrós1, Poli M. Spritzer4,5. 1Gynecology and Obstetrics, Medical School of Universidade de Passo Fundo, Passo Fundo, Brazil; 2Hospital São Vicente de Paulo, Passo Fundo, Brazil; 3Gynecological Endocrinology Unit, Division of Endocrinology, Hospital de Clinicas de Porto Alegre, Porto Alegre, Brazil; 4National Institute of Hormones and Women’s Health, Conselho Nacional de Desenvolvimento Científico e Tecnológico., Porto Alegre, Brazil; 5Laboratory of Molecular Endocrinology, Department of Physiology, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil

Objective: The aim of this study was to assess whether clinical variables are associated with CAC in pre-, menopause transition and postmenopausal women. Design: This is a cross-sectional study nested in a longitudinal population-based study. Setting and participants: include 295 women in the city of Passo Fundo, Southern Brazil. The first examination was conducted in 1995-1996 and the present study used data from the third examination, realized between 2010 and 2011. Risk factors and clinical endpoints: Demographic and clinical variables (i.e. medical history, gynecologic data, hormone replacement therapy) were obtained by questionnaires and anthropometric and metabolic profile was evaluated. Habitual physical activity was assessed by pedometer, during seven days. Coronary computed tomography: Scanning center assessed CAC by multi-detector computed tomography system. A radiologist read all CT scans at a central reading center. We used the average Agatston Score. Calciumization was considered present if participants had CAC=0 and absent if CAC>0. Statistical analysis: Poisson regression model with random effects was used to assess the relation between CAC and cardiovascular risk factors. We conducted additional Poisson regression analyses, adjusting for covariates that were found in crude analysis to be strongly related. Data were considered to be significant at P<0.05. Results: Women presenting CAC=0 (34.7%) were older (58.7±5.4 versus 56.3±5.2, p<0.001), had higher prevalence of central adiposity (71 versus 59%, p=0.04), hypertension (71 versus 52%, p=0.002) compared to CAC>0 (table).Smoking, physical activity, educational level, menopausal status, BMI, diabetes and alcohol intake did not differ between the groups. Hormone therapy (HT) was more prevalent in the group of CAC=0 (19.7 versus 9.8%, p=0.029). Prevalence ratio for presence of CAC, obtained by general linear models and adjusted for age, educational level, smoking, alcohol intake, physical activity were: HT: 0.545 (CI:0.309-0.962, p=0.036); hypertension: 1.752 (CI:1.270-2.451, p=0.003); waist-to-hip ratio 1.364(CI:1.095-1.755, p=0.092). Conclusion: In this population-based sample of pre, menopause transition and postmenopausal women, HT was associated with protection for CAC and hypertension with risk for CAC, independently of age.

Table 1. Clinical and social characteristics of the sample, according to CAC

<table>
<thead>
<tr>
<th>Variable</th>
<th>CAC=0</th>
<th>CAC=1 (65.3%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>56.3±5.2</td>
<td>58.7±5.4</td>
<td>0.001</td>
</tr>
<tr>
<td>White skin color</td>
<td>160 (83.7)</td>
<td>85 (77.9)</td>
<td>0.052</td>
</tr>
<tr>
<td>Educational level</td>
<td>8.7±4.3</td>
<td>8.6±3.9</td>
<td>0.012</td>
</tr>
<tr>
<td>Labor</td>
<td>93 (48.2)</td>
<td>37 (34.8)</td>
<td>0.030</td>
</tr>
<tr>
<td>Hormonal Therapy</td>
<td>50 (25.3)</td>
<td>39 (36.0)</td>
<td>0.029</td>
</tr>
<tr>
<td>Menopausal status</td>
<td>17 (86.0)</td>
<td>7 (69.0)</td>
<td>0.172</td>
</tr>
<tr>
<td>Alcohol intake</td>
<td>115 (58.6)</td>
<td>75 (71.6)</td>
<td>0.124</td>
</tr>
<tr>
<td>Smoker</td>
<td>34 (17.6)</td>
<td>24 (23.5)</td>
<td>0.224</td>
</tr>
<tr>
<td>Hypertension</td>
<td>108 (52.2)</td>
<td>72 (82.1)</td>
<td>0.002</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>28.9±6.64</td>
<td>28.2±6.12</td>
<td>0.548</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>94.8±13.3</td>
<td>96.1±14.4</td>
<td>0.092</td>
</tr>
<tr>
<td>Waist-to-hip ratio</td>
<td>0.87±0.86</td>
<td>0.88±1.07</td>
<td>0.138</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>86.9±79.6</td>
<td>86.0±73.7</td>
<td>0.218</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>198±115</td>
<td>211±115</td>
<td>0.056</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>32.9±8.1</td>
<td>34.0±7.4</td>
<td>0.016</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>113±51</td>
<td>142.5±70.5</td>
<td>0.107</td>
</tr>
<tr>
<td>Physical activity</td>
<td>61 (32.6)</td>
<td>32 (32.6)</td>
<td>0.988</td>
</tr>
</tbody>
</table>

P-83. Evaluation of Toll-like Receptor 2 and 4 and RNA Expression and the Cytokine Profile in Postmenopausal Women with Metabolic Syndrome
Cláudio L. Orsatti1, Eliana A. Nahus, MD, Jorge Nahus-Neto1, Vanessa Giorgi2, Flavia B. Dias1, Steven S. Witkin3. 1Gynecology and Obstetrics, Botucatu Medical School-Sao Paulo State University, Botucatu, Brazil; 2Department of Obstetrics and Gynecology, Division of Immunology and Infectious Diseases, Cornell Medical College, New York, NY

Objective: To evaluate the gene expression of Toll-like (TLR-2 and TLR-4) receptors and cytokine profile in postmenopausal women with or without metabolic syndrome (MetS). Design: In this cross-sectional study, 311 Brazilian women (age ≥45 years and amenorrhea ≥12 months) were included. Exclusion criteria included: recurrences or current history of cancer, tuberculosis, diabetes, chronic kidney disease, autoimmune diseases and cancer. Women showing three or more of the following diagnostic criteria were diagnosed as positive for MetS: waist circumference ≥88 cm, triglycerides >150 mg/dL, LDL cholesterol <50 mg/dL, blood pressure ≥130/85 mmHg, and fasting glucose ≥100 mg/dL. The expression of TLR-2 and TLR-4 was evaluated by real time PCR (polymerase chain reaction) analysis. The cytokine profile, tumor necrosis factor alpha (TNF-α) and interleukins 1β, 6, and 10, were measured by ELISA. Statistical analyses used the chi-square test, Kruskal-Wallis test, Mann-Whitney test and Spearman correlation. Results: The expression of TLR-2 and TLR-4 RNA was demonstrated in 32.5 % and TLR-4 in 20.6% of the subjects. There was no association between the expression of TLR-2 and TLR-4 and the presence or absence of MetS (P=0.05). There was greater IL-6 (P=0.044) and TNF-α (P=0.048) production in women expressing TLR-2 and TLR-4, respectively, than those who were TLR-2 or TLR-4 negative. There were positive correlations between IL-6 levels and high blood pressure (P=0.036) and hyperglycemia (P=0.047). No association was observed between the expression of TLR-2 or TLR-4 and markers of MetS conclusion: TLR-2 expression was associated with increased pro-inflammatory cytokines, IL-6 and TNF-α, and TLR-4 negatively correlated with elevated blood pressure and hyperglycemia, biomarkers of metabolic syndrome.

P-85. Association between levels of serum ferritin and bone mineral density in Korean premenopausal and postmenopausal women: KNHANES 2008-2010

Seok Kyo Seo1, Byungsuek Lee1, Kihyun Park1,2. Obstetrics and Gynecology, Severance Hospital, Yonsei University, Seoul, Republic of Korea; 1Obstetrics and Gynecology, Sam General Hospital, Ahnyang, Republic of Korea

Objective: As women go through menopause, serum estrogen decreases and ferritin increases. Despite the increase in serum estrogen is well known to cause detrimental effects on bone health, but data on the associations between serum ferritin with BMD before and after menopause are still lacking. Therefore, this study aimed to investigate the association between serum ferritin levels and BMD in pre- and postmenopausal Korean women.

Design: A study performed using data collected from the 2008-2010 Korean National Health and Nutrition Examination Survey, including 7305 women (4229 premenopausal and 3076 postmenopausal). BMD was measured using dual X-ray absorptiometry at femur and lumbar spine, and serum ferritin levels were measured by chemiluminescent immunoassay.

Results: Median serum ferritin levels in postmenopausal women were higher than those in premenopausal women despite the same age ranges. Serum ferritin levels were significantly correlated with BMD on lumbar spine (beta = -0.199, P = 0.003) in premenopausal women after adjusting confounding factors. Additionally, BMD on lumbar spine had a tendency to decrease as serum ferritin quartiles increase (P for trend = 0.036) in premenopausal women after adjusting confounding factors. On the other hand, there were no significant associations between serum ferritin levels and BMD on total femur, femur neck in premenopausal women, and BMD on total femur, femur neck and lumbar spine in postmenopausal women. Conclusion: Increased serum ferritin levels were significantly associated with BMD in premenopausal women, particularly on lumbar spine, but not in postmenopausal women.

