S-1. Association of coronary artery vitamin D receptor expression and Systemic Risk Factors for Coronary Artery Atherosclerosis

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Objective: The results of previous studies have determined that an inverse correlation exists between coronary artery vitamin D receptor (VDR) expression and the degree of coronary artery atherosclerosis (CAA). It is not clear whether VDR decreases after CAA develops, suggesting a local response to CAA, or whether systemic factors lead to decreased VDRs suggesting the VDR quantity may be an indicator of future CAA. The current study analyzes the association between coronary artery VDR expression (as an H-score) and systemic CAA risk factors. Design: Premenopausal cynomolgus monkeys (n=39) were fed atherogenic diets containing the equivalent of 1,000 IU/day of 25OHD3. After 32 months consuming the diets, each monkey underwent surgical menopause. After 32 post-menopausal months, CAA was measured in the left circumflex artery (LCX) and left anterior descending artery (LAD). VDR expression was quantified in the LAD and monocyte chemotactic protein-1 (MCP-1), an inflammatory marker, was assessed. Concurrently, plasma 25OHD3 and lipid profiles were assessed. Correlations were analyzed with Spearman’s rho (R) and differences between groups were evaluated with Kruskal-Wallis and post hoc Games-Howell tests using alpha=0.05. Results: In postmenopausal monkeys receiving an atherogenic diet, MCP-1 was significantly elevated compared with monkeys at baseline (p<0.001) and in those at the start of menopause (asymptomatics) (p<0.001). Coronary VDR expression was inversely correlated with MCP-1 (R=-0.328, p=0.042). When VDR expression was grouped by tertile, as VDR quantity increased, there was a corresponding decrease in MCP-1 (p=0.039). Additionally, the change of postmenopausal MCP-1 (from baseline to necropsy) was significantly reduced in the group with higher, compared to the median, VDR H Score quantification (p=0.038). The combination of plasma 25OHD3 and TPC:HDL-C were subsequently broken into low-, moderate-, and high-risk groups; as the risk increased, VDR quantity decreased (p=0.04), see figure 1. Conclusion: Coronary artery VDR expression was inversely correlated with systemic CAA risk factors. These findings suggest that an increased level and/or severity of systemic CAA risk factors may lead to a loss of coronary artery VDR, either with or after CAA progression. This, in turn, would support the translational hypothesis that women who would most benefit from 25OHD3 supplementation would be those in the pre-menopausal years, before they develop significant CAA and hence lose substantial coronary artery VDR expression.

Figure 1. VDR (H-score) by ratio of Vitamin D to TPC:HDL-C

S-2. Safety and Efficacy of Low-dose Mesylate Salt of Paroxetine (LDMP) for the Treatment of Vasomotor Symptoms (VMS) Associated With Menopause: A 24-week, Randomized, Placebo-controlled Phase 3 Study

James A. Simon, MD1,2, Gerard Sanacora, MD1,2, S. Jaihail Bhaskar, RPh, PhD3, Joel Lippman, MD, MPH4, George Washington University School of Medicine, Washington, DC; 2Yale University School of Medicine, New Haven, CT; 3Noven Pharmaceuticals, Inc., New York, NY

Objective: Vasomotor symptoms (VMS), including hot flashes and night sweats, affect quality of life in 75% to 88% of menopausal women. Hormonal treatments may improve VMS, but some patients are unable or unwilling to take them creating an unmet need for effective non-hormonal therapy with favorable safety and tolerability profiles. In an earlier Phase 2 study, LDMP (7.5 mg daily at bedtime for 8 weeks) was safe and efficacious in treating VMS associated with menopause. Results of this Phase 3 study confirm and extend those findings. Design: This was a 24-week, multicenter, double-blind, randomized, placebo-controlled. Phase 3 study of LDMP in postmenopausal women ≥ 40 years old with moderate to severe VMS (≥ 7-8 moderate to severe hot flashes daily). After an initial screening period, eligible subjects entered a 12-day, single-blind run-in period, during which they received placebo once daily at bedtime and recorded the number and severity of hot flashes in daily diaries. Subjects compliant with diary entry and with at least one hot flash eligibility criterion were randomized 1:1 to LDMP or placebo for 24 weeks. Primary efficacy endpoints were mean changes in frequency and severity of moderate to severe VMS from baseline to Week 4 and Week 12. Receiver operator characteristic (ROC) responder analysis was conducted to evaluate clinical meaningfulness of VMS frequency. Persistence of treatment benefit at Week 24 was evaluated with a responder analysis, where a responder was defined as a subject with ≥ 50% reduction in VMS frequency from baseline to Week 24. Safety assessments included treatment-emergent adverse events (TEAEs), vital signs, and clinical laboratory abnormalities. Results: Overall, 370 participants (285 per group) were randomized, and 453 (235 [82.5%] LDMP, 218 [76.5%] placebo) completed the study. The intent-to-treat population comprised 568 subjects (284 LDMP, 284 placebo); mean age was 54 years. Mean weekly reductions in VMS frequency were significantly greater for LDMP than placebo at Week 4 (–28.9 and –19.0, respectively; P<0.0001) and at Week 12 (–37.2 and –27.6, respectively; P<0.0001). Daily reductions in VMS frequency were clinically meaningful per ROC responder analysis, with significantly more responders treated with LDMP than placebo at Week 4 (68% vs 48%, respectively; P=0.0072) and at Week 12 (61% vs 45%, respectively; P=0.0001). Mean weekly reductions in VMS severity were also significantly greater for LDMP than placebo at Week 4 (–0.089 and –0.056, respectively; P=0.0452) and at Week 12 (–0.123 and –0.067, respectively; P=0.0114). Significantly more subjects treated with LDMP than placebo were responders at Week 4 (47.5% vs 36.3%, respectively; P=0.0066), demonstrating persistence of treatment benefit. Overall, 56.5 % (161/285) of subjects in the LDMP group reported ≥ 50% improvement in 25.4% (156/608) of subjects in the placebo group. Most TEAEs were nasopharyngitis (5.1% vs 4.9%), headache (4.3% vs 3.7%), nausea (3.8% vs 1.4%), fatigue (3.4% vs 1.5%), diarrhea (2.9% vs 2.5%), and dizziness (2.0% vs 0.8%). No significant changes were observed in laboratory values, vital signs, or electrocardiograms for either group. Conclusion: LDMP was safe, well tolerated, and efficacious in reducing both the frequency and severity of VMS associated with menopause at Week 4 and Week 12 and demonstrated persistence of treatment benefit at Week 24. Reductions in frequency of VMS associated with menopause at Week 4 and Week 12 were clinically meaningful.

S-3. Improving sleep in post-menopausal women: Outcome from a randomized trial of Clinical Hypnosis

Gary Elkins, Ph.D., Aimee K. Johnson, William Fisher, MA, Jim Sliwinski. Baylor University, Waco, TX

Objective: Sleep dysfunction is one of the most common complaints of the climacteric. Traditionally, it is believed that the primary cause of sleep disturbance among postmenopausal women is nocturnal vasomotor symptoms (hot flashes). Over 66% of post-menopausal women experience hot flashes. Hypnosis is one mind-body therapy that seems particularly promising for treating hot flashes, and secondary analyses suggest that it may have additional benefits, such as improved sleep. The present study investigates the efficacy of clinical hypnosis versus structured-attention control in improving the sleep of post-menopausal women with hot flashes. Design: In a study of 187 post-menopausal women experiencing moderate to severe (50+)(7-8) hot flashes, participants were randomized to receive either five sessions of clinical hypnosis or five sessions of structured-attention control, which served as an active control. To investigate the potential impacts of the treatment on the quality of sleep, patients were given the Pittsburg Sleep Quality Index, (PSQI; Buysse, Reynolds, Monk, Berman, & Kupfer, 1989) at baseline, 6-weeks, and at 12-week follow-up. The PSQI has 19 items that generate seven scales: sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of other sleeping medication, daytime dysfunction, and a global score. A higher score indicates greater levels of sleep dysfunction. Results: To evaluate the quality of patients’ sleep post-intervention, the global score from the PSQI was tabulated at baseline, 6-weeks, and 12-week follow-up. In the clinical hypnosis group, patients reported a global score improvement of 5.6 (43.49%) at week six of the intervention, compared to a 1.04 (6.5%) improvement in the structured attention control group. At follow-up, the clinical hypnosis patients continued to improve, showing a reduction in global score of 6.27 (53.12%) from baseline as compared to a 1.23 (9.17%) improvement in the control group. Sleep quality, as determined by the global score of the PSQI was significantly improved over the control group (p<0.01, CI 3.65 to 5.84). Conclusion: The results of this study suggest that clinical hypnosis may be an excellent treatment option for post-menopausal women who suffer from sleeplessness or disrupted sleep. Though the results of this study are encouraging, they should be interpreted cautiously as this study was limited by a lack of objectively measured sleep outcomes. Future study should investigate the mechanism of the change in hypnosis in sleep quality using self-reported and objectively measured sleep outcomes, to develop a model for dissemination.

S-4. A Negative View of Menopause: Does the Type of Symptom Matter?

Richa Sood, MD, Brandon R. Grossardt, Stephanie Faubion, MD, Jacqueline Thielen, MD, Mary L. Marnach, Sharonne Hayes, MD, Lynne Shuster, MD. Mayo Clinic, Rochester, MN

Objective: Menopausal symptoms can be numerous, varied, prolonged and bothersome. Although hot flashes and night sweats are the most commonly reported symptoms, they are often not the most bothersome. The degree of symptom bother, which is not completely explained by symptom severity and frequency, can be an important determinant of symptom impact on quality of life. Our study was aimed to assess if...
women's view of menopause is influenced by the type of symptoms experienced. Design: From July 2005 to July 2011, all women seen for menopausal concerns at the Mayo Clinic Women's Health Clinic in Rochester, Minnesota were given the North American Menopause Society Menopause Health Questionnaire (MHQ), which assesses medical, reproductive and gynecologic history, family history, personal habits, and menopausal symptom occurrence and severity. Information was entered into an electronic database for those women who provided research authorization. We used self-reported responses to the 33 items in section 13 of the MHQ to assess how bothersome each of the symptoms was. For statistical analysis, those symptoms reported as “not at all” or “a little bit” bothersome were coded as not bothersome, whereas those symptoms reported as “quite a bit” or “extremely” bothersome were coded as “bothersome”. To assess information related to overall menopausal experience, we used the Cleveland Clinic Menopause Questionnaire (ClintMenQ) to assess self-reported changes in 12 different aspects of menopause (e.g., vaginal itching; OR=2;1; reported as bothersome in only 7% of women) and the OR and the frequency of endorsement were combined into a composite impact measure of degree of bother. The highest impact symptoms in the negative menopausal view group were found in to be anxiety (30.9% bothersome; OR=2.3, 95% CI: 1.7–3.1; p<0.0001); irritability (29.4% bothersome; OR=2;4, 95% CI: 1.8–3.2; p<0.0001); and difficulty concentrating (34.9% bothersome; OR=2;1; 95% CI: 1.6–2.9; p< 0.0001). Despite the frequency with which hot flashes (42.7%) and night sweats (37.9%) were reported as bothersome, the ORs were relatively small (OR=1.2 with p=0.19; and p=0.15, respectively). Conclusion: A negative view of menopause was associated most commonly with reported symptoms of anxiety, irritability and difficulty with concentration. This was followed closely by memory concerns, weight gain, depressed mood, frequent awakenings, and sexual concerns. Vasonomotor symptoms, although frequently reported, were less likely to be associated with a negative view of menopause. Some symptoms appear to influence the overall positive or negative view of menopause more than others, regardless of their frequency of occurrence.