P-86. Melatonin and Other Circadian Rhythm Disturbances in Menopausal Depressed Patients vs. Normal Control Women

Barbara L. Parry, M.D., Charles Meliska, Ph.D, Diane Sorenson, Henry Orff, Fernando Martinez, Ana Lopez, Richard Hauger. Psychiatry, University of California, San Diego, La Jolla, CA

Objective: To test the hypothesis that the amplitude or phase (timing) of melatonin and other circadian rhythms (sleep, cortisol, Thyroid Stimulating Hormone-TSH, prolactin) differ in menopausal depressed patients (DP) vs. normal control (NC) women.

Design: In 38 (24 NC, 14 DP) peri- or post-menopausal women (as assessed by serum Follicle Stimulating Hormone-FSH), we measured plasma melatonin and serum cortisol, TSH and prolactin every 30 minutes from 18:00-0:00 h in dim light (< 30 lux) or dark, serum gonadotropins and steroids-estradiol, progesterone, FSH, luteinizing hormone-LH (18:00, 06:00 h), mood (Hamilton and Beck depression ratings) and subjective (logs) and objective (polysomnography-PSG) sleep.

Results: Multi- and univariate analyses of covariance (MANCOVA, ANCOVA) showed melatonin offset time was delayed (P = 0.045) and morning plasma melatonin was elevated in DP compared with NC (P = 0.044). Multiple regression analyses showed that years past Menstrual Period (FMP) predicted melatonin duration, and that melatonin duration, body mass index (BMI), years past FMP, FSH level and sleep end time were significant predictors of baseline Hamilton (P = .0003) and Beck (P = .0004) depression scores. Cosinor acrophase, amplitude and mesor for cortisol, TSH and prolactin were not significantly different in DP vs. NC. Sleep logs showed no significant differences in sleep variables in DP vs. NC. Conclusion: Increased melatonin secretion that is phase-delayed into the morning characterized menopausal DP vs. NC. Years past FMP, FSH, sleep end time and BMI may modulate effects of altered melatonin secretion in menopausal depression. Cortisol, TSH and prolactin circadian rhythms were not significantly different in DP vs. NC. DP had poorer sleep quality by subjective, but not objective, assessments.

P-87. Presenting Symptoms among Premenopausal and Postmenopausal Women with Vulvodynia

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Objective: Vulvodynia is a chronic vulvar pain condition that may be localized to the vulvar vestibule (vestibulodynia) or generalized to a wider area of the vulva and may be provoked (e.g., intercourse or tampon use) or nonprovoked (spontaneous) Vulvodynia affects both reproductive and non-reproductive-aged women, with a prevalence of 15.6% in women over 65 years of age. In symptomatic postmenopausal women, vulvodynia should be considered in a postmenopausal or estrogenic state. Vulvodynia has been ruled out. Our objective was to determine whether there were differences in the clinical presentation of symptoms and vulvar pain ratings in postmenopausal women compared to premenopausal women with provoked vestibulodynia (PVD) enrolled in a clinical trial. Design: Pre-treatment data in 42 self-identified premenopausal and 9 postmenopausal women were analyzed prior to trial entry. Subjects were clinically confirmed to have PVD by pelvic exam. Those with atrophic vaginitis by presence of a 10% parabasal cells were treated with local estrogen therapy for 6 weeks and rescreened clinically for adequate estrogen therapy symptoms did not resolve. Women completed a standardized questionnaire describing their vulvar symptoms and rated daily pain on a visual analogue scale (0 = no pain to 10 = worst pain imaginable) from sexual intercourse, tampon insertion (as a surrogate measure of intercourse) and 24-hour vulvar pain. Chi-Square was used to determine differences between pre- and postmenopausal women in the questionnaire characteristics and unprovoked, intercourse and tampon use scores. Manova was used to analyze pain ratings by (0-10) numeric rating scale (NRS). Results: The average ages of premenopausal and postmenopausal women were (31.2 ± 9.4 years) and (55.3 ± 7.5 years), respectively. The groups did not differ in years of education (p = .24), race (p = .67), marital status (p = .57) or on repeated if symptoms for vaginal dryness and irritation differences were observed in clinical presentation for post- compared to premenopausal women in vulvar burning (77.8% vs. 54.8%, p = .026), vulvar itching (33.5% vs. 23.8%, p = .51) and vulvar stinging (44.4% vs. 49.5%, p = .47), and vulvar aching (44.4% vs. 59.5%, p = .46) in menopausal (2.56 ± 1.33 vs. 2.48 ± 1.42, p = .088). Similarly, there were no significant differences in mean (± SD) NRS pain ratings of postmenopausal compared to premenopausal women for vulvar insertion (5.56 ± 1.64 vs. 5.69 ± 2.37, p = .088), daily vulvar pain (2.39 ± 2.32 vs. 3.67 ± 2.55, p = .025) and sexual intercourse (5.33 ± 3.79 vs. 5.93 ± 2.52 p = .071). Conclusion: Our preliminary findings suggest that the clinical presentation of symptoms and vulvar pain severity are similar in postmenopausal and premenopausal women with PVD. The statistical power of our conclusion is limited by the small number of postmenopausal women in the study. Further research on the vulvar pain experience of the older woman is warranted.
Objective: To quantify compounded bioidentical hormone therapy (CBHT) use among menopausal US women and to explore their knowledge of CBHT vs FDA-approved hormone therapy. Design: Two Internet surveys were conducted—one by Rose Research (Rose) in April 2010 and the other by Harris Interactive (Harris) in January 2013—to identify patterns of menopausal hormone therapy (MHT) use. To quantify CBHT use, we extrapolated findings from Rose to the general population of US women using census data. Source Healthcare Analytics PHAST 2.0. Pharmaceutical Data. 2013. 1. 2010 US Census Data.

Results: Sales, usage, and prescribing of CBHT are not systematically tracked, so extrapolations were required to quantify the use of CBHT among US women. In Rose, 5% of respondents (883/17,825) were current MHT users. Extrapolating to the general population suggests at least 3.6 million US women per year use MHT (Table 1). Multiplying 3.6 million by the average number of drugs current MHT users in Rose were taking per year indicates 57 million prescriptions for MHT may be filled annually. Subtracting the ~36 million FDA-approved MHT prescriptions filled annually2 from the estimated 57 million annual MHT prescriptions suggests 21 million CBHT prescriptions may be filled annually. Further, dividing the ~21 million annual MHT prescriptions by mean duration of treatment by number of products being used suggests at least 1.4 million women use CBHT. Multiplying CBHT prescriptions filled annually by the average amount paid for MHT as reported in Rose (~$49) indicates more than $1 billion per year may be spent on CBHT in the United States. Harris and Rose surveys were consistent with each other, indicating that 9% to 9.5% of respondents were prior MHT users and 5% to 6% were current users. At least 2/3 of MHT users in each survey said their physician had recommended it. Most Harris completers (78%) had or were having a menopausal symptoms. Similarly, treating symptoms was the main reason Rose completers gave for starting MHT (53%) or continuing MHT (43%). In Rose, 21% (378/1771) of completers believed their MHT had been “specifically formulated, personalized, or compounded” based on their hormone levels and 27% (476/1771) did not know whether their MHT was custom-compounded. Most CBHT users in both surveys obtained CBHT at a local pharmacy; however, 15% of CBHT users in Rose obtained MHT at their physician’s office. Most importantly, 76% of Harris completers were unsure whether CBHT obtained at a specialty pharmacy was FDA-approved (10% incorrectly said it was). Conclusion: Based on these surveys, an estimated 1.4 million US women are current or former users of MHT. The Rose and Harris surveys were funded by TherapeuticsMD.

Table 1. Rose Data Applied to the General Population4

<table>
<thead>
<tr>
<th>From Rose</th>
<th>Usage in US women using MHT</th>
<th>Extrapolated CBHT use</th>
<th>Proportion of MHT use that is CBHT</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of MHT prescriptions filled annually</td>
<td>37 million</td>
<td>57 million</td>
<td>38 million</td>
</tr>
<tr>
<td>No. of FDA-approved drugs filled annually</td>
<td>56 million</td>
<td>56 million</td>
<td>56 million</td>
</tr>
<tr>
<td>No. of MHT prescriptions filled annually</td>
<td>21 million</td>
<td>21 million</td>
<td>21 million</td>
</tr>
<tr>
<td>No. of MHT prescriptions filled annually</td>
<td>1 million</td>
<td>1 million</td>
<td>1 million</td>
</tr>
<tr>
<td>Extrapolated cost of MHT use (1-54 prescriptions)</td>
<td>$1.2-$11.8 million</td>
<td>$1.2-$11.8 million</td>
<td>$1.2-$11.8 million</td>
</tr>
</tbody>
</table>

Table 1. Rose Data Applied to the General Population

References
1. 2010 US Census Data.

P-90. Hypoactive sexual desire disorder and sexual dysfunction in indigenous women in climacteric from Latin-America

Katherine Portela, Lizeel Ulique-Camaamo, Alvaro Monterrosa-Castro, Juan Blumel-Mendez. Grupo de Investigacion Salud de la Mujer, Cartagena, Colombia

Objective: To estimate the prevalence of SD in Latin-American indigenous women in climacteric. Design: Cross-sectional study carried out Zenesis (Colombian) and Quechua (Peruvian) indigenous aged between 40 and 59 years who had sexual partner and regular coital activity. The Female Sexual Function Index (FSFI) evaluated 6 domains (Desire, arousal, lubrication, orgasm, satisfaction and pain). Score ≥2.65 indicates presence of SD. The scale allows establishing the presence of HSDD when the score of the desire domain is ≤5. They were assessed in their own communities. Data analysis was performed using the EPI-INFO 7. The p<0.05 was statistically significant.

Results: 234 indigenous women were included, 157 (63.3%) Zenesis and 309 (66.7%) Quechua. Age: 47±6.3 years, BMI: 23.6±2.8, offspring: 4.0±1.7, diabetes: 2.7%, arterial hypertension: 0.6%, Never smokers: 96.7%, hormonal therapy: 3.8%. The average age of the last menstruation in postmenopausal women 43±2.9 and the number of years in postmenopausal phase 9±4.1. The most damaged domains was sexual satisfaction, followed by the desire and lubrication. The average score of FSFI: 22.7±3.9. SD: 87.1% [CI95%:83.6-89.9%. and HSDD: 93.9% [CI95%:91.3-95.9]. DS appeared in 52.4% [CI95%:47.4-57.4] of women premenopausal and 47.5% [CI95%:42.6-52.5] postmenopausal. The HSDD was observed in 52.5% [CI95%:47.7-57.2] of premenopausal, and 47.4% [CI95%:42.7-52.8] of postmenopausal women Conclusion: The prevalence of SD and HSDD in a group of Colombian and Peruvian indigenous in climacteric was high. For both sexual disorders, significant differences were not observed with the change of the menopausal status.

P-91. Efficacy and Safety of a New Low-Dose Estradiol Vaginal Cream Administered 2 Times a Week for the Treatment of Vaginal Dryness Associated with Menopause

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Objective: Use of estrogen alone is one of the recommended therapies for moderate to severe symptoms of vulvovaginal atrophy (VVA) associated with menopause, including vaginal dryness. This 12-week, double-blind, placebo-controlled study assessed the efficacy and safety of a new low-dose estradiol vaginal cream (0.003%) in women with moderate to severe vaginal dryness. Design: Post menopausal women (N=488) experiencing vaginal dryness of moderate to severe intensity, which was self-identified as the subject’s most bothersome symptom of VVA, that had a vaginal pH greater than 5.0 and less than or equal to 5% superficial cells on vaginal wall cytology smear were randomly assigned to 1 of 2 treatment groups: 15 mcg estradiol as estradiol vaginal cream (n=237) or vehicle cream (n=248). The subjects were dosed once daily for 2 weeks followed by 2 times per week for an additional 10 weeks. The three co-primary efficacy assessments were the mean change in subjects’ self-assessed severity of vaginal dryness, mean change in vaginal pH, and the mean change in the percentage of superficial cells on vaginal wall cytology. Additionally, vaginal pH was assessed by the investigator by visual inspection of the vagina for signs of atrophy, pallor, dryness, friability, and petechiae. Results: The subjects in the study had a mean age of 60 years and median weight of 152 pounds. The demographic characteristics and VVA symptoms were comparable between the 2 treatment groups at baseline. Change from baseline in participant assessment of vaginal dryness improved significantly at Week 4 (p=0.0309), Week 8 (p=0.0004), Week 12 (p=0.0061) and Week 12/Final Assessment (p=0.0125) in the estradiol vaginal cream group vs the vehicle group. Vaginal pH and the percentage of parabasal and superficial cells improved significantly in the estradiol vaginal cream group from baseline to Week 12 and Week 12/Final Assessment compared with the vehicle group (p<0.0001). The investigator’s assessment of vaginal health also showed significant improvements for the estradiol vaginal cream group vs vehicle from baseline to Week 12 and Week 12/Final Assessment (p<0.0001). Among the subjects who experienced adverse events (46.9% estradiol vaginal cream; 45.3% vehicle) almost all were mild or moderate in severity. Most frequently reported adverse events were urinary tract infection and vulvovaginal mycotic infection (5.2% each) for estradiol vaginal cream and urinary tract infection (5.2%) and application site pain (5.5%) for vehicle. Two subjects in each treatment group experienced treatment-emergent SAEs (0.7%) that were unlikely related to study drug. Eight (2.8%) subjects treated with estradiol vaginal cream and 5 (1.7%) subjects treated with vehicle experienced AEIs that led to discontinuation from the study. The new low-dose estradiol vaginal cream significantly improved the severity of vaginal dryness in post menopausal women and was well tolerated.
Evidence-based pharmacologic treatment options and no approved pharmacologic options for the treatment of HSDD. Tribulus terrestris and Tribolone may be evaluated as an alternative therapeutic option for women with HSDD because of their potential hormonal activity. Despite these treatment limitations, health care providers can address the sexual health concerns of post-menopausal women.

P-95. Vaginal health and menopausa: isoflavones derived from Glycine max (L.) Merr versus placebo

Sonia Maria R. Rolim-Lima1, Bianca Franco Augusto Bernardo1, João Duvilio de Biazi Andreotti2, Camila Matsuura Endo1, Suzette Matiko Sasagawa2, Silvia Saito Yamada1, Suely Mitoi Ykko Ueda1. 1Gynecology and Obstetrician, Santa Casa Medical School Sao Paulo, Sao Paulo, Brazil; 2Microbiologist, Santa Casa Medical School Sao Paulo, Sao Paulo, Brazil

Objective: Isoflavones derived from Glycine max (L.) Merr are the most studied of the phytoestrogens and some trials involving its oral form for treating climacteric symptomatology have shown no change in vaginal epithelium or endometrium. Similarly, topical preparations for the prevention and delay of skin maturation in postmenopausal women have shown satisfactory outcomes. Estrogen similar effect of this pharmacological type, associated with the topical route of administration, without systemic interaction may represent a new therapeutic for women whose hormone therapy is contraindicated. The aim of the current investigation was to evaluate the effects of vagal administration of isoflavones derived from Glycine max (L.) Merr as a treatment option for vaginal symptomatology, the vaginal pH and vaginal microbiota of postmenopausal women.

Design: Double-blind, randomized, placebo-controlled, clinical trial. The authors of this study supported by the Federal University of Sao Paulo, Sao Paulo, Brazil, and the Foundation for Research Support of the State of Sao Paulo (FAPESP). It was selected 55 women in the postmenopausal period with exclusive complaints of genital atrophy without indications or contraindications to oral hormone therapy. The women were divided into two groups according to vaginal gel used: Group I (n = 29), use of Glycine max (L.) Merr (isoflavones - Hebron 80®) and Group II (n = 26), placebo. Each gel was administered vaginally on a daily basis throughout the 12-week trial. During both T0 and at visits T1 and T2, patients filled out a questionnaire regarding the symptoms of vaginal dryness and dyspareunia, which were subsequently classified as follows: 0 = none, 1 = mild, 2 = moderate, 3 = severe. Vaginal secretion from the vaginal fornix was collected on T0, T1 and T2 for analysis of microbiota, and vaginal pH only in the Isoflavone group (Table II). There was no change in FSH, estradiol and endometrial safety (endometrial thickness as measured by transvaginal ultrasonography) were evaluated at T0 and T2. Data was analyzed via Epi Info™ 7 and SPSS Statistics, the confidence interval of 95% and the t-distribution paired, McNemar and chi-square. Results: In the Isoflavone group there was an improvement in vaginal dryness and dyspareunia and in the placebo group, only vaginal dryness (Table I). The most prevalent microorganisms in both groups were Enterococcus sp, coagulase-negative Staphylococcus and Escherichia coli, there was variation in the vaginal microbiota only in the Isoflavone group for Enterococcus sp when comparing T0 vs T1 (p=0.03) and Bacinella sp when comparing T1 vs T2 (p=0.01). There was a reduction of the vaginal pH only in the Isoflavone group (Table II). There was no change in FSH, estradiol and endometrial ECO in both groups after treatment (Table II). Conclusion: Isoflavone improves vaginal pH and vaginal symptoms of urogenital atrophy and alters the vaginal microbiota, without changing FSH, Estradiol and endometrial ECO, representing a therapeutic option to improve the genital epithelium.