THURSDAY CONCURRENT SESSION #1

S-5

Longitudinal Assessment of the Menopausal Transition, Endogenous Estradiol, and Perception of Physical Functioning: The Study of Women’s Health Across the Nation

Samantha M. Gomez, MPH1, Candace McClure, PhD, Trang VoPham, MPH1, Barbara Sterinfeld, PhD1, Jane Cauley, DrPH2, Carrie Karvonen-Gutierrez1, Naila Khalil, PhD1, Kim Sutton-Tyrrell, DrPH3. 1University of Pittsburgh Graduate School of Public Health, Pittsburgh, PA; 2Kaiser Permanente Division of Research, Oakland, CA; 3University of Michigan School of Public Health, Ann Arbor, MI; 4Wright State University, Dayton, OH

Objective: Physical functioning (PF) limitation has been reported more frequently in women compared to men, even at relatively young ages. The menopausal transition is a unique period of a woman’s life during which several physiological, psychological, and social role changes occur. Whether the menopausal transition and related hormonal changes can be considered as major factors that impact the level of PF in women at mid-life is still not clear. Longitudinal associations between menopausal status, level and change from visit 04 (to assess between-woman variation) and change since visit 04 (to assess within-woman transition) were modeled separately. HT users were excluded from endogenous E2 models. Final models were adjusted for age, time since visit 04, site, race, income, ability to pay for basics (BMI) (level and change since visit 04), physical activity (level and change since visit 04), hypertension, diabetes, osteoarthritis, and depressive symptoms. In addition to the above covariates, E2 models were also adjusted for cycle day of the blood draw.

Results: In fully adjusted models for menopausal status, compared to premenopausal status (OR=1.05, 95% CI 0.95-1.14), natural postmenopausal status (OR=0.96, 95% CI 0.86-1.07) and surgical menopause (OR=1.88; 95% CI 1.10-3.23) women had significantly higher odds of reporting greater PF limitation. Additionally, in fully adjusted E2 models, both higher levels of E2 at visit 04 (OR=0.88; 95% CI 0.80-0.98) and less reduction in E2 over time (OR=0.85; 95% CI 0.72-0.99) were significantly associated with lower odds of reporting greater PF limitation. Interactions with race or BMI were not significant. Conclusion: The menopausal transition, starting at the late peri-menopausal stage, and lower and higher reduction in E2 over the transition were significantly associated with lower PF at menopause. These associations were not explained by aging, race, body size, level of physical activity, or existing comorbid conditions.

S-6

Disruptions in Ovarian Function are Related to Depression and Cardio-metabolic Risk during Pre-menopause

Maria E. Blei, PhD1, Joyce T. Bromberger1, Melissa D. Latham1, Nancy E. Adler1, Lauri A. Pasch1, Steven E. Gregorich2, Barbara Sterinfeld1, Mitchell P. Rosen3, Marcelle I. Cedars1. 1Psychiatry, University of California San Francisco, San Francisco, CA; 2Epidemiology, University of Pittsburgh, Pittsburgh, PA; 3Medicine, University of California San Francisco, CA

Objective: Abnormalities in menstrual cycle characteristics are common among women with psychiatric disorders; and menopausal cycle irregularity is an independent risk factor for cardiovascular disease (CVD). Here, we examined the extent to which disruptions in ovarian function among healthy, regularly-cycling women may relate to depression and cardiometabolic risk factors assessed in the Study of Women’s Health Across the Nation (SWAN) study. We examined whether the association between symptoms of menopausal transition and depression was influenced by baseline depression, baseline menopausal symptoms, menopausal status, and menopausal symptoms; however, the etiology of menopausal insomnia is poorly understood. Many women who were previously good sleepers experience insomnia during menopause. Even among healthy, regularly-cycling women, subtle disruptions in ovarian function may relate to changes in menstrual cycle length observed during menopause. Some symptoms appear to influence the overall positive or negative view of menopause more than others, regardless of their frequency of occurrence.

S-7

Reduced slow wave activity during sleep in women with menopause-induced insomnia

Magdalena Baker, PhD1,2, Stephanie A. Sassoon, Ph.D1, Benjamin Mayer1, Rebecca A. Cur1, David S. Sugarbaker1, Ian M. Colrain1,3. 1Human Sleep Research Program and Neuroscience Program, SRI International, Menlo Park, CA; 2Brain Function Research Group, School of Physiology, University of the Witwatersrand, Johannesburg, South women, lifetime depression diagnosis (OR=2.982, 95% CI:0.970-0.995). Each 1 cm increase in WC was associated with a 1.3% increase in the probability of experiencing a change in menstrual cycle length (OR=1.013, 95% CI=1.000-1.027) and having a hypertension diagnosis was associated with a 79.2% increase in the probability of experiencing a change in menstrual cycle length (OR=1.792, 95% CI:0.990-3.245). In addition, endorsement of any one of the depression indicators was associated with more than a 2-fold increase in the probability of experiencing a change in menstrual cycle length: CESD score ≥ 16 (OR=2.098, 95% CI:3.131-5.598); lifetime depression diagnosis (OR=4.631, 95% CI:1.727-5.079); and lifetime anti-depressant medication use (OR=2.869, 95% CI:1.470-5.598). In multivariable logistic regression analyses, there was a relation between depression and HDL (b=1.807, p=0.045) that attenuated (b=0.064, p=0.133) when change in menstrual cycle length was covaried, suggesting disruptions in ovarian function may partially mediate this association. Depressed menopause was related to the other cardio-metabolic risk factors (p>0.05). All analyses included covariate adjustment for age, race/ethnicity, socioeconomic status, cigarette smoking, past use of hormone-containing medication for birth control, and menstrual cycle length. Conclusion: Even among healthy, regularly-cycling women, subtle disruptions in ovarian function marked by changes in menstrual cycle length are related to increases in depression and CVD risk. In addition, disruptions in ovarian function may mediate associations between depression and HDL. The current findings have implications for the identification of women who may benefit from early intervention in order to more effectively prevent or delay the emergence of CVD.
that develops in the context of the menopausal transition. Patients who reported menopause, 41.1%; BMI, 29.4). A total of 397 patients completed 24 weeks of treatment (MHT) with either oral conjugated estrogens or transdermal estradiol in over 700 recently menopausal women. Here we examine changes in sexual function over time in the KEEPS cohort and determine whether type of hormone therapy influenced changes in sexual function. 

**Conclusion:** 727 menopausal women who were within 3 years of their final menstrual period were randomized to either: oral conjugated estrogen 0.45mg (n=230) or transdermal estradiol 30mcg (n=225), both with micronized progesterone 200mg daily for 12 months, control group (n=275). Nine recruitment sites from across the USA participated in the KEEPS trial. Participants completed the Female Sexual Function Inventory (FSFI) at baseline, 18, 36 and 48 months. **Results:** Desire, arousal, orgasm, lubrication and pain improved in combined treatment groups at 18 months compared to the placebo group. Differences in FSFI status between study groups were statistically significant. **Conclusion:** Sexual function, as measured by the FSFI, improved overall in the first 18 months of follow-up. Sexual function over the 4 year follow up in KEEPS and differences between regimens will be presented.

**THURSDAY CONCURRENT SESSION #2**

**S-10. Gynecologic Safety of Bazedoxifene/Conjugated Estrogens: Pooled Results of Phase 3 Trials**

David F. Archer1, JoAnn V. Pinkerton2, Risa Kagan, MD3, Kelly A. Ryan1, John Thompson4, James H. Pickar5, Sebastian Mirkin6. 1Clinical Research Center, Eastern Virginia Medical School, Norfolk, VA; 2University of Washington, Seattle, WA; 3Surgery & Physiology, Mayo Clinic, Rochester, MN; 4Obstetrics & Gynecology, New York University, New York, NY; 5Obstetrics & Gynecology, Albert Einstein College of Medicine, Bronx, NY; 6Obstetrics & Gynecology, University of Colorado School of Medicine, Aurora, CO

**Objective:** The Kromos Early Estrogen Prevention Study (KEEPS) is a multicenter trial designed to test the effects of 4 years of randomized, double-blind menopausal hormone treatment (MHT) with either oral conjugated estrogens or transdermal estradiol in over 700 recently menopausal women. Here we examine changes in sexual function over time in the KEEPS cohort and determine whether type of hormone therapy influenced changes in sexual function. **Conclusion:** 727 menopausal women who were within 3 years of their final menstrual period were randomized to either: oral conjugated estrogen 0.45mg (n=230) or transdermal estradiol 30mcg (n=225), both with micronized progesterone 200mg daily for 12 months, control group (n=275). Nine recruitment sites from across the USA participated in the KEEPS trial. Participants completed the Female Sexual Function Inventory (FSFI) at baseline, 18, 36 and 48 months. **Results:** Desire, arousal, orgasm, lubrication and pain improved in combined treatment groups at 18 months compared to the placebo group. Differences in FSFI status between study groups were statistically significant. **Conclusion:** Sexual function, as measured by the FSFI, improved overall in the first 18 months of follow-up. Sexual function over the 4 year follow up in KEEPS and differences between regimens will be presented.

**S-9. Effects of Oral vs Transdermal Estrogen vs Placebo on Sexual Function Over Time in the Kronos Early Estrogen Prevention Study (KEEPS)**

Hugh S. Taylor, MD1, SD Mitchell Harman, MD2, Lubna Pal3, Mary Jane Minkin, MD3, Erin Wolf3, Dennis Black4, Elliot Brinton, MD5, Matthew Budoff, MD6, Mercarel Cedars, MD7, John Hods, MD8, Rogerio Lobo, MD9, JoAnn V. Pinkerton6, George Merriam, MD10, Virginia M. Miller, Ph.D.11, Frederick Naftolin, MD,Ph.D.12, Genevieve Neal-Perry, MD, PhD13, Nanette Santoro, MD14. 1OB/GYN, Yale School of Medicine, New Haven, CT; 2Kronos Longevity Research Institute and Phoenix VA Medical Center, Paradise Valley, Arizona; 3Epidemiology & Biostatistics, University of California, Berkeley, California; 4Cardiovascular Genetics, University of Utah School of Medicine, Salt Lake City, UT; 5Medicine, Los Angeles Biomedical Research Institute, Torrance, CA; 6Obstetrics & Gynecology, University of California at San Francisco, San Francisco, CA; 7Atherosclerosis Research Unit, University of Southern California, Los Angeles, CA; 8Obstetrics & Gynecology, Columbia University School of Medicine, New York, NY; 9Medicine, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA; 10VA Puget Sound HCS and Division of Metabolism, Endocrinology, and Nutrition, University of Washington, Seattle, WA; 11Surgery & Physiology, Mayo Clinic, Rochester, MN; 12Obstetrics & Gynecology, New York University, New York, NY; 13Obstetrics & Gynecology, Albert Einstein College of Medicine, Bronx, NY; 14Obstetrics & Gynecology, University of Colorado School of Medicine, Aurora, CO