P-94. The effects of Tribulus terrestris and Tribolone in postmenopausal women with hyoactive sexual desire disorder

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Objective: To study the effects of Tribulus terrestris and Tribolone in post menopause women with HSDD. Design: This is a prospective, randomized, double blind study with 66 postmenopausal women with HSSD. Women were allocated randomly into three groups: Control Group (n = 20) received placebo; Tribulus group (n=22) received 750 mg/oral administration/day; and Tribolone group (n=24) 1.25 mg/oral administration/day. The Female Sexual Quotient (Quociente Sexual Feminino - QSF) was applied to evaluate the sexual function, before and after 90 days of treatment. The women considered as being post-menopausal were those with amenorrhea for 1 year and FSH ≥30mIU/mL. All patients signed a voluntary informed consent form prior to participation in the study, which was approved by the Medical Ethics Committees at the Faculty of Medical Sciences at Santa Casa de Sao Paulo and the Foundation for Research Support of the State of Sao Paulo (FAPESP).

Results: In Groups Control Tribulus all patients completed the study; in Tribolone Group four women did not complete it, three due to side effects. In Tribulus and Tribolone Groups there was a significantly improvement in the sexual function, after 90 days treatment the Control Group kept the same pattern, Tribolone Group showed a regular-good pattern and Tribolona Group to a good-excellent pattern. Conclusion: There are only modest
Cortisol awakening response differs for midlife women with objective vasomotor symptoms versus without vasomotor symptoms
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Objective: We previously reported the novel finding that cognitive performance relates significantly to the number of objective vasomotor symptoms (VMS) women experience but not to the number of VMS they report. Recently, we also found that reductions in objective VMS were associated with improvements in subjective cognitive performance. These findings suggest that physiological factors related to VMS, rather than psychological factors, predict poorer cognitive function. One potential mechanism that might mediate the relationship between objective VMS and cognitive performance is cortisol. Increases in cortisol are associated with decrements in cognitive performance and higher VMS frequency. Here we aimed to test the hypothesis that objective VMS will relate to higher cortisol awakening response (CAR) and that higher CAR and total daily cortisol will predict worse cognition.

Additionally, we aimed to examine whether the relationship between cortisol and cognitive performance differs between women with and without objective VMS.

Design: In an observational study, 40 midlife early post- and perimenopausal women (mean age, 52.1 years) with either self-reported moderate to severe hot flashes (n=20; >30 hot flashes/week) or none-to-few hot flashes (n=20; <7 hot flashes/week) completed measures of objective hot flushes with an ambulatory hot flash monitor, subjective hot flashes with a diary and questionnaire, and a standardized neuropsychological test battery. Women were also asked to provide saliva samples for three days. On each of the 3 days, participants provided samples at the following points: wake time, wake time plus 15 minutes, wake time plus 30 minutes, and 15, 30, and 45 minutes post waking and 3, 6, 9, and 12 hours post waking. These samples were shipped to an outside laboratory that measures cortisol according to standard procedures and using standard calculations for both CAR and total cortisol (area under the curve—AUC).

In order to examine VMS group differences on the CAR, we conducted a series of mixed effects regressions (MRRM), Variables included in the analysis are: Subjective: mild to severe hot flushes for the cohort, average daily cortisol level at baseline (LNG-IUD placement), and again at 90 days post treatment; Objective: hot flash frequency, number of hot flushes per day and number of hot flushes per week (self-reported) as well as the number of hot flushes per week (self-reported). We performed correlation analysis for objective VMS to total cortisol level and subjective VMS to cortisol level. We also performed correlation analysis for subjective VMS to total cortisol level and objective VMS to total cortisol level. These analyses were performed after removing women with missing data. Women were divided into four groups.

**Design:** Double-blind randomized controlled pilot trial. Regularly cycling women ages 40-52 with at least one of the following (hot flashes, bloating, headache, or adverse mood, or poor sleep (self-reported)) were enrolled and randomized to either LNG-IUD plus low-dose estrogen gel (intervention) to LNG-IUD alone (control). Estradiol was administered once daily as a 0.06% gel containing 0.75mg of estradiol per 1.25gm. Estradiol levels for the cohort climbed from a baseline of < 15 pg/ml to an average E2 of 36.5 pg/ml. Participants maintained a daily diary of estradiol levels for the 180 day study period. Women were followed up at 3, 6, 9, and 12 months post-randomization.

**Results:** A total of 38 women were enrolled; 20 were randomized to TDE. The average age was 42.9±2.7 years and mean BMI was 24.7±3.3 kg/m2; the groups were similar with regard to these measures. Women receiving TDE demonstrated significantly improved FSS scores between days 90 and 140 (mean difference: TDE-0.8±0.2 vs. placebo-0.1±0.7; p=0.026) and borderline significant improvement in HFRDIS scores (mean difference TDE: -5.5±15.3 vs. placebo: 4.2±13.1; p=0.076). CESD and PSQI scores were not associated with TDE use. There were no reported unexpected adverse events.

**Conclusion:** The impact of perimenopausal symptoms was observed with estradiol and low-dose estrogen intervention in combination with LNG-IUD use in this pilot study. Such a ‘minimalist’ approach to management of the perimenopause holds promise for reducing common, bothersome menopausal symptoms while maintaining effective contraception.

Transdermal Progesterone: The Impact of Dose and Duration of Use on Endometrial Histology in Postmenopausal Hormone Therapy
Carolyn V. Shaak, MD1, Charlotte M. Walsh, PhD2, WomanWell, Inc, Needham, MA; 2Gynecology, Faulkner Brigham and Women’s Hospital, Boston, MA.

Objective: Studies of the endometrial protective effect of transdermal micronized progesterone have not been reassuring. However, we have investigated the use of transdermal progesterone at the FDA approved oral dose strengths of 100-200 mg. Although adverse effects of intrauterine progesterone have previously been limited to duration. There are no published reports of transdermal progesterone use for a 2 year duration as required by the FDA for pregestin approval. The objective of this retrospective cohort study was to examine the endometrial impact of transdermal progesterone (P) when administered, along with estradiol (E2), continuously for a minimum of 2 years in daily doses equal to the FDA approved oral doses.

**Design:** The records of 192 menopausal patients using a customized transdermal estradiol and progesterone cream were selected for review because the patients underwent endometrial evaluation by ultrasound or endometrial biopsy in 2012 or 2013. The average age of the cohort was 61 years. All members used an E2 transdermal hormone cream for a minimum of 24 months (average=4.5 years). The most frequently prescribed E2 formulation utilized 1 mg of estradiol contained with 100 mg of progesterone at the site of application and was administered most commonly as 1cc twice daily to the hip/high region. Total daily hormone doses ranged from 1.5 to 3 mg E2 and 100 to 300 mg P. The 192 patient cohort was subdivided into four groups according to the type of endometrial data obtained: GROUP 1: ultrasound for bleeding, <5mm endometrium, no biopsy (n=86); GROUP 2: ultrasound unrelated to bleeding, <5mm lining, no biopsy (n=50); GROUP 3: ultrasound any reason, >5mm endometrium, biopsy (n=45); GROUP 4: biopsy for bleeding without antecedent ultrasound (n=11).

**Results:** AUC levels:

- Baseline: 1 for all groups
- +180min: 0.8
- +360min: 0.8
- +540min: 0.8
- +720min: 0.8
- 3, 6, 9, and 12 hours post-waking: 0.8

Women with objective VMS, but not subjective VMS were associated with improvements in cognitive function. One potential mechanism that might mediate the relationship between objective VMS and cognitive performance is cortisol. Increases in cortisol are associated with decrements in cognitive performance and higher VMS frequency. Here we aimed to test the hypothesis that objective VMS will relate to higher cortisol awakening response (CAR) and that higher CAR and total daily cortisol will predict worse cognition.

Additionally, we aimed to examine whether the relationship between cortisol and cognitive performance differs between women with and without objective VMS.

Design: In an observational study, 40 midlife early post- and perimenopausal women (mean age, 52.1 years) with either self-reported moderate to severe hot flashes (n=20; >30 hot flashes/week) or none-to-few hot flashes (n=20; <7 hot flashes/week) completed measures of objective hot flushes with an ambulatory hot flash monitor, subjective hot flashes with a diary and questionnaire, and a standardized neuropsychological test battery. Women were also asked to provide saliva samples for three days. On each of the 3 days, participants provided samples at the following points: wake time, wake time plus 15 minutes, wake time plus 30 minutes, and 15, 30, and 45 minutes post waking and 3, 6, 9, and 12 hours post waking. These samples were shipped to an outside laboratory that measures cortisol according to standard procedures and using standard calculations for both CAR and total cortisol (area under the curve—AUC).

In order to examine VMS group differences on the CAR, we conducted a series of mixed effects regressions (MRRM), Variables included in the analysis are: Subjective: mild to severe hot flushes for the cohort, average daily cortisol level at baseline (LNG-IUD placement), and again at 90 days post treatment; Objective: hot flash frequency, number of hot flushes per day and number of hot flushes per week (self-reported) as well as the number of hot flushes per week (self-reported). We performed correlation analysis for objective VMS to total cortisol level and subjective VMS to cortisol level. Women with objective VMS were divided into five groups.