**Objective:** The Kronos Early Estrogen Prevention Study (KEEPS) is a multicenter trial designed to test the effects of 4 years of randomized, double-blind menopausal hormone treatment (MHT) with either oral conjugated estrogens or transdermal estradiol in over 700 recently menopausal women. Here we examine changes in sexual function over time in the KEEPS cohort and determine whether type of hormone therapy influenced changes in sexual function. **Conclusion:** 727 menopausal women who were within 3 years of their final menstrual period were randomized to either: oral conjugated estrogen 0.45mg (n=230) or transdermal estradiol 30mcg (n=225), both with micronized progesterone 200mg daily for 12 months, control group (n=275). Nine recruitment sites from across the USA participated in the KEEPS trial. Participants completed the Female Sexual Function Inventory (FSFI) at baseline, 18, 36 and 48 months. **Results:** Desire, arousal, orgasm, lubrication and pain improved in combined treatment groups at 18 months compared to the placebo group. Differences in FSFI status between study groups were statistically significant. **Conclusion:** Sexual function, as measured by the FSFI, improved overall in the first 18 months of follow-up. Sexual function over the 4 year follow up in KEEPS and differences between regimens will be presented.
and the incidence of ovarian cyst (assessed by TVU) was similar for BZA/ACE and PBO. The incidence of breast-related AEs with both BZA/ACE doses was comparable to those with PBO. The incidence rates for breast cancer (per 1,000 woman-yr) with BZA 20 mg/CE 0.45 mg (1.0 [95% CI, 0.0-3.2]) and BZA 20 mg/CE 0.625 mg (0.2 [95% CI, 0.0-1.5]) were not different from that with PBO (1.4 [95% CI, 0.0-4.2]). Based on daily diary data, both BZA/ACE doses showed low rates of breast pain and tenderness (range, 5.8-13.0%) that were comparable to those with PBO (5.4-10.9%).

**Conclusion:** Pooled phase 3 trial data showed that BZA 20 mg/CE 0.45 and 0.625 mg were associated with an acceptable gynecologic safety profile, adequate endometrial protection, and no evidence of breast stimulation in postmenopausal women with a uterus.

**Table. Summary of Gynecologic Safety (Pooled Phase 3 Study Data)**

<table>
<thead>
<tr>
<th>Study</th>
<th>BZA 20 mg/CE 0.45 mg</th>
<th>BZA 20 mg/CE 0.625 mg</th>
<th>PBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>TVUs</td>
<td>29.8% (95% CI, 21.3-40.5)</td>
<td>31.5% (95% CI, 22.6-40.5)</td>
<td>32.5% (95% CI, 24.1-40.5)</td>
</tr>
<tr>
<td>Endometrial biopsies</td>
<td>12.7% (95% CI, 8.7-18.3)</td>
<td>12.1% (95% CI, 7.7-18.5)</td>
<td>10.8% (95% CI, 6.5-17.3)</td>
</tr>
</tbody>
</table>

*Does not include data from SMART-4 due to formulation change.*

**S.11. Differential Effects of Bazedoxifene/Conjugated Estrogens and Hormone Therapy on the Endometrium**

Sebastian Mirkin1, Hugh S. Taylor2, David F. Archer3, James H. Pickar4, Barry S. Komrn3, Pfizer Inc, Collegeville, PA; Yale University School of Medicine, New Haven, CT; 1Clinical Research Center, Eastern Virginia Medical School, Norfolk, VA; 2Columbia University Medical Center, New York, NY; 3Pfizer Inc, Groton, CT

**Objective:** Bazedoxifene/conjugated estrogens (BZA/CE) is a tissue selective estrogen complex (TSEC) with demonstrated efficacy in treating menopausal symptoms and preventing postmenopausal osteoporosis. BZA has been shown to inhibit endometrial proliferation in a mechanistically different manner than progestins. Here we describe the endometrial effects of BZA/CE compared with CE/medroxyprogesterone acetate (MPA) in non-hysterectomized women enrolled in two phase 3 studies.

**Design:** The 2-year Selective estrogens, Menopause, And Response to Therapy (SMART)-1 (N = 3,397) and SMART-5 (N = 1,843) trials were randomized, double-blind, placebo (PBO)- and active-controlled studies in non-hysterectomized postmenopausal women. Transvaginal ultrasounds (TVUs) and endometrial biopsies were performed at screening and Month 12 (also Month 24 in SMART-1; TVUs were performed at selected sites in SMART-1). Uterine bleeding and spotting were evaluated using daily diaries. Results are presented for BZA 20 mg/CE 0.45 mg, BZA 20 mg/CE 0.625 mg, CE 0.45 mg/MPA 1.5 mg, and PBO.

**Results:** The incidence of endometrial hyperplasia with BZA 20 mg/CE 0.45 mg and BZA 20 mg CE 0.625 mg was low (<0.4%) and similar to that with PBO and CE 0.45 mg/MPA 1.5 mg (Table). In SMART-1, neither BZA/ACE dose showed differences from PBO in the adjusted mean change from baseline in endometrial thickness at 1 or 2 years.

**Possible Endometrial Effects of BZA/CE Compared with CE/MPA in Two Phase 3 Clinical Trials**

<table>
<thead>
<tr>
<th>Study</th>
<th>Month</th>
<th>BZA 20 mg/CE 0.45 mg</th>
<th>BZA 20 mg/CE 0.625 mg</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>SMART-1</td>
<td>12</td>
<td>0.0 (0.22)</td>
<td>0.0 (0.22)</td>
<td>0.0 (0.22)</td>
</tr>
<tr>
<td>SMART-5</td>
<td>12</td>
<td>0.0 (0.15)</td>
<td>0.0 (0.15)</td>
<td>0.0 (0.15)</td>
</tr>
</tbody>
</table>

**Conclusion:** BZA 20 mg/CE 0.45 and 0.625 mg were associated with lower incidences of bleeding and higher rates of cumulative amenorrhea compared with CE/MPA. Findings indicate that BZA/ACE effectively protects the endometrium similar to conventional hormone therapy without the addition of a progestin in non-hysterectomized postmenopausal women.

**S.12. Pooled Cardiovascular Safety Results from Phase 3 Trials of Bazedoxifene/Conjugated Estrogens**

James H. Pickar1, Roggero Lobo1, Ben Ebede2, John Thompson2, Sebastian Mirkin1, 1Columbia University Medical Center, New York, NY; 2Pfizer Inc, Collegeville, PA; 3Pfizer Inc, Groton, CT

**Objective:** In a series of phase 3 clinical trials, the tissue selective estrogen complex (TSEC) pairing bazedoxifene (BZA) with conjugated estrogens (CE) was shown to be effective for the treatment of menopausal symptoms and prevention of postmenopausal osteoporosis, with a favorable safety/tolerability profile. In this analysis, the cardiovascular safety of BZA/CE was evaluated using pooled data from the Selective estrogens, Menopause, And Response to Therapy (SMART) trials.

**Design:** Data were summarized using a meta-analytic approach from five phase 3 studies of 12-week to 2-year duration, conducted in generally healthy, non-hysterectomized postmenopausal women, including SMART-1 (N = 3,397), SMART-2 (N = 318), SMART-3 (N = 652), SMART-4 (N = 1,061), and SMART-5 (N = 1,843). Reports of specified cardiovascular, cerebrovascular, and venous thromboembolic adverse events (AEs) were reviewed by 3 independent adjudication committees. Adjudicated results are presented for the BZA 20-mg/CE 0.45- and 0.625-mg and placebo groups. Results: Overall, the incidence of venous thromboembolic events (VTEs) with BZA/ACE was comparable to that with placebo. The incidence (per 1,000 woman-years) of VTEs was 0.25 (95% CI, 0.01-1.00) for BZA 20 mg/CE 0.45 mg, 0.28 (95% CI, 0.01-0.96) for BZA 20 mg/CE 0.625 mg, and 0.29 (95% CI, 0.01-1.00) for placebo (Table). The relative risk of VTEs versus placebo was 0.86 (95% CI, 0.71-1.04) for BZA 20 mg/CE 0.45 mg and 0.52 (95% CI, 0.38-0.71) for BZA 20 mg/CE 0.625 mg. The incidence (per 1,000 woman-years) of deep vein thrombosis was similar with BZA 20 mg/CE 0.45 mg (0.30 [95% CI, 0.00-2.23]) and placebo (0.30 [95% CI, 0.00-2.03]) for BZA 20 mg/CE 0.625 mg (0.30 [95% CI, 0.00-2.23]) and placebo (0.30 [95% CI, 0.00-2.03]). There were no reports of pulmonary embolism or arterial thrombosis in the BZA/ACE or placebo groups. The incidence (per 1,000 woman-years) of adjudicated fatal and non-fatal coronary heart disease-related AEs was low and similar for BZA 20 mg/CE 0.45 mg (2.57 [95% CI, 0.00-5.55]), BZA 20 mg/CE 0.625 mg (4.14 [95% CI, 0.00-9.31]), and placebo (2.01 [95% CI, 0.00-5.21]). The incidence (per 1,000 woman-years) of myocardial infarction was 1.83 (95% CI, 0.00-4.45) for BZA 20 mg/CE 0.45 mg, 0.41 (95% CI, 0.00-1.69) for BZA 20 mg/CE 0.625 mg (0.41 [95% CI, 0.00-1.69]), and placebo (0.41 [95% CI, 0.00-1.69]). BZA 20 mg/CE 0.45 mg (0.44 [95% CI, 0.00-2.37]) and BZA 20 mg/CE 0.625 mg (0.20 [95% CI, 0.00-1.86]) was low and similar to that with placebo (0.00 [95% CI, 0.00-2.02]). BZA 20 mg/CE 0.45 mg and 0.625 mg were associated with an acceptable cardiovascular safety profile in postmenopausal women based on a meta-analysis of data from five phase 3 clinical trials. The risks of VTEs, superficial thromboembolism, arterial thrombosis, and stroke with BZA/ACE were found to be comparable to those for placebo. Similarly, the incidence of adjudicated coronary heart disease-related AEs with BZA/ACE was low and similar to that with placebo.
S-13. Patient Preference Survey of Local Estrogen Therapy: Attitudes and Insights of Postmenopausal Women Previously Treated with Other Local Estrogen Formulations and Presently on Vaginal Estradiol Tablets

Mary Jane Minkin, MD1, Jeffrey Goldstein2, Ricardo Maamari2. 1Yale University School of Medicine, New Haven, CT; 2Novo Nordisk, Inc., Princeton, NJ

Objective: To evaluate women’s adherence to local estrogen therapies (LET) and identify reasons based on products’ attributes for patients to switch from local formulations to vaginal estradiol tablets. Design: 6,974 women who previously had opted-in on the Vagifem10.com website were contacted by email and asked to participate in a quantitative, online survey. 423 women responded, of which 79 met the specific eligibility criteria: postmenopausal, presently on vaginal tablets, and formerly treated with another LET formulation. Eligible participants responded to an online survey consisting of 34 questions that explored: duration of multi-product therapy; frequency and reasons for non-compliance with prior treatment; reasons to switch to vaginal tablets; comparative compliance behavior on vaginal tablets; and overall “user-friendly” attributes with all formulations. The results were tabulated based on age group, previous treatment, reason for switching to vaginal tablets, and sexual activity status using a confidence interval of 95%.