**Design:** Double-blind randomized controlled pilot trial. Regularly cycling women ages 40-52 with at least one of the following (hot flashes, bloating, headache, or adverse mood, or poor sleep (self-reported)) were enrolled and randomized to either LNG-IUD plus low-dose estrogen gel (intervention) to LNG-IUD alone (control). Estradiol was administered once daily as a 0.06% gel containing 0.75mg of estradiol per 1.25gm. Estradiol levels for the cohort climbed from a baseline of < 15 pg/ml to an average E2 of 36.5 pg/ml. Participants maintained a daily diary of estradiol levels for the 180 day study period. Women were followed up at 3, 6, 9, and 12 months post-randomization.

**Results:** A total of 38 women were enrolled; 20 were randomized to TDE. The average age was 42.9±2.7 years and mean BMI was 24.7±3.3 kg/m2; the groups were similar with regard to these measures. Women receiving TDE demonstrated significantly improved FSS scores between days 90 and 140 (mean difference: TDE-0.8±0.2 vs. placebo-0.1±0.7; p=0.026) and borderline significant improvement in HFRDIS scores (mean difference TDE: -5.5±15.3 vs. placebo: 4.2±13.1; p=0.076). CESD and PSQI scores were not associated with TDE use. There were no reported unexpected adverse events.

**Conclusion:** The impact of perimenopausal symptoms was observed with estradiol and low-dose estrogen intervention in combination with LNG-IUD use in this pilot study. Such a ‘minimalist’ approach to management of the perimenopause holds promise for reducing common, bothersome menopausal symptoms while maintaining effective contraception.
P-100.
Role of gabapentin in menopausal vasomotor symptoms
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Objective: Hot flashes are the main reason for seeking treatment during menopause. There are various hormonal and non hormonal options for the same. objective was to evaluate the effect of gabapentin on menopausal hot flashes. Design: - Study was conducted on 50 women in menopausal age group (40-60 years) presenting with hot flashes. The patients were given 900 mg of gabapentin divided in three doses of 300 mg each. At enrollment they were interviewed in details regarding hot flashes, sleep disturbances, depression, anxiety as per greene climaetric scale. Hot flash score was calculated as- (No of mild hot flash in a day X1) + (No of moderate hot flashes in day X2) + (No of severe hot flashes in day X3). The patients were followed at 2, 4, 8 and 12 weeks. At each visit rescoring was done and hot flash, anxiety, depression, somatic and vasomotor scales were calculated. Ultrasound (Uterus, adnexa, endometrial thickness) and lipid profile was one at enrollment and at 12 weeks. Results: Mean age was 50.96 ± 4.49 years. All the patients presented with hot flashes associated with sleep disturbances, depression and sexual problems in 92%, 82% and 38% respectively. There was significant improvement (p value <0.05) in hot flash score which fell by 8%, 44.7%, 64.3% and 82% at end of 2, 4, 8 ad 12 weeks respectively. As per Greene Climaetric Scale, anxiety, depression, somatic, vasomotor and sexual scales fell by 81.81%, 44.44%, 100%, 75.4% and 75% at the end of 12 weeks. There was improvement in cholesterol, HDL, LDL, VLDL and triglyceride levels at end of 12 weeks but it was not significant (p values >0.05). Conclusion: Gabapentin is an effective treatment option for menopausal vasomotor symptoms.

P-101.
Atypical Presentation Of Pyometra Due To Leiomyoma In Post Menopausal Women
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Objective: A pyometra is a rare disorder seen in 0.01-0.5% of patients 1. Various causes especially in post menopausal women are stenosed cervical os, cervical malignancy, radiotherapy, endometrial carcinoma, forgotten intrauterine device, genital tuberculosis etc.2 Design: A postmenopausal woman presenting with pyometra due to fibroid uterus and the pus discharge continued even after one month of continuous pus drainage, which was managed by hysterectomy is presented. Results: A 60 years old woman, para two, menopausal for five years presented with progressively increasing mass abdomen for four months, blood stained foul smelling discharge and loss of weight for two months and fever for one month. On examination she was febrile, and the uterus was enlarged to 22 week size and was firm, non tender and mobile with no adnexal mass. Vaginal examination showed foul smelling copious pus coming through the cervix which was flushed with vault and cervical os was admitting tip of finger through which an irregular mass was felt just above the internal os. Provisional diagnosis of endometrial growth with pyometra was made. Ultrasound showed enlarged uterus with a large hyperechoic lesion with multiple echogenic foci in it suggesting pyometra with uterine growth. Vaginal swabs sent for culture and sensitivity. The patient was administered broad spectrum antibiotics and continuous drainage of pus was done by putting self retaining catheter in the uterus. Daily about 80-100 ml pus drained and pus drainage did not subsided even after 15 days of continuous drainage. Cervical biopsy and endometrial aspiration (biopsy not possible due to pus in uterine cavity) were sent for histopathology and cytology respectively and reported as chronic cervicitis and large number of inflammatory cells, endometrial cells could not be seen. Even after one month of admission, pus discharge, low grade fever and loss of weight continued so, exploratory laparotomy was performed. The uterus was soft, enlarged to 22 week size, with normal fallopian tubes and ovaries. On cut section, whole of the uterus was filled with pus and a large necrotic growth and the cervix appeared normal (Figure- 1). Total abdominal hysterectomy and bilateral salpingo oophorectomy was done. Post operative period was uneventful. Histopathology reported as infected leiomyoma with no evidence of malignacy. Conclusion: Usual treatment of pyometra in menopausal woman is hysterectomy. Which is usually performed when there is no more pus and histopathology report is available. If the patient is not responding to symptomatic treatment for long and is deteriorating, hysterectomy might be needed in some cases of pyometra with the pus in uterus.

P-102.
Post hysterectomy Vault prolapse- A review over three years
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Objective: To study the clinical profile, surgical details of hysterectomy and the etiology of the prolapse, in the patients who presented with vault prolapse after hysterectomy. Design: It is a retrospective study over a period of three years in department of gynecology at post graduate institute of medical science, Rohtak, India. All the patients who presented with vault prolapse after hysterectomy were included in the study. There were total of 30 patients. The demographic profile, duration of symptoms, type of hysterectomy, who performed the hysterectomy whether general surgeon or gynecologist and the treatment offered for vault prolapse were studied in detail. The cause for vault prolapse if any was tried to find out. Results: The patients were in age group of 45-65 years with mean age 54.73 ± 5.89 years. Most of the patients belonged to rural background (73.33%) and were illiterate (53.33%). Mean duration of symptoms was 6.39 ± 6.35 years and mean duration of hysterectomy was 9.5 ± 4.95 years. Most of the patients had symptoms within one year of hysterectomy (46.66%, n=14) followed by within five years (20.0%, n=6), ten years (20%, n=6) and more than ten years (13.33%, n=6). Eighteen patients (60.0%) had developed prolapsed after abdominal hysterectomy, ten patients (33.33%) after vaginal hysterectomy and two (6.66%) after laparoscopic assisted hysterectomies. Most of the hysterectomies (56.67%, n=17) were done by general surgeon and these all were abdominal hysterectomies, 26.67% (n=8) were performed by gynecologist and in five cases (16.66%) specialty of doctor could not be elicited from records as majority of patients were illiterate. All the patients who came within one year had undergone abdominal hysterectomy and that was done by general surgeons. Procedures done for vault prolapse at presented in case were sacrospinous fixation transvaginally (SSF) with enterocoe repair (36.67%, n=11), SSF with anterior colporrhaphy and posterior colpopereinephoraphy (23.33%, n=7) and abdominal meshplasty (23.33%, n=7). It is further observed that all the cases which presented with symptoms within one year of surgery had abdominal hysterectomies and all these were performed by general surgeons. As, the patient had vault prolapsed within one year so the reason seems to be technical, either mild enterocele present at time of surgery was missed and not repaired or vault suspension was not performed. In India, sometimes abdominal hysterectomy is done by general surgeons (who are not so conversant with both pelvic floor surgery) especially in private set up for financial reasons. Conclusion: Surgical technique is important factor in etiology of post hysterectomy prolapsed, presence of mild enterocele should be corrected even at time of abdominal hysterectomy and vault should be properly suspended for prevention of vault prolapse. The hysterectomy should be performed by gynecologist who are more conversant with pelvic pathology and not by general surgeon.