Table: Summary of Cardiovascular Safety (Pooled Phase 3 Study Data*)

<table>
<thead>
<tr>
<th>E2A 20 μg/CUR 0.05 mg (n=969)</th>
<th>PLA 15 mg/CUR 0.625 mg (n=1,088)</th>
<th>PLA (n=1,175)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Incidence</strong> (95% CI)</td>
<td><strong>Incidence</strong> (95% CI)</td>
<td><strong>Incidence</strong> (95% CI)</td>
</tr>
<tr>
<td>MI</td>
<td>0.30 (0.00-1.04)</td>
<td>0.00 (0.00-1.00)</td>
</tr>
<tr>
<td>PE</td>
<td>0.00 (0.00-1.00)</td>
<td>0.00 (0.00-1.00)</td>
</tr>
<tr>
<td>CHD VTE</td>
<td>0.00 (0.00-1.00)</td>
<td>0.00 (0.00-1.00)</td>
</tr>
</tbody>
</table>

*Based on cumulative meta-analysis of data from five phase 3 studies with inverse variance weighting.

**Incidence rates per 1,000 woman-years.

S-14. 25(OH) Vitamin D Concentrations and Plasma Cholesterol Profiles in the Women’s Health Initiative

Peter F. Schnatz, D.O.1,2, Yuxi Zhang, MD,1 Sharon Vila-Wright, M.D.,1 Aaron K. Araghi MD,2, Matthew Naulty1,2 David M. O’Sullivan, PhD,1 Rebecca D. Jackson, M.D., Erin LeBlanc, M.D., MPH, Jennifer G. Robinson, MD, MPH, James M. Shikany, Dr.P.H.1, Catherine R. Womack, M.D.1, Lisa W. Martin, M.D.1, Marian L. Neuhauser, PhD,1 Mara Z. Vitillanos, Dr.P.H., MPH, RD,2 Yingq Song, M.D., ScD,1 Stephen Korthuis MD,1 MD,2, JoAnne E. Manson, ScD,1 Deborah Hospital & Medical Center, Reading, PA; 2OBGyn & Int Med, Jefferson Medical College, Philadelphia, PA; 6Division of Public Health Sciences, Fred Hutchinson Cancer Research Center, Seattle, WA; 7Int Medicine, The Ohio State Univ, Columbus, OH; 8Center for Health Research, Kaiser Permanente, Portland OR; 9Dept of Epidemiology & Med, Univ of Iowa, Iowa City, IA; 10Dept of Prev Med, Univ of Alabama at Birmingham, Birmingham, AL; 11Dept of Prev Med, Univ of TN, Memphis, TN; 11Int Medicine, George Washington Univ, Washington, DC; 12Dept of Epid & Prev, Wake Forest Univ, Winston-Salem, NC; 13Medicine, Harvard Medical School, Boston, MA

Objective: The relationship between 25-hydroxyvitamin D (25OHD) and plasma cholesterol is poorly understood. The objective of this study, therefore, was to evaluate the association between vitamin D concentrations and total and free fatty acid (VFA) level in plasma lipids in a cohort of postmenopausal women not selected for high risk of coronary heart disease. Design: This cohort was selected from the WHI CaD study, a double-blinded, randomized, placebo-controlled trial designed to test the effects of CaD supplementation (1,000 mg of elemental calcium plus 400 IU of vitamin D3) versus placebo on multiple health outcomes in postmenopausal women. We randomly selected 300 White, 200 African-American, and 100 Hispanic participants (n=1,753), ensuring there were equal numbers from each arm (representing 6% of the population). Serum and plasma was tested for 25OHD (Diassor assay) and lipids, respectively (fasting plasma triglycerides (TG), high density lipoprotein cholesterol (HDL-C), and calculated low density lipoprotein cholesterol (LDL-C)). Participants had available plasma at both baseline (prior to CaD randomization) and two years after randomization. Among the 576 participants with evaluable data, 275 (49.5%) received CaD and 285 (49.5%) received placebo. We analyzed the prospective effect of CaD on LDL-C and the mediating effect of 25OHD. To ensure the relationship between 25OHD and LDL-C was correctly specified, we investigated the association of 25OHD concentrations with LDL-C at randomization and year 2 with nonparametric regression splines. Since previously published WHI results showed no effect of CaD on TG and HDL-C, we did not determine whether the 25OHD concentration was a mediating variable between CaD and these lipids; rather, here we present nonparametric associations of 25OHD concentration with LDL-C at randomization and year 2 (without adjustment for randomization effects). Calcium plus vitamin D (CaD) supplementation was 1.38 times higher (95% CI 1.29-1.47, p<0.001) for women randomized to CaD compared with placebo, with unadjusted mean achieved concentrations of 24.3 ng/mL in the intervention arm vs. 18.2 ng/mL in the control arm. This effect of CaD on mean 25OHD concentrations was not modified by age, BMI, race/ethnicity, hormone therapy use or other factors known to be associated with vitamin D deficiency. Women randomized to CaD had a 4.46 mg/dL mean decrease in LDL-C (p=0.03). When 25OHD was included in the model, the effect of CaD was attenuated to 3.24 mg/dL and was no longer statistically significant. However, 25OHD was a significant predictor of LDL-C (p=0.04). When examining change in vitamin D concentrations regardless of randomization arm, there was an association between vitamin D concentration and TG, HDL-C, and LDL-C. As the achieved concentration of 25OHD increased, HDL-C increased in a linear fashion (p=0.003) while LDL-C and TG decreased (p=0.02 and p<0.001, respectively). Conclusion: Supplemental CaD significantly increased concentrations of 25OHD. Overall, women with increasing 25OHD appeared to have a better lipid profile, including increased HDL-C as well lower LDL-C and TG. This study, from this analysis support the hypothesis that higher concentrations of 25OHD, in response to oral CaD supplementation, are associated with improved LDL-C profiles.

Multivariable adjusted effect of CaD on LDL-C, with and without 25OHD in the regression model, after randomization into WHI CaD trial

FRIDAY CONCURRENT SESSION #1

S-15. Comparing Sexual Function at Midlife in Hispanic and Non-Hispanic Women in West Texas

Beth Prairie, MD, MPH, Yan Zhang, PhD,1 Sahar Morgan,2 Marjorie R. Jenkins, MD,1 ‘Obstetrics and Gynecology, University of Pittsburgh, Pittsburgh, PA; 2Family and Community Medicine, Texas Tech University, Amarillo, TX; 2Laura Bull. Institute for Women’s Health, Texas Tech University, Amarillo, TX

Objective: Using the Greene Climacteric Scale® (GCS), which independently measures psychological, somatic, and vasomotor symptoms, we measured menopausal symptoms in Hispanic and non-Hispanic women in West Texas. The Greene Climacteric Sexual Function Index (FSFI) are well-validated survey instruments available in both Spanish and English for gathering information on menopausal symptoms and sexual function. We assessed menopausal symptoms and sexual function of Hispanic women and compared...
their experience with non-Hispanic women. Design: This is a blind de-identified survey that enrolled anonymous subjects who voluntarily complete and return a mailed survey. Hispanic women and non-Hispanic women aged 40-60 speaking either English or Spanish were eligible. The study was eligible for non-Hispanic women aged 40-60 years, males, and language other than English or Spanish. We expect a return rate of approximately 30% on our questionnaires and have mailed questionnaires to 1000 women (500 Hispanic and 500 non-Hispanic). A sample size of at least 55 women in each group (a total of 110) is needed to provide 80% power to detect a 0.80 with significance set at 0.05 based on previous studies for the GCS and the FSFI. All data were de-identified and analyzed in SPSS. Descriptive statistics were used to assess all variables. Independent t-tests were used to compare the GCS and FSFI score differences between Hispanic and non-Hispanic women. Chi-square tests were used to compare menopausal and socio-demographic characteristics differences between Hispanic and non-Hispanic women. Results: Preliminary results showed that 2 weeks after initial survey mailing, 106 surveys have been returned. Of all respondents, 42% were Hispanic and 58% were non-Hispanic women. The number of surveys returned for Hispanic women does not yet meet our power analysis requirement. The mean age of the sample was 50.7 (SD=3.3) years. Significantly more non-Hispanic women had a college or above education level (44% versus 21%, p=0.005) and Hispanic women were significantly more likely to live in households with 4+ people. There were no significant differences between the groups for other demographic variables including age, menopausal status, household income, self-rated health status, having health insurance or type of health insurance. From answers to questions based on the Stages of Reproductive Aging Workshop (STRAW) to determine menopausal status, 18% of the sample were premenopausal (26.8% of Hispanic, 11.9% of non-Hispanic respondents), 12% were perimenopausal (12.2% Hispanic, 11.9% non-Hispanic), 51% were menopause (41.5% Hispanic, 57.6% non-Hispanic) and the remaining 19% were indeterminate from menopause and overall GCS score was 18.7+/-2.1, 12.5, 16.4, 17.6, 15.2, 17.6 and 15.5 for Hispanic women and 20.2 +/- 12.5 for non-Hispanic women. There was no significant difference between the Hispanic and non-Hispanic women in their mean GCS scores or in the GCS sub-scales. However, on the FSFI, Hispanic women had higher scores on arousal (mean 1.18 +/-0.22 versus 8.4+/=5.2, p=0.006), lubrication (14.0 +/-6.5 versus 10.8 +/-5.5, p=0.007), orgasm (10.1 +/-0.48 versus 7.8 +/-4.5, p=0.021), and pain subscales (7.0 +/-0.66 versus 3.9 +/-0.48, p=0.011), indicating better sexual function. There was no difference in the satisfaction or desire domains or in the overall FSFI score (14.5 +/-5.9 for Hispanic and 17.4 +/-6.8 for non-Hispanic women, p=0.05). Conclusion: Preliminary results from this survey of 106 Hispanic and non-Hispanic middle age women in the Texas Panhandle suggest significantly better sexual functioning in the Hispanic sample. This significant difference exists despite no difference on the GCS scale scores, age or menopausal status between the two groups. Additional analysis including multivariable analysis will be required to evaluate the relationships between demographic variables and menopausal status and sexual function and climacteric symptoms. There is a significant gap in our knowledge of sexual function in Hispanic women in the US. Similarly, the relationship between menopausal symptoms and sexual function in Hispanic women has not been well-studied. This study begins bridging this gap.

S-16. Is a sexual revolution cohort effect masking an increase in HPV detection at menopause in the US?
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Objective: New sexual norms and sexual behavior/relationships may be occurring at menopause. It has previously been demonstrated that estrogen (dehydroepiandrosterone; DHEA) and estrogens exert beneficial effects on vulvovaginal atrophy (VVA) symptoms. Prasterone, in addition, has been shown to improve the four domains of sexual function, an effect not recognized for estrogens. The goal of this study was to determine if prasterone could specifically modify innervation density in the rat vagina, thus providing an explanation for the improvement of sexual dysfunction in postmenopausal women reported. Methods: Prasterone, estrogen and estrogens administered in combination. Vaginae were fixed by intravaginal administration of the steroid precursor prasterone and to compare the innervation of the rat vagina was examined 9 months after ovariectomy (OVX) and was compared to intact animals as well as to OVX animals treated daily routine gynecologic care in Baltimore, MD USA were enrolled into a 2-year semi-annual follow-up study. Demographics, as well as reproductive, sexual, and cervical cancer screening histories were collected from all women by interview. A cervical swab was collected and tested for 37 HPV genotypes by the Roche HPV Linear Array test. Age-specific any and HR HPV prevalence was estimated in the total population and in strata defined by lower risk of prior infection (< 5 self-reported lifetime sex partners (LTPS)) and higher risk of prior infection (>=5 LTPS). Results: Women reporting a recent new sex partner had higher odds of prevalent HPV in both younger and older women, but the general trend risk (PAR) was <30% in women aged 35-49 years and in women aged 50-60 years. The number of LTPS decreased with increasing age. HPV age-specific prevalence declined with age in women <5 LTPS, but not in women with 5+ LTPS. The relative difference in prevalence between women with <5 versus 5+ LTPS was greatest in the younger age. The PAR due to a higher lifetime number of sex partners was higher in older compared with younger women. Conclusion: We observed an interaction between age and LTPS on prevalent HPV detection that is consistent with an age-associated increased risk of HPV reactivation. A lower cumulative lifetime HPV infection probability in older women with sexual debut before the 1965-1975 sexual revolution may be masking an age-related increase in HPV reactivation in the US. Given the large number of women from the baby-boomer generation who are currently entering the menopausal transition, further evaluation of this cohort effect on HPV and cervical cancer will be required.
parameter. OXV decreased the area of the PGP 9.5 nerve fibers to 41% (p<0.0001) of the intact value, an effect which was completely reversed by prasterone and prenarin treatment. The addition of AROL to prasterone induced a significant further 48% (p=0.0008) increase of the PGP 9.5 fiber area, thus leading to a value 39% above intact controls while the stimulatory effect of prenarin on PGP 9.5 fiber area in the lamina propria was reversed by 81% (p<0.0001). Most importantly, when looking at the ratio of the area of PGP 9.5 fibers per total area of lamina propria (PGP 9.5 fiber density), treatment with prasterone significantly increased PGP 9.5 fiber density by 60% (p=0.0074) compared to OXV animals while a further 27% increase (total increase of 87%; p<0.0001) was observed when AROL was combined with prasterone. Premarin, on the other hand, had no significant effect on the density of PGP 9.5 fibers. Conclusion: The relatively potent stimulatory effect of prasterone on vaginal nerve fiber density provides a possible explanation for the beneficial effects of intravaginal prasterone on sexual dysfunction observed in postmenopausal women treated by a low intravaginal dose of prasterone (Labte, Archer et al, Menopause 16, 925-931, 2009). Taking into account the observation that progestin causes adhesions in the rat vagina while almost completely blocking the stimulatory effect of prenarin, the present data suggest that prasterone exerts its beneficial effect on nerve fiber density through an androgenic action in agreement with previous findings with testosteronex.

S-19. LibiGel® (Testosterone Gel) Safety Study Continues in Fifth Year in Postmenopausal Women with a Low CV Event Rate
Michael C. Snares, M.D.,1 Joanne Zborowski,2 William White, M.D.2, 3BioSante Pharmaceuticals, Inc., Lincolnshire, IL; 4School of Medicine, University of Connecticut, Farmington, CT
Objective: LibiGel®, testosterone gel, is in Phase III development for treatment of postmenopausal women with Hypoactive Sexual Desire Disorder (HSDD). FDA approval requires demonstration of cardiovascular (CV) and breast safety and herein we report on the post-placebo-controlled, long-term safety study in postmenopausal women with HSDD.
Design: Design: This is a randomized, double-blind, placebo-controlled, multi-center CV events-driven, adaptive design comparison of daily LibiGel® testosterone gel (which increases serum free testosterone into the normal premenopausal range, approximately 4-5 pg/ml) verses identical placebo gel in postmenopausal women with HSDD and at least 2 points of CV risk. Design of the study incorporated enrollment completion prior to the maximum of 4,000 subjects if the unblinded, independent Data Monitoring Committee (DMC) statistician calculated the predictive probability of study success to be >90% after completing the study for an additional 12 months after enrollment completion using prospectively designed Bayesian modeling of the distribution of endpoint CV events. The primary safety outcome measure is the effect of treatment on the incidence of a composite of adjudicated CV events including death, myocardial infarction, stroke, coronary revascularization (stent or coronary artery bypass graft), or venous thromboembolic events (venous thrombosis or pulmonary embolism). Results: Based on the results of the adaptive design sample size algorithm, enrollment was completed at 3,656 randomized subjects. In addition, the DMC has recommended that the study continue as planned after each of the 8 separate, unblinded data evaluations. The mean age of subjects currently in the study is 60.2 year: two thirds are hypertensive, 19.4% smokers and 22% diabetic. More than 6,300 women-years of exposure have accrued to date. The rate of adjudicated, protocol-defined CV events is 0.54% and the breast cancer rate is 0.32%.

S-21. vasomotor symptoms and insulin resistance in the Study of Women’s Health Across the Nation
Rebecca C. Thurston, PhD,1, 2 Samar R. El Khoudary, PhD MPH,3 Kim Sutton-Tyrrell, PhD,4 DiPHT, Carolyn J. Crandall, MD MS,4 Barbara Sternfeld, PhD,4 Hadime Joffe, MD, MS,5 Ellen B. Gold, PhD,4 Faith Selzer, PhD,4 Karen A. Matthews, PhD,3 1Department of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, PA; 2Department of Medicine, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA; 3Division of Research, Kaiser Permanente, Oakland, CA; 4Department of Psychiatry, Massachusetts General Hospital/Harvard Medical School, Boston, MA; 5Division of Public Health Sciences, University of California Davis School of Medicine, Davis, CA
Objective: Emerging research suggests links between menopausal hot flashes and cardiovascular risk. The mechanisms underlying these associations are unclear, due in part to incomplete understanding of the physiology of hot flashes. We examined the longitudinal associations between hot flashes/nights sweats and fasting glucose and insulin resistance, controlling for cardiovascular risk factors and reproductive hormone concentrations.
Design: Participants were drawn from the Study of Women’s Health Across the Nation (SWAN) (N=3075), a longitudinal cohort study, were ages 42-52 years at cohort entry. Women completed questionnaires (hot flashes, night sweats: none, 1-5, ≥6 days, past 2 weeks), physical measures (blood pressure; height; weight), and a fasting blood draw (serum glucose, insulin, estradiol) (E2), follicle stimulating hormone (FSH) yearly for 8 years. The Homeostasis Model Assessment (HOMA) was calculated. Among women free of cardiovascular disease, free of hormone use, and free of insulin or glucose-lowering medications, hot flashes/nights sweats were examined in relation to glucose and HOMA in linear mixed models adjusting for demographics, age, site, education, menopausal status, alcohol use, physical activity, anxiety, BMI, medication use, and additionally E2 or FSH
Results: Compared to reporting no flashes, reporting hot flashes was associated with higher glucose, with higher glucose, hot flashes 1-5 days: % difference (95% CI):0.33(-0.15,0.82), p=0.2; ≥6 days: % difference (95% CI): 1.25(0.60-1.90), p<0.0001) and a higher HOMA index (hot flashes 1-5 days: % difference (95% CI):2.37(0.36-4.43), p=0.02; ≥6 days: % difference (95% CI):5.91(1.78-10.22), p<0.0001; see Figure) in multivariable models. Findings persisted after adjusting for E2 or FSH. Night sweats were similarly associated with higher glucose and HOMA. Conclusion: Hot flashes and night sweats were associated with higher serum glucose and indicators of insulin resistance that could not be explained by other cardiovascular risk factors. Metabolic factors may be relevant to understanding the link between hot flashes and cardiovascular risk. SWAN has grant support from the National Institutes of Health (NIA), the National Institute on Aging (NIA), the National Institute of Nursing Research (NINR) and the NIH Office of Research on Women’s Health (ORWH) (Grants NR004061; AG102550, AG012535, AG012531, AG012539, AG012546, AG012553, AG012554, AG012495). The content of this abstract is solely the responsibility of the authors and does not necessarily represent the official views of the NIA, NINR, ORWH or the NIH.

FRIDAY CONCURRENT SESSION #2
S-20. Efficacy of Gabapentin Extended Release in the Treatment of Menopausal Hot Flashes: Results of the Breeze 3 Study
JoAnn V. Pinkerton, MD,1 Joanne Zborowski,2 Michael Sweeney, MD,3 Department of Obstetrics and Gynecology, University of Virginia, Charlottesville, VA; 2East Bay Physicians Medical Group, Altabates Summit Medical Center, Berkeley, CA; 3Columbia Center for Women’s Health Research, Columbus, OH; 4Depomed Inc, Menlo Park, CA
Objective: To assess the efficacy and safety of gabapentin extended release (GER) 1800 mg daily in a divided dose (600 mg AM, 1200 mg PM), compared with placebo (P) in reducing the average daily frequency and severity score of moderate-to-severe hot flashes in postmenopausal women at Weeks 4 and 12 of the efficacy treatment period, compared with Baseline. Design: Prospective, multicenter, randomized, double-blind, placebo-controlled study of 24 weeks duration. Primary endpoints frequency and severity of hot flashes at Weeks 4 and 12 using the last observation carried forward (LOCF) imputation method. Secondary endpoints observed frequency and severity of hot flashes at Week 24. Secondary outcome: Mild: sensation of heat without sweating, able to continue activity (score 2); Moderate: sensation of heat with sweating, able to continue activity (score 2); Severe: sensation of heat with sweating, causing cessation of activity (score 3). Patient Global Impression of Change (PGIC) and daily sleep interference (Likert scale 0-10) were also recorded.
Results: Breeze 3 recruited 600 patients (mean age 54.0 years; mean time since LMP: 114 months; surgical menopause, 41.1%; BMI, 29.4 ). A total of 397 patients completed 24 weeks of treatment—206 (68.9%) in the G-ER arm and 191 (65.0%) in the P arm. Baseline daily hot flash frequency was 11.8 for patients in the G-ER arm and 12.0 for patients in the P arm, and baseline severity was 2.55 for patients in the G-ER arm vs. 2.54 for the P arm. Sleep interference was marked at baseline: 7.3 (G-ER) and 7.4 (P) on a scale of 1-10. There was a greater reduction in LOCF hot flash frequency and severity at 4 weeks and 12 weeks, mean reduction (95% CI) in hot flash frequency G-ER vs. P was -1.69 (-2.29, -1.09; p=0.0004) [4 weeks] and -1.14 (-1.8, -0.48; p=0.0097) [12 weeks]. Corresponding reductions in severity were -0.21 (-0.31, -0.1; p=0.0001) [4 weeks] and -0.19 (-0.33, -0.04; p=0.012) [week 12]. These reductions were maintained out to 24 weeks. Patients reporting much/very much improved on PGIC were 68% vs 54% G-ER/P; p=0.0036 at 12 weeks and 74% vs 54% p=0.0001 at 24 weeks Sleep was markedly improved by G-ER at week 12 (3.6 vs 4.6, p= 0.0035). G-ER was well tolerated with only 5% more patients withdrawing due to adverse events (AE’s) than placebo (16.7% vs 11.5%). Most common AE’s (%-G/ER/P were dizziness (13%), headache (9.8%), somnolence (6.3%) and upper respiratory tract infections (URTI) (6%). Mean weight gain over 24 weeks was 0.8 kg higher in G-ER than placebo (p<NS). Conclusion: G-ER was effective at reducing frequency and severity of hot flashes at 4, 12 and 24 weeks. Patient Global Impression and sleep were both significantly improved at 12 weeks. G-ER was well tolerated over 24 weeks for the treatment of patients with moderate-to-severe hot flashes and may offer an alternative for patients unable or unwilling to take hormone therapy.
**S-22. Caffeine and Menopausal Symptoms: What’s the Association?**
Stephanie Faubion, MD1, Richa Sood, MD1, Jacqueline Thielen, MN1, Sharonne Hayes, MD, PhD1