P-103.
BMD Changes after hormone therapy on Turner syndrome
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Objective: Turner syndrome (TS), which is caused by partial or total monosomy X, is associated frequently with osteoporosis. We designed this study to analyze the effects of hormone replacement therapy (HT) on bone mineralization in patients with TS by measuring bone mineral density (BMD). Design: Thirty three women were diagnosed as TS during last 13 years at Seoul St. Mary’s hospital, the Catholic University of Korea. Twenty women with TS had received HT and follow-up data of BMD were available in 15 women. All of their medical records about HT and bone mineral density were reviewed retrospectively. Results: The average age at diagnosis and start of HT were 17.9 ± 6.8 and 25.1 ± 6.4, respectively. The mean duration of HT was 7.7 ± 7.4 years and mean BMD at start of HT was 22.5 ± 3.0(kg/m2). 73.3%(11/15) and 20% (3/15) were prescribed calcium/VD and bisphosphonate, respectively. At the beginning of HT, cut open uterus showing fibroid and pus
total lumbar BMD, the lowest lumbar BMD, Lt femur BMD (total/ the lowest) and Rt femur BMD (total/ the lowest) were increased 19.81, 18.28, 22.36 & 22.68, 14.91 & 13.04, 13.95 & 12.94, 17.48 & 16.36 and 14.01 & 13.51 %, respectively. According to the duration of HT, lumbar and Lt femur BMD were proportionally increased significantly. Conclusion: HT could effectively increase bone mineral density in TS. It is important to emphasize to young women with TS and their caregivers that HT is critical for bone health.

P-104. PEGASUS - Prevalence and severity of genitourinary symptoms and impact on sexual function and quality of life in postmenopausal women receiving adjuvant endocrine therapy for early stage breast cancer - A prospective study

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Objective: Postmenopausal women with breast cancer may experience significant symptoms associated with genitourinary atrophy. The symptoms can occur as an adverse effect induced by anti-cancer treatments, particularly endocrine therapy, which can exacerbate menopausal symptoms due to reduced estradiol levels that tend to be more pronounced than in women without breast cancer. The impact of such symptoms in breast cancer survivors can be enormous as they can markedly challenge women’s physical and emotional health leading to potentially life-long burdens. In order to provide appropriate and adequate care for breast cancer survivors, it is important to understand that genitourinary symptoms in this population may differ in frequency, severity and impact on quality of life (QoL) and sexual function. Thus, it is clear that this issue still needs to be more carefully addressed in a focused and well-designed study. Using standardized instruments, we measure prevalence and severity of genitourinary symptoms, impact on QoL and sexual function in postmenopausal women receiving adjuvant endocrine therapy for early stage breast cancer. Design: Multi-center prospective study. A total sample of 280 postmenopausal women with early breast cancer and estrogen-receptor positive tumors is expected to complete self-administered questionnaires consisting of validated measures of genitourinary symptoms, including urinary frequency, urgency, incontinence, dysuria, recurrent urinary tract infections, dysuria and pelvic floor dysfunction, in addition to sexual function and QoL. Questionnaires are completed at baseline, (prior to the commencement of an aromatase inhibitor or tamoxifen) and 6-month, 1- and 2-year follow-ups. Results: Data collection is ongoing. To date, 151 women have been invited and of those, 19 declined participation. Baseline questionnaires were completed by 132 women; 44 were randomized to TDE. The average age was 42.9 ± 11.3 years and mean BMI was 24.7 ± 4.7 kg/m2. Further data will be presented. We will report on the prevalence and severity of genitourinary symptoms and their evolution over time in postmenopausal women on adjuvant endocrine therapy. Conclusions: Genitourinary symptoms are common among breast cancer survivors; high prevalence of symptoms is reported after adjuvant treatment, but prior to the commencement of endocrine therapy. It is likely to impact on quality of life and sexual activity. The results will be used to plan intervention studies as well as to identify patients at risk of developing significant genitourinary symptoms.

P-105. Incidence of Endometrial Spotting and Bleeding during Continuous Combined Estrogen plus Progestin Therapy in Normotensive versus Hypertensive Postmenopausal Women

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Objective: Endometrial spotting or bleeding (S/B) is a common side effect among postmenopausal women using continuous combined estrogen plus progestin therapy (ccEPT). While the cause is unknown, it requires further investigation and leads to hormone therapy discontinuation. Renin-Angiotensin-Aldosterone System (RAAS) known to play a major role in hypertension is also present in endometrium and has a potential role in regulating uterine vasculature through angiotensin II receptors. We investigated the incidence of S/B in hypertensive compared to normotensive postmenopausal women using ccEPT during the first 12 months in the Women’s Health Initiative (WHI) study. We hypothesized that hypertensive postmenopausal women will have a higher incidence of S/B compared to normotensive postmenopausal women due to the impact of RAAS which contributes to small uterine vessel dysfunction. Design: We used the WHI clinical trial database which is a randomized double-blind study investigating ccEPT in postmenopausal women. There were 16,608 postmenopausal women with intact uterus between 50 and 79 years of age enrolled in the ccEPT trial. We used multivariate mixed effect logistic regression models to estimate the relationship of hypertensive status or use of antihypertensive drugs with endometrial S/B after controlling for baseline clinical characteristics. The statistical analyses were performed using SAS version 9.3 with a two-sided alpha level of 0.05. Results: A total of 8,506 postmenopausal women randomized to the ccEPT arm had 28,660 visits over a period of 12 months. The mean number of episodes of endometrial S/B was significantly higher among hypertensive versus normotensive women. Hypertensive women were found to be more likely to experience endometrial S/B compared to normotensive women (OR=1.07, 95% confidence interval [CI]: 1.02, 1.13) independent of age, race, menopausal status, body mass index and endometrial thickness. Hypertensive women taking angiotensin medication were more likely to have endometrial S/B (OR=1.24, 95% CI: 1.05, 1.45). There was less endometrial S/B among those using angiotensin II receptor antagonists (OR=0.53, 95% CI: 0.33, 0.85) or beta blockers (OR=0.82, 95% CI: 0.68, 0.98), while women using diuretics, angiotensin converting enzyme inhibitors, and calcium channel blockers had similar endometrial S/B compared to non-users of these drugs. Conclusion: Almost half of postmenopausal women who began ccEPT at any age or any interval from LMP experienced at least one episode of endometrial S/B within the first year. Hypertensive postmenopausal women were more likely to bleed than normotensive postmenopausal women. Hypertensive women taking angiotensin II receptor antagonists or beta blockers were less likely to experience bleeding. This is unique and supports our hypothesis that RAAS plays a role in the uterine vasculature via angiotensin II receptors and it is contributes to endometrial S/B in postmenopausal women using continuous combined hormone therapy.

P-106. LNG-IUD plus Estrogen—A Little Dab Will You Do In the Perimenopause

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Objective: To compare perimenopausal symptomatology using a levonorgestrel-containing IUD (LNG-IUD) plus low-dose transdermal estrogen (TDE) to LNG-IUD alone. Design: Double-blind randomized controlled pilot trial. Regularly cycling women ages 40-52 with at least one of the following (hot flashes, blotting, headache, or adverse mood, or poor sleep (self-reported)) were enrolled and randomized to either LNG-IUD plus estrogen gel (TDE) or LNG-IUD alone. The gel was administered once daily as a 0.06% gel containing 0.75mg of estradiol per 1.25gm. The gel was administered once daily as a 0.06% gel containing 0.75mg of estradiol per 1.25gm; 28,660 visits over a period of 12 months. There were 16,608 postmenopausal women with intact uterus between 50 and 79 years of age enrolled in the ccEPT trial. We used multivariate mixed effect logistic regression models to estimate the relationship of hypertensive status or use of antihypertensive drugs with endometrial S/B after controlling for baseline clinical characteristics. The statistical analyses were performed using SAS version 9.3 with a two-sided alpha level of 0.05. Results: A total of 8,506 postmenopausal women randomized to the ccEPT arm had 28,660 visits over a period of 12 months. The mean number of episodes of endometrial S/B was significantly higher among hypertensive versus normotensive women. Hypertensive women were found to be more likely to experience endometrial S/B compared to normotensive women (OR=1.07, 95% confidence interval [CI]: 1.02, 1.13) independent of age, race, menopausal status, body mass index and endometrial thickness. Hypertensive women taking angiotensin medication were more likely to have endometrial S/B (OR=1.24, 95% CI: 1.05, 1.45). There was less endometrial S/B among those using angiotensin II receptor antagonists (OR=0.53, 95% CI: 0.33, 0.85) or beta blockers (OR=0.82, 95% CI: 0.68, 0.98), while women using diuretics, angiotensin converting enzyme inhibitors, and calcium channel blockers had similar endometrial S/B compared to non-users of these drugs. Conclusion: Almost half of postmenopausal women who began ccEPT at any age or any interval from LMP experienced at least one episode of endometrial S/B within the first year. Hypertensive postmenopausal women were more likely to bleed than normotensive postmenopausal women. Hypertensive women taking angiotensin II receptor antagonists or beta blockers were less likely to experience bleeding. This is unique and supports our hypothesis that RAAS plays a role in the uterine vasculature via angiotensin II receptors and it is contributes to endometrial S/B in postmenopausal women using combined continuous hormone therapy.