**Objective:** To determine whether there is an association between caffeine intake and menopausal symptoms, particularly vasomotor symptoms. **Design:** Data was collected using the Menopause Health Questionnaire (MHQ), a comprehensive survey of menopause-related health information, including baseline demographics, reproductive and gynecologic history, personal habits, abuse, medications, family history, and vasomotor symptom presence and severity. The study population is a consecutive sample of women with menopausal concerns presenting for consultation to the Women’s Health Clinic at Mayo Clinic in Rochester, Minnesota between July 2005 and July 2011. Questionnaires were sent to patients in advance of their appointment or provided at the time of their visit. The MHQ paper forms were subsequently entered into an electronic database. Information relating to the presence and severity of menopausal symptoms was assessed in a set of 33 questions with each symptom rated from 1-4 in terms of symptom bother (1=not at all, 2=a little bit, 3=quite a bit, and 4=extremely). Hot flashes and night sweats were the primary symptoms of interest. Caffeine intake and current tobacco use were assessed as present or absent (yes/no). Menopausal status was assessed as pre-menopausal (before menopause, having regular periods), peri-menopausal (changes in periods, but not having gone 12 months in a row without a period), or post-menopausal. Data are summarized using mean (SD) for continuous variables and frequency percentages for nominal variables. Menopausal symptom ratings were analyzed as continuous variables and compared between women who used caffeine versus not using the two-sample t-test. In addition, analysis of covariance (ANCOVA) was used to assess whether caffeine use was associated with increased menopausal symptoms after adjusting for smoking and menopausal status. In all cases, two-tailed p-values <0.05 were considered statistically significant. **Results:** A total of 2507 MHQ questionnaires were completed during the study period. After eliminating questionnaires completed by the same individuals at subsequent visits and questionnaires with incomplete data regarding caffeine intake and menopausal symptoms, a total of 1925 questionnaires were included. Of these 1925 women (mean age 52.5, range 19 to 82), 84% used caffeine and 7% were current smokers. Women who used caffeine had higher mean symptom scores for hot flashes [2.35 (1.03) versus 2.22 (1.04), p=0.045] and night sweats [2.26 (0.98) versus 2.09 (1.02), p=0.009]. After adjusting for smoking and menopausal status, caffeine use was significantly associated with night sweats (p=0.020) but not hot flashes (p=0.066). **Conclusion:** Caffeine intake is positively associated with night sweats, though not with hot flashes in women presenting to a specialty clinic for menopausal concerns. This study helps clarify the association of caffeine and vasomotor symptoms.

**S-23. Equol-Producer Status and Self-Reported Vasomotor Symptoms**
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**Objectives:** Studies of the impact of soy isoflavones on vasomotor symptoms (VMS) have yielded mixed results. Daidzein, one of the major phytoestrogens in soy foods, can be metabolized by gut bacteria to equol, a phytoestrogen that more strongly binds to estrogen receptors than daidzein. About 20% of U.S. women harbor bacteria that can produce equol, and it has been suggested that equol-producer status may modify the effect of soy on VMS. The purpose of this study was to evaluate the association between equol-producer status and VMS frequency among women with adequate soy intake to classify equol-producer status. **Design:** We performed a prospective observational study. Women were recruited via a mailed eligibility questionnaire, and for those who remained eligible, a follow-up phone screen and survey. Eligibility criteria included: age 45-55; in the menopause transition or post-menopause; not using oral or transdermal estrogen, oral contraceptives, or SERMs; consuming ≥3 soy servings/week based on a soy-food questionnaire; no severe liver or kidney disease; no history of becoming pregnant; willing to come to study clinic and willing to complete a 24 h urine collection. VMS were collected over 3 days via diary. Urine samples (2 mL) were analyzed for isoflavones by gas chromatography-mass spectrometry. Equol-producers were defined as participants with urine equol concentrations above the lowest level of quantification of the assay (i.e. ≥0.6 mg/mL). In addition, women needed to have urine daidzein or genistein concentrations ≥100 mg/mmol to allow for accurate equol-producer classification. We calculated the mean number of VMS per day for the all women combined, and we then evaluated the association of total VMS, dichotomized as below or above the whole group mean (c.33, vs. ≥ 2.33 VMS/day), within quartiles of daidzein intake, stratified by equol-producer status. We hypothesized that among equol producers, but not non-producers, higher daidzein intake would be associated with lower VMS frequency. **Results:** 355 women were eligible for this analysis and 36% (n=129) were equol producers. There were few differences in the characteristics of women who were and were not equol producers – mean age was 53 years, 61% were postmenopausal, 17% had a hysterectomy, 70% reported ever having VMS, and 94% had greater than a high school education. Among equol producers, compared to those in the lowest quartile of daidzein intake, those in the highest quartile of daidzein intake were 76% more likely to have fewer than the mean number of VMS/day (Table). The test for trend across levels of daidzein intake just missed statistical significance (p=0.06). Among equol non-producers there were no associations between level of daidzein intake and VMS per day. **Conclusion:** We found that higher levels of daidzein intake were associated with fewer VMS but only among equol producers. These findings suggest that among US women equol producers, higher equol availability (due to higher soy consumption) is associated with fewer VMS, whereas in equol non-producers level of soy consumption has no impact on VMS symptoms.

**S-24. Effect of four years of oral conjugated equine estrogen or transdermal 17β-estradiol combined with micronized progesterone on platelet-associated proteins in women of the Kronos Early Estrogen Prevention Study (KEEPS)**
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**Objectives:** Adherence of activated platelets with the concomitant release of vasoactive and mitogenic factors to vascular endothelium contributes to development and progression of cardiovascular disease. In ovariocystinized experimental animals, platelet expression and secretion of adhesion molecules, mitogenic proteins and vascular remodeling enzymes decrease with estrogenic treatments suggesting an additional mechanism by which menopausal hormone treatments might limit progression of vascular disease. Experiments were designed to evaluate effects of menopausal hormone treatments on secretion of adhesion molecules and mitogenic factors to vascular endothelium in women of the Kronos Early Estrogen Prevention Study (KEEPS) trial. **Design:** Platelets were isolated from venous blood of women enrolled in the KEEPS trial at Mayo Clinic prior to and 48 months following randomization to either oral conjugated equine estrogen (0.45 mg/day, n = 8), transdermal 17β-estradiol (50 µg patch; n = 8) with progesterone (200 mg/day for the first 12 days of the month) or placebo (n=10). Expression of proteins in platelet lysate was assessed using a customized protein array for 30 proteins involved in inflammation, cell adhesion, migration, proliferation and vascular remodeling including interferon gamma, vascular cell adhesion molecule-1, regulated upon Activation, Normal T-cell Expressed, and Secreted (RANTES), platelet-derived growth factor, and matrix metalloproteinase 9. Using the paired baseline and follow-up measures, the signed-rank test was used to assess significant change within each treatment group. Group differences were assessed using analysis of covariance. Given the number of proteins analyzed, principal component analysis (PCA) was used to reduce the dimensionality of these data. In the overall sample, the set of normalized “delta” values were orthogonally-transformed into a small number of linearly uncorrelated principal components, which account for as much of the variability in these data as possible. Analysis of variance was then used to test for a group difference in the first few principal components. **Results:** Over the course of 48 months, KEEPS participants receiving estrogen treatments demonstrated a significant change (based on F = 0.1) in 22 of 30 proteins of which 6 were decreases. In contrast, only 5 of 30 proteins changed significantly in the placebo treated group, with all 5 representing increases. For 8 proteins, the change over time was found to differ between the placebo and the combined estrogen groups. The first principal component derived from the PCA, which represented a weighted average of all 30 proteins, was not significantly different in the oral, transdermal, and combined estrogen groups compared to those on placebo (p=0.02, 0.04, and 0.01, respectively). In general, plasma
proteins did not change significantly across groups. Conclusion: Consistent with results in ovariecctional experimental animals, in this randomized trial of menopausal women, decreases in the platelet content of proteins related to processes of vascular remodeling associated with estrogenic treatments. It is likely that these effects are specific to platelets and reflect transcriptional and translational changes at the level of platelet precursor; bone marrow megakaryocytes, as there were no comparable changes in levels of these various proteins in the plasma. Decreases in inflammatory, mitogenic, and vascular remodeling platelet functions were observed in patients with estrogenic treatments and slow progression of vascular disease in newly menopausal women using menopausal hormone treatments.

BASIC SCIENCE POSTER PRESENTATIONS

P-1.

Immunohistochemical expression of estrogen and progesterone receptors in endometrial polyps: comparison between benign and malignant polyps in the postmenopause

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Objective: To evaluate ER and PR expression in the glandular epithelium and stroma of benign and malignant endometrial polyps in the postmenopause Design: A total of 1050 women underwent surgical hysteroscopy in the Prof. Dr. Aristodemou Pinotti Women’s Hospital—CARSM/UNICAMP from January 1998 to December 2008. Of the total number, 390 postmenopausal women with endometrial polyps were included in the study. Polypoid lesions were histologically classified as benign (endometrial polyps, polyps with simple hyperplasia, atypical complex hyperplasia) and malignant and malignant lesions (polyps with simple hyperplasia or atypical complex hyperplasia and carcinomatous polyps). PR and ER expression was evaluated by immunohistochemistry according to stained cells, intensity of nuclear staining and final score. The final score of receptor expression was compared between benign and premalignant/malignant polyps. Results: The prevalence of malignancy in endometrial polyps was 7.1% and was associated with postmenopausal bleeding. Only the final score of ER expression in the stroma of endometrial polyps was higher in the benign group than in the premalignant/malignant group and this difference was significant. There was no difference in PR expression. The risk of malignancy in endometrial polyps was significantly higher when both ER and PR receptor expressions were negative in the stromal component of the polyp (p<0.01). Conclusion: Malignancy of endometrial polyps was associated with a low expression of stromal estrogen receptor. PR expression did not show any association with the risk of malignancy.

P-2.

Evaluation of hyaluronic acid on the vagina of rats treated with estrogen and isoflavones: early and late effects

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Objective: To investigate the action of different doses of isoflavones on the endometrium of castrated adult rats. Design: 40 ovariecctional virgin rats were treated by gavage during 30 consecutive days with vehicle or different doses of genistein: 42, 125 or 250 μg/g body weight per day. Animals were killed, weighed, vaginal and uterine samples were taken for cytologic evaluation, and serum levels of 17β-estradiol and progesterone were determined. The middle third of the uterine horns was dissected, fixed in 10% formaldehyde and processed for paraffin inclusion; 5-μm thick sections were obtained and stained with HE for further histological study under light microscopy. The endometrial morphology and area, number and area of glands, and number of eosinophils in the lamina propria were analyzed. ANOVA and the Tukey-Kramer test were performed for statistical analyses. Results: Endometrial glandular area, and number of glands and eosinophils in 250 μg/g and 125 μg/g of isoflavone were higher than in the other groups (p < 0.05). Morphological data showed signs of endometrial proliferation upon treatment with genistein, especially in animals in in 250 μg/g and 125 μg/g of isoflavone compared to the vehicle group. Conclusion: Our data suggested that raloxifene alone or combined with estrogen may increase the expression of Kiss1 and receptor of Kiss1, androgen and insulin receptors on the endometrium of castrated rats.

P-3.

Early and late effects of estrogen or isoflavone on the uterus of castrated rats

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Objective: The aim of this study was to evaluate changes on the uterus of ovariecctional rats after early and late treatment with soybean concentrate extract or conjugated equine estrogen Design: 60 ovariecctional rats were randomly divided into six groups of 10 animals each: GI-immediate received vehicle, GII-immediate received conjugated equine estrogen (50 μg/kg, per day), GIV-received vehicle after 30 days of ovariecction, GV-received conjugated equine estrogen (50 μg/kg, per day) after 30 days of ovariecction and GVI-received conjugated equine estrogen (50 μg/kg, per day) after 30 days of ovariecction. The substances were administered by gavage immediately after oophorectomy or after 30 days for 60 days. The animals were killed under anesthesia and the uterus was removed for the hyaluronic acid analysis with an ELISA-like method. The ANOVA and Tukey-Kramer test were applied Results: Regardless of treatment time, all isoflavone- or estrogen-treated animals had significant enhance in the concentration of hyaluronic acid (GI = 662.0; GII = 1416.3; GIII = 2341.8; GIV = 355.7; GV = 1731.24; GVI = 1126.31). In early treatment, the estrogen treatment were more effective than the isoflavone one, but the data not for late treatment (the isoflavone action was superior to estrogen one). Conclusion: Our data showed that the animal response to estrogen and isoflavone is different in relation to treatment time in the uterine hyaluronic acid of castrated animals. In fact the estrogen and isoflavone are more effective, respectively, in early and late treatment for increasing the hyaluronic acid of ovariecctional rats.
P-6. The effects of sex steroid on the uterus of ovariec-tomized metocolopramide-induced hyperprolactinemia mice

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Objective: To evaluate the effects of metocolopramide-induced hyperprolactinemia on the morphology of the uterus of ovariec-tomized mice treated with steroid hormones. Design: 120 female mice were used: 20 non-ovariec-tomized were divided randomly into groups: GI control: 0.2 ml 0.9% saline, subcutaneously, GII: 6.7 mg of metocolopramide dissolved in 0.2 ml 0.9% saline, subcutaneously. The groups were divided into: GIII-OVX / S: 0.2 ml 0.9% saline subcutaneously; GIV-OVX / M: 6.7 mg of metocolopramide dissolved in 0.2 ml 0.9% saline, subcutaneously; GV-OVX / S + P: 0.2 ml 0.9% saline, subcutaneously and 2mg/kg/day micronized progesterone by gavage; GVI-OVX / S + P + M: 6.7 mg of metocolopramide dissolved in 0.2 ml of saline solution to 0% estrogen, progesterone receptors, histological and immunohistochemical analyses. The results were evaluated by analysis of variance (ANOVA) and, subsequently, by Tukey’s multiple comparison test for analyzing variables to identify the groups with statistically significant differences. Results: Histomorphometric data revealed a significant increase of degenerating follicles, and presence of antral and nonantral follicles in the GI group. The data of experimental group were three times different than control one.

P-7. The effect of estrogen compounds on the In vitro differentiation of human embryoid bodies

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Objective: Human embryonic stem cells (hESCs) are derived from the inner cell mass of pre-implantation embryo by the blastocyst stage and their differentiation occurs through an intermediate stage treatment to embryoid bodies (EBs) that is a clumps of ES cells. hEBs can provide a new experimental model for pharmaceutical drug testing and studies of human development and we aimed to investigate the effect of estrogen compounds on the differentiation of long-term cultured EBs in vitro. Design: For this study, 30-day old EBs were subjected to estradiol (E2), estrol (E3) and selective estrogen receptor modulator (raloxifene, RLX) in culture media every 48 hours for 7 days. To confirm the effects of estrogen treatment, ICI 182780 was added to the respective EBs every 48 hours for additional 7 days following estrogen treatment. Reverse transcription (RT)-PCR and quantitative PCR (qPCR) were performed to analyze the relative expression of differentiation marker genes representing the three germ layers.

Results: The expression of 7 marker genes, which included e-fetoprotein (AFP), hepatocyte nuclear factor (HNF)-3α, HNF-4α (endoderm), brachyury, cardiac actin (cACT) (mesoderm), nestin (ectoderm), and Oct-4 (undifferentiated), was measured. Significantly lower expression of HNF-4α was observed in EBs after treatment of RLX and E3 in long-term cultured EBs, compared to control and E2-treated EBs (P<0.02). The lower expression of HNF-4α was negated by ICI 182780 treatment. Conclusion: These findings suggest that E3 and RLX have effects on the proliferation and differentiation of long-term cultured EBs.

P-8. Beneficial effects of hormone replacement therapy in postmenopausal animal model

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Objective: Much controversy surrounds the use of hormone replacement therapy to alleviate menopausal symptoms, and prevention of breast cancer particularly taboo. Our study aimed to investigate the role of estradiol, bioidentical progesterone, and testosterone on a spectrum of postmenopausal health factors including cognition, physical activity, cardiovascular health, and bone metabolism. Design: Ten-week-old nude mice were ovariec-tomized to mimic postmenopausal condition. The mice were treated with different concentrations and doses of steroids for 10 months. The treatments were given either constantly, or cyclically to mimic estrus and menstrual cycles. Mice were terminated and analyzed for cardiovascular health markers, bone formation, and general health at different timepoints. Results: Performance on running wheels was significantly increased in the hormone-treated animals compared to untreated mice. Mice showed better performance in the Morris water maze than the ovariec-tomized controls. Free cholesterol and LDL/LDL levels in serum were reduced in hormone-treated groups, whereas HDL was increased significantly. We were not able to observe any trend in serum triglyceride levels linked to hormone treatment. Total alkaline phosphatase was not altered by hormone treatment, but bone specific alkaline phosphatase was increased. Conclusion: Overall, our data demonstrates that bioidentical administration of bioidentical hormones to mice mimicking postmenopausal status results in higher cognitive capacity as well as better general, cardiovascular, and bone health.

P-9. Analysis immunohistochemical of Ki-67 and c-kit the ovarian follicles of pinealec-tomized rats treated with melatonin

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Objective: to evaluate the morphometry and expression of Ki-67 and c-kit on the ovarian follicles of pinealec-tomized rats treated with melatonin. Design: Forty adult rats were equally divided into groups: GI – control; GII – sham pinealec-tomized; GIII – pinealec-tomized and GIV – pinealec-tomized and melatonin administration. After two months of treatment the animals were euthanized and their ovaries were dissected out for histology. Morphometry was evaluated by analysis of variance (ANOVA) and a multiple comparison test for analyzing variables to identify the groups with statistically significant differences. Results: Histomorphometric data revealed a significant increase of degenerating follicles, and presence of antral and nonantral follicles in the GI group.

P-10. Ovarian gene expression after melatonin supplementation on the adult female rats in proestrus

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Objective: the aim of this study was to evaluate the ovarian gene expression after melatonin supplementation on the adult female rats. Design: Thirty female rats (Rattus norvegicus) were divided into two treatment groups: GI - control that received vehicle (n=15); GII - experimental that received melatonin supplementation (10 μg/animal), during consecutive 60 days daily (n=15). The animal were sacrificed under anesthesia and their ovaries were dissected out. The tissues were processed for histology. The data of experimental group were three times different than control one.

Results: The data were normalized and confirmed by GeneChips® Operating software (Affymetrix Inc., Santa Clara, CA, USA) and NC-Chip Analyzer (dChip) software (www.dchip.org). We considered as positive or negative, when the data of experimental group were three times different than control one. Results: 80 and 12 genes of the experimental were up and down regulated, compared to control group, respectively. In relation to steroidogenesis, the pregnancy-zone protein (FPZ) were down regulated and dual specificity phosphatase 1 (DUSP1), lutinizing hormone/choriogonadotropin receptor (LH/GCR), gonadotropin releasing hormone receptor (GnRHR) were up regulated. Conclusion: Our results suggested that melatonin supplementation interfered with ovarian gene expression and may influence the expression of hormonal receptors on the ovarian tissue.

P-11. Ovarian gene expression after melatonin repletion on the adult female pinealec-tomized rats in proestrus

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Objective: to evaluate the ovarian gene expression after melatonin repletion on the adult female pinealec-tomized rats. Design: Thirty pinealec-tomized female rats (Rattus norvegicus) were divided into two treatment groups: GI - control that received vehicle (n=15); GII – experimental that received melatonin supplementation (10 μg/animal), during consecutive 60 days. After that, all animal were sacrificed under anesthesia and the
P-12. Differences in estrogen and progesterone receptor expression in the endometrial polyp and atrophic endometrium of postmenopausal women exposed and not exposed to tamoxifen  

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Objective: To compare the expression of estrogen receptors (ER) and progesterone receptors (PR) in endometrial polyps of tamoxifen users to atrophic endometrium. 

Design: Among women undergoing surgical hysterectomy, 84 tamoxifen users were benign endometrial polyp selected. This group was compared to 84 samples of atrophic endometrium and 252 benign polyps of postmenopausal women who were non-users of tamoxifen. ER/PR expression was assessed by immunohistochemistry study according the percentage of stained cells. 

Results: Polyps of tamoxifen users had a higher expression of ER and PR in the glandular epithelium and stroma, in relation to the atrophic endometrium. Regarding polyps of women not treated with tamoxifen, users had a higher PR expression in the epithelium (p=0.0014) and stroma (p=0.0056), without any difference in ER expression. 

Conclusion: Polyps frequently exhibit increase in ER expression, independent of atrophy status. 

P-13. Estrogen and progesterone receptors, Ki67, Bcl-2 and Cox-2 markers in benign endometrial polyps in pre and postmenopausal women and their association with obesity  

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Objective: To evaluate the immunoexpression of estrogen and progesterone receptors, Ki67, Bcl-2 and Cox-2 in benign endometrial polyps in pre and postmenopausal women and their association with obesity. 

Design: It was observed that among 1050 women who underwent hysterectomy surgery at the “Prof. Dr. José Aristodemo Pinotti” Women’s Hospital-CAISM-UNICAMP from January 1998 to December 2008, 800 were confirmed to have endometrial polyps. Of this total amount, it was decided to select 252 endometrial polyps. This group was compared to 84 samples of atrophic endometrium. 

Results: The hormonal receptors median final scores (0 to 8 and the Ki67 from 0 to 3). The ER, PR, Bcl-2, Cox-2 and Ki67 median final scores in the glandular epithelium and stroma of the polyps were compared among obese and nonobese women, in pre and postmenopausal condition, using the Chi-square Fisher’s exact test or nonparametric Mann-Whitney test. 

Results of this study were submitted to Student t test (p<0.05). 

Conclusion: Our data suggest that melatonin increased the proliferation of epithelial tissue and decreased in the connective tissue of pMenopausal female rats.

P-14. Expression of Ki-67 in the endometrium of pMenectomized rats treated with melatonin during the preovulatory period  

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Objective: To evaluate the expression of Ki-67 in the uterus of female pMenectomized rats treated with melatonin. 