Results: A total of 38 women were enrolled; 20 were randomized to TDE. The average age was 42.7 years and mean BMI was 24.7 ± 3.3 kg/m2; the groups were similar with regard to these measures. Women receiving TDE demonstrated reduced FSS scores between days 90 and 140 (mean difference TDE: -0.8 ± 1.2 vs. placebo: 0.1 ± 0.7; p=0.026) and borderline significant improvement in HFRDS scores (mean difference TDE: -5.5 ± 1.3 vs. placebo: 4.2 ± 1.3; p=0.08). CES-D, PSQI and FSS scores correlated with TDE use. There were no reported adverse events.
Conclusion: Improvement of perimenopausal symptoms was observed with a brief, low-dose estrogen intervention in combination with LNG-IUD use in this pilot trial. Such a ‘minimalist’ approach to management of the perimenopause holds promise for reducing common, bothersome menopausal symptoms while maintaining effective contraception.

P-107. A Pilot Study of S-equol Supplement (SES-OH) on Reproductive Health in Postmenopausal Japanese Women
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Objective: Equol, which is an active metabolite of soy isoflavone “daidzein”, has similar estrogenic activity and exhibits cardiac effects of SERMs like sulindac in the binding to estrogen beta-receptor. Equol can be produced by intestinal bacteria in approximately 50% of Japanese and 20–30% of the US population. Using a lactic acid bacterium, Lactobacillus plantarum 20-92, that metabolizes daidzein to equol, we successfully produced a fermented soy ingredient containing S-equol (SES-OH). Clinical studies have suggested that the daily 10mg S-equol supplement alleviates menopausal symptoms such as hot flashes, muscle or joint pain, depression, and urinary incontinence. Although the meta-analysis and systematic reviews confirmed the significant effect of estrogen therapy in the management of urogenital atrophy, some women are not confident receiving hormone therapy because of their side effects. The objective of this study was to evaluate the effect of a S-equol supplement on the vaginal epithelium cytorugosity and endometrial thickness in postmenopausal Japanese women.

Design: One hundred five post-menopausal Japanese women without equol-producer were divided into one of four groups; 2 mg of S-Equol /day: EQ2 (n=26), 6 mg of S-Equol /day: EQ6 (n=25), 10 mg of S-Equol /day: EQ10 (n=27) and placebo (n=27), after the baseline assessment at menopause, 6 weeks, the end of treatment in the 12 weeks study, and after 4 weeks follow up. Transvaginal sonography was performed to evaluate endometrial thickness. Results: At baseline and after 12 weeks of intervention, percentage of superficial cells was 8.1±7.3 and 4±2.4% (p<0.05). In the placebo group, 7.8±13.9 and 6±9.1 (2.2%) for the EQ2 group, 4.2±9.6 and 6.9±6.4 (2.7%) for the EQ6 group, 7.7±14.3 and 13.5±2.6 (6.3%) for the EQ10 group, respectively. EQ groups were increasing with dose-response manner, and the EQ10 group showed the trend to superiority compared to placebo (p<0.05). In the vaginal cytoturgosity, no increase of abnormality was observed in all subjects. Endometrial thickness after 12 weeks of intervention was 3.6±1.1mm in the placebo group, 4±1.1mm for the EQ2 group, 3.8±2.3 for the EQ6 group, 4.6±2.4mm for the EQ10 group, respectively. No significant difference among the groups was observed. Nine subjects experienced greater than 5mm of endometrial thickness, but it was slight increase. No significant difference was observed in serum E2, FSH, testosterone, T, T4 and T3 levels among the groups. No side effects were observed significantly. Conclusion: To evaluate the effect of the S-equol supplement use during 12 weeks exerts estrogenic action on the vaginal epithelium assessed by maturation value. However, it neither increased the incidence of genital bleeding nor caused significant change in endometrial thickness. Daily 10mg S-equol supplement may contribute the reproductive health in postmenopausal women.

P-108. Correlation between menopausal symptoms and the perception of psychological stress in women from the Colombian Caribbean
Lzielillo Ullaque-Caamano, Joulen Mo-Carrascal, Alvaro Monterrosa-Castro, Enrique Ramos-Clason. Universidad de Cartagena, Cartagena, Colombia
Objective: To estimate the best score of the PSS-10 that predicted severe deterioration of the somatic, psychological and urogenital domains as well as of the QoL. Design: Cross-sectional study part of the CAVIMEC (Calidad de Vida en la Menopausia y Enferas Colombianas) research project carried out in resident women from Cartagena and Monteria in the Colombian Caribbean, between 40-59 years of age. They voluntarily completed the questionnaire in their own communities. There were considered socio-demographic variables and the scales: Perceived Stress Scale 10 items (PSS-10) and the Menopause Rating Scale (MRS), both in Spanish version. To greater score of the PSS-10, greater perceived psychological stress. The MRS comprises the following domains: somatic, psychological, urogenital symptoms, deterioration of the domains and worse QoL. The severe deterioration is established with somatic score > 7, psychological score > 6, urogenital score > 3 and the QoL > 15. The statistical analysis was carried out with Epi-info-7 and MedCalc. Results: 471 women were studied with average age of 48.3±5.1y. 92.5% had sexual partner, 23.9% were in premenopause, 11.7% in perimenopause and 65.3% in postmenopause. 38.0% of women were in overweight or obesity, 7.2% were diabetic women, 15.5% had hypertension and 9.4% suffered from bilateral oophorectomy. 67.6% of the women manifested to have felt fairly often or very often that things were going her way, 65.7% expressed to have felt herself nervous and “stressed”. The total addition of PSS-10 was 16.4±4.2. A score > 16 in the PSS-10 was related with severe deterioration of the QoL [sensibility: 91.6%; Specification: 30.3; Area under the curve (AUC): 0.63; C95%:0.58-0.67], p<0.001. A score > 15 in the PSS-10 was related with severe deterioration of the somatic domain [sensibility: 98.9%; Specification: 92.2%; AUC: 0.95 C95%:0.94-0.96], p<0.0001. A score > 18 in the PSS-10 was related with severe deterioration of the psychological domain [sensibility: 75.2%; Specification: 42.9%; AUC: 0.69 C95%:0.56-0.80], p<0.0002. A score > 16 in the PSS-10 was related with No 50 years and time living with partner /g42/ to estimate Pearson’s Correlation Coefficient was carried out with the statistical programs Epi-info 7 and MedCalc. Study without ethic impact in the participants. Results: 471 women were studied. Average age: 48.3±5.1. They were distributed according the menopausal status: premenopause: 23.9%, perimenopause: 11.7% and postmenopause: 64.3%. 61.9% of the women were in overweight or obesity, 7.2% were diabetic women, 15.2% had arterial hypertension, 15.7% had bilateral oophorectomy and 50.3% had been hysterectomized. 69.4% of the women manifested to have felt fairly often or very often that things were going her way and the 57.5 % expressed to have felt herself confident in handling her personal problems. The average of the MRS score was 13.4±6.4, being the physical and mental exhaustion (84.5%), the hot flushes and sweating (84.5%) and the joint and muscular discomfort (84.3%), the most frequent symptoms. A weak positive correlation was found between hot flushes, heart discomfort, sleep problems, joint and muscular discomfort, depressive mood, insecurity, anxiety, poor physical and mental exhaustion, sexual problems, bladder problems, dryness of vagina and the total score of the domains and of the quality of life with the total addition of the PSS-10 (p<0.005). Quality of life: r= 0.41 [C95%: 0.33-0.48], p<0.0001. Urogenital domain: r= 0.39 [C95%: 0.32-0.43], p<0.0001. Psychological domain: r= 0.38 [C95%: 0.31-0.46], p<0.0001. Conclusion: Significant and positive correlation was found between the score of the PSS-10 and the menopausal symptoms in women from the Colombian Caribbean.

P-110. Perceived psychological stress and severe deterioration of the quality of life in climacteric women from the Colombian Caribbean
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Objective: To evaluate the association between metabolic syndrome and low sexual function in climacteric women and factors associated with sexual function in this population. Design: Cross-sectional study with 256 women of 40 to 60 years utilizing a questionnaire on socio-demographic, behavioral data and evaluation of sexual function using the Short Personal Experiences Questionnaire (SPEQ). Women had been also submitted to anthropometric measurements, blood pressure and serum dosages of fasting glucose, HDL cholesterol, triglycerides, FSH and TSH. Results: The prevalence of Metabolic Syndrome was 62.1% and 31.4% of the entire group had low sexual function. The only factor of female sexual function associated with the metabolic syndrome was the weekly alcohol consumption associated with the metabolic syndrome was the weekly alcohol consumption associated with the metabolic syndrome was 62.1% and 31.4% of the entire group had low sexual function. The only factor of female sexual function associated with the metabolic syndrome was the weekly alcohol consumption associated with the metabolic syndrome was 62.1% and 31.4% of the entire group had low sexual function. The only factor of female sexual function associated with the metabolic syndrome was the weekly alcohol consumption. The prevalence of Metabolic Syndrome was 62.1% and 31.4% of the entire group had low sexual function. The only factor of female sexual function associated with the metabolic syndrome was the weekly alcohol consumption. The prevalence of Metabolic Syndrome was 62.1% and 31.4% of the entire group had low sexual function. The only factor of female sexual function associated with the metabolic syndrome was the weekly alcohol consumption. The prevalence of Metabolic Syndrome was 62.1% and 31.4% of the entire group had low sexual function. The only factor of female sexual function associated with the metabolic syndrome was the weekly alcohol consumption. The prevalence of Metabolic Syndrome was 62.1% and 31.4% of the entire group had low sexual function. The only factor of female sexual function associated with the metabolic syndrome was the weekly alcohol consumption. The prevalence of Metabolic Syndrome was 62.1% and 31.4% of the entire group had low sexual function. The only factor of female sexual function associated with the metabolic syndrome was the weekly alcohol consumption. The prevalence of Metabolic Syndrome was 62.1% and 31.4% of the entire group had low sexual function. The only factor of female sexual function associated with the metabolic syndrome was the weekly alcohol consumption. The prevalence of Metabolic Syndrome was 62.1% and 31.4% of the entire group had low sexual function. The only factor of female sexual function associated with the metabolic syndrome was the weekly alcohol consumption. The prevalence of Metabolic Syndrome was 62.1% and 31.4% of the entire group had low sexual function. The only factor of female sexual function associated with the metabolic syndrome was the weekly alcohol consumption. The prevalence of Metabolic Syndrome was 62.1% and 31.4% of the entire group had low sexual function. The only factor of female sexual function associated with the metabolic syndrome was the weekly alcohol consumption.
P-111. Metabolic syndrome in climacteric women with and without HIV: a cross sectional study
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Objective: To determine the prevalence of metabolic syndrome (MetS) and associated factors in climacteric women at two HIV referral centers. Design: a cross sectional study of 273 HIV infected and 264 HIV negative outpatients women. MetS was diagnosed with waist circumference ≥80cm and two or more of the following factors: triglycerides ≥150 mg/dL, HDL cholesterol < 50 mg/dL, systolic blood pressure ≥ 130 mmHg or diastolic ≥ 85 mmHg and glycemia ≥ 100 mg/dL. ID.F.Sociodemographic, clinical and behavioral factors were evaluated. In HIV - group factors associated with infections were analysed. Bivariate and multiple regression analysis were used. Results: The prevalence of MetS in the HIV group was 46.9% compared to 42.2% in the control group. The bivariate analysis did not show an association of MetS and HIV infection. There was a MetS association with being aged 50-60 years (p=0.001), formal education <8 years (p<0.001), being overweight (p=0.002), worst health self-perception (p=0.036), BMI>25 (p=0.001). Multiple analysis showed association of MetS with BMI ≥25 kg/m2 (RP=2.34, 95% CI: 1.70-3.21, p<0.001), aging (RP=1.05, 95% CI: 1.02-1.07, p<0.001) and the use of highly active antiretroviral therapy (HAART) (RP= 1.48, 95% CI: 1.13-1.94, p<0.005). Conclusion: There was no association of MetS and HIV status. The main factors associated with MetS being overweight, aging and using HAART. There's a need of a better approach, awareness and education of both HIV positive and negative women in relation to lifestyle to prevent weight gain and MetS.

Variables associated with the presence of Metabolic Syndrome (n=491) - Multiple regression analysis

PR: prevalence ratio; 95% CI: confidence interval of 95%. Variables considered: age (years), skin color (white / other), physical activity (0-2 times per week / 2 3 times per week), education (0-7 years / 2 8 years), family income (≤ US$ 750.00 / > US$ 750.00), number of residents in a house (up to 2 / > 2), smoking (yes / no), alcohol consumption (yes / no), menopausal status (pre or perimenopause / menopause), weight gain (yes / no), hormone therapy (yes / no), self-rated health (excellent or good / not so good or bad), HAART (yes / no), other chronic diseases (yes / no), BMI (≤ 25 / > 25 kg/m2), FSH (<40 / ≥ 40), TSH (<4.5 / ≥ 4.5), free T4 (<0.90 vs ≥ 1.80 / 90 to 1.80), group (HIV+ / HIV-).

P-112. Symptom Clusters: Midlife Women’s Health
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Objective: Many women experience multiple co-occurring symptoms during the menopausal transition (MT) and early postmenopause (PM), yet little is known about the heuristics women use to account for, understand and manage them. Our objective was to explore heuristics that women use to: 1) characterize the relationships among symptoms in a cluster; 2) group, frame, and name symptoms as a cluster; 3) attribute clusters to causes; and 4) identify factors exacerbating and ameliorating symptom clusters. Design: 30 midlife women between the ages of 40 and 60 experiencing symptoms they associated with menopause were recruited through flyers posted on campus and in gynecology and women’s clinics. Women completed the Computerized Symptom Capture Tool (C-SCAT) application based on their symptom experience in the previous 24 hours. The C-SCAT app guided women to identify and draw the symptom clusters they experienced and relationships between symptoms as well as respond to questions about their heuristics. Data generated from the C-SCAT app were transmitted to an Amazon Web Services account as graphical screen shot images and Excel files containing text responses for analysis. Results: Women described their final diagrams very/extremely accurately (77%) accurate in depicting their symptoms and relationships among them. They reported from 1 to 31 symptoms (median =11) and grouped them into 1 to 4 clusters of 2 to 18 symptoms. Hot flashes were the most commonly reported symptom as well as the most bothersome symptom in any cluster. Women named their symptom clusters based on the symptoms in each cluster (e.g. “hot flashes”), the impact of the cluster (e.g. “really annoying symptoms, “night problems”), and emotional aspects of symptoms (e.g. “blue mornings” and “feel like I am crazy”). Causal attributions of the clusters included psychological/physical changes and effect of hormonal changes. Factors exacerbating their clusters included drinking alcohol, eating specific foods, lack of sleep, stress, having too much to do, and aging. Self management strategies women used to alleviate their symptoms were avoiding fat, exercising, sleeping, and taking herbal therapies as well as acupuncture. Conclusion: Although statistical methods are most commonly used to identify symptom clusters, women could group symptoms into a cluster, framing and naming the clusters. Moreover, all offered relational maps among symptoms, identified causal attribution factors and could describe exacerbating and ameliorating factors, and self-management strategies. Future testing of reports generated by the iPad app may reveal its utility in helping women prepare for health care provider visits to help manage their symptoms.

P-113. Effect of oral hormone therapy on the degree of oxidative stress in postmenopausal women with metabolic syndrome
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Objective: To determine the effect of oral hormone therapy [HT] on the degree of oxidative stress [OS] in postmenopausal women with metabolic syndrome. Design: A randomized, double blind controlled trial was carried out. We evaluated 46 postmenopausal women without metabolic syndrome [WOMS] and 44 postmenopausal women with MS [WMS] that were assigned to treatment [Tx] (0.625 mg/d of synthetic conjugated estrogens [Sthrough6%/g42] plus 5 mg/10d of medroxyprogesterone [MPA])or placebo [P]. Then we conformed four groups: Group 1: 21 women WOMS in Tx; Group 2: 25 participants WMS in Tx; Group 3: 25 women WOMS in P; Group 4: 19 participants WMS in P. We measured lipoperoxides levels [LPO] by TBARS assay as OS biomarker. Tests were carried out at the beginning and at 6 months of treatment. An alternative cut-off value of LPO α0.320 μmol/L was defined on the basis of the 90th percentile of young healthy subjects. Results: Of the participants enrolled, 4 of each assignment group dropped out in different time, leaving 21 subjects in group 1 and 2; 22 in group 3 and 18 in group 4, who completed all the assessments (basal and 6 mo.). At basal time, LPO levels were highest in the women WMS (0.356±0.06 vs. 0.318±0.06 μmol/L, p=0.01). The proportion of women with high LPO levels were also higher among the group WMS (73%) vs 48% p<0.05. After 6 months of treatment, LPO levels decreased significantly in groups 1 and 2: WOMS 0.310±0.05 to 0.260±0.4 μmol/L [p=0.001], and WMS 0.355±0.06 to 0.29±0.05 μmol/L [p<0.05]. In placebo groups LPO did not change. We found that the proportion of women with high LPO at baseline reduced 40% using HT (p<0.05); in group 1 the women with high LPO also diminished 18% and in P groups these proportions did not change after 6 mo. (Figure) Conclusion: Our findings suggest that oral HT decreases LPO as an OS biomarker, but this effect is proportionally higher in postmenopausal women with metabolic syndrome than without metabolic syndrome. This work was supported by grant DGAPA-UNAM IN222213. Trial registration: COF001220.

Figure. Effect of treatment in the proportion of women with high lipoperoxides (≥ 0.320 μmol/L) after 6 months. *chi square test, p< 0.05.