Design: Forty adult rats were equally divided into groups: GI – pMenectomized with vehicle administration; GII – pMenectomized with melatonin administration (10 μg/animal) during the night. After 60 days of treatment, all animals were anesthetized, and the uterus were removed and fixed in 10% formaldehyde (phosphate buffered) for histological processing and paraffin embedding. Sections (5 μm thick) were collected on silanized slides and submitted to immunohistochemical methods for the detection of proliferation index (Ki-67). 

Results: The percentage data of proliferation were submitted to Student t test (p<0.05). 

Conclusion: Reactivity of Ki-67 was expressed at a higher percentage in the pMenectomized rat with melatonin administration in the superficial (GI = 85.2 ± 3.4 vs. 5.7 ± 2.7%: p<0.001) and glandular (GI = 82.4 ± 6.3 vs. 7.9 ± 5.8%: p<0.001) epithelium. However, it was proved to be low in the lamina propria of the melatonin treated animals (GI = 4.8 ± 2.5 vs. GI = 54.8 ± 9.7%: p<0.001). 

P-15. Neurotic personality traits and disorders are associated with menopause-induced insomnia in absence of current depression  

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Objective: Insomnia is one of the most common and bothersome symptoms of the menopause transition. The etiology of menopause-induced insomnia is poorly understood and may involve several predisposing factors including sensitivity to hormonal changes, hot flashes, mood, and personality. Given that not all women experience insomnia during the menopause transition, an important question is what personality traits and psychological disorders predispose certain women to experience insomnia during perimenopause. This study examined the relationship of personality traits and disorders in women with and without insomnia due to menopause. We hypothesized that perimenopausal women with insomnia would be more likely to have past mood disorder history, greater incidence of personality disorders, and greater trait neuroticism than perimenopausal women without insomnia. 

Design: We recruited two groups of perimenopausal women, matched in age, years of education, ethnicity, and body mass index: 30 women meeting DSM-IV criteria for Sleep Disorder due to Menopause (Insomnia) and 22 control women without sleep complaints. The majority of women (80%) were in the early stage of the menopause transition. Participants were administered the Structured Clinical Interview for DSM-IV (SCID) to exclude Axis I disorders other than insomnia and document past history of Axis I disorders; the Greene Climacteric Scale (GCS) to assess current perimenopausal symptoms; the Beck Depression Interview II (BDI-II) to assess current depressive symptoms; the Structured Interview for DSM-IV Personality Disorders (SIDP-IV) to determine personality disorders; the Neuroticism Five Factor Inventory (NEO-FFI) to assess personality traits. 

Results: Perimenopausal women with insomnia had higher scores on the GCS, reflecting more severe menopausal symptoms overall than women without sleep complaints (p < .001), with 24% of women with insomnia had had past history of depression compared to 9% of controls (p < .001), and had significantly higher BDI-II scores than controls (p < .001), although mean BDI-II scores for both groups reflected minimal depressive symptomatology (M = 9.8, SD = 6.1 for insomniacs, and M = 3.8, SD = 4.0 for controls). 

Furthermore, perimenopausal women with insomnia had a higher incidence of personality disorders (39%) compared to controls (0%: p = 0.01), with 24% of women with insomnia diagnosed with personality disorders related to neurotic styles (Obsessive Compulsive Personality Disorder and Depressive Personality Disorder). Women with insomnia scored significantly higher on the NEO-FFI Neuroticism factor (p = 0.001) and lower on the Agreeableness factor (p = 0.003) than controls. Neuroticism was a significant predictor of insomnia diagnosis status over Agreeableness (p = 0.02). 

Conclusion: Results of this study corroborate findings of previous studies reporting a relationship between neuroticism and insomnia, and extend these findings to women who develop insomnia as they transition to menopause. Women with higher trait neuroticism, a personality disorder particularly within the neurotic spectrum, and a past history of depression in absence of a current diagnosis of depression, are more likely to experience insomnia during perimenopause. Women with greater neuroticism or with a personality disorder may be more vulnerable to, and/or less tolerant of, the symptoms of menopause such as insomnia, and could benefit from early identification so that they may be targeted with strategic interventions to prevent or minimize menopausal symptom impairment.
P-16. Vitamin D and conjugated equine estrogen (CEE), the Association with Coronary Artery Atherosclerosis (CAA)

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Objective: The objective of the current study is to analyze daily 25OHD3 supplementation in a cohort of monkeys randomized to oral CEE vs. control and the association with CAA.

Design: All menopausal cynomolgus monkeys (n=50) were fed an atherogenic diet containing a women’s equivalent of 1000 IU/day of 25OHD3. The monkeys were ovarectomized and randomized to receive CEE (equivalent of 0.45 mg/day, n=25) or placebo (n=25). Plasma concentrations of 25OHD3 were measured at baseline and 20 months post-randomization (equivalent to 6 human years). At 20 months CAA was assessed in the right coronary (RCA), the left circumflex (LCX), and the left anterior descending (LAD) arteries. The outcomes were assessed by measuring atherosclerotic plaque area (A), American Heart Association atherosclerotic lesion classification, and evaluating coronary artery (CA) remodeling.

Results: The percent change in 25OHD3 concentrations from baseline to 20 month post-randomization was inversely correlated with the plaque area of the RCA (r = -0.30, p<0.04), LCX (r = -0.30, p=0.036), LAD (r = -0.33, p=0.02) and maximum AHA lesion severity score (AHA-LADmax). (r = -0.34, p=0.017). The RCA, LCX, and LAD plaque area and AHA-LADmax were significantly decreased in monkeys with CEE treatment and higher percent changes in 25OHD3 vs. those with lower percent changes in 25OHD3 without CEE over the course of the study (p=0.016, p=0.02, p=0.029, and p=0.021) respectively). In addition, those with larger 25OHD3 percentage changes with CEE had the least severe CAA and a greater ability to maintain normal luminos by remodeling, compared to the other three groups listed in the fig. The correlations between 25OHD3 percentage changes and CAA were also assessed in the control group only, in order to eliminate the covariate effect of CEE, and the 25OHD3 percentage changes were also inversely correlated with AHA-LADmax (r=0.49, p=0.013). Conclusion: Monkeys that had a greater percent increase in 25OHD3 had significantly less CAA, lower AHA severity scores, and better CA remodeling. In addition, monkeys who had higher percent increases in 25OHD3 with CEE had significantly decreased AHA lesion scores, decreased artery plaque size, and greater CA remodeling. The atheroprotective effect of 25OHD3 was still present without the CEE effect. If these translational findings are present in women, it suggests that achieving higher 25OHD3 concentrations may be cardioprotective and that there may be a synergistic effect with CEE.

P-18. Metoclopramide-induced hyperprolactinemia may change the effects of sex steroid on the uterine hyaluronic acid of ovariectomized mice

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Objective: To identify and quantify the hyaluronic acid of uterine matrix of ovariectomized female mice with metoclopramide-induced hyperprolactinemia after ovariectomy.

Design: 120 female mice were used: 20 non-ovariectomized were divided randomly into two groups of 10 animals each: GI-control: 0.2 ml 0.9% saline, subcutaneously; GII-experimental: 6.7 mg of metoclopramide, subcutaneously. The other 100 animals were submitted to ovariectomy and randomly divided into 10 groups with 10 animals each: GIII-OVX / S: vehicle subcutaneously; GIV-OVX / M: mg 6.7 mg of metoclopramide dissolved in 0.2 ml 0.9% saline, subcutaneously, GV OXV / S + P: vehicle subcutaneously and 2 mg /Kg /day micronized progesterone by gavage; GVI-OXV / M + P: 6.7 mg of metoclopramide dissolved in 0.2 ml of saline solution to 9% subcutaneous and 2mg/kg/day micronized progesterone by gavage; GVII OXV / S + E: 0.2 0.9% saline, subcutaneous and subcutaneous 50g/kg/day of 17β-estradiol by gavage; GVIII OXV / M + E: 6.7 mg of metoclopramide dissolved in 0.2 ml 0.9% saline subcutaneously and 50g/kg/day of 17β-estradiol and 2mg/kg/day of micronized progesterone by gavage; GX OXV / Q + M + E: 6.7 mg of metoclopramide dissolved in 0.2 ml 0.9% saline, subcutaneously and 50g/kg/day of 17β-estradiol and 2mg/kg/day of micronized progesterone by gavage; GX OXV / Q + M + E: 6.7 mg of metoclopramide dissolved in 0.2 ml 0.9% saline, subcutaneously and 50g/kg/day of 17β-estradiol and 2mg/kg/day of micronized progesterone by gavage; GX OXV / Q + M + E: 6.7 mg of metoclopramide dissolved in 0.2 ml 0.9% saline, subcutaneously and 50g/kg/day of 17β-estradiol and 2mg/kg/day of micronized progesterone by gavage; GX OXV / Q + M + E: 6.7 mg of metoclopramide dissolved in 0.2 ml 0.9% saline, subcutaneously and 50g/kg/day of 17β-estradiol and 2mg/kg/day of micronized progesterone by gavage.

Average volume of the right and left hypothalamus in baseline scan (left graph) and scan 8 weeks later (right graph) in subjects with MDD vs. healthy age-matched controls. At baseline individuals with MDD presented a tendency to have a larger right hypothalamus than healthy controls [p = 0.06, F = 3.56]. Eight weeks later, following treatment with SNRI, the hypothalamus of patients with MDD decreased to a size comparable to healthy controls.

Conclusion: Metoclopramide-induced hyperprolactinemia may change the effects of sex steroid on the uterine hyaluronic acid of ovariectomized mice.

P-20. Free subjects (p=0.06), with a subsequent normalization in size following 8 weeks of treatment with SNRI and alleviation of depressive symptoms. The menopause transition (MT) and early postmenopausal years have been associated with the occurrence of vasomotor symptoms (VMS) and a heightened risk for depressive disorder and vasomotor symptoms (VMS). The present study examined the presence of volumetric hypothalamic differences in midlife women presenting with MDD (untreated, medication-free) with and without concomitant VMS (N=14) and healthy controls (N=18).

Design: Volumetric hypothalamic measures were completed using high-resolution MRI images, with volumes of interest being manually drawn onto the MRI images. Participants were categorized into 4 groups based on their clinical history of VMS and MDD (MDD+/VMS-, MDD+VMS-, MDD-+/VMS+, MDD+VMS+). Hypothalamic volumes were compared across the groups using age, VMS scores and depressive scores as covariates. Measures were repeated for the MDD group after treatment with antidepressants. Results: Overall, no significant difference in hypothalamic volume were found among the four groups studied. However, there was a trend towards a larger right hypothalamus in MDD, medication-free subjects (p=0.06), with a subsequent normalization in size following 8 weeks of treatment with SNRI and alleviation of depressive symptoms. Conclusion: Hyperactivity in the hypothalamic-adrenal-pituitary axis is a common neuroendocrine abnormality observed in patients with MDD. Volumetric increases have been shown in the pituitary and adrenal glands of patients with MDD. This preliminary research supports the hypothesis that functional abnormalities in the HPA axis correlate to structural abnormalities in hypothalamic areas. Further, larger studies should explore the extent to which the presence of VMS and MDD might result in distinct structural and functional brain correlates.

P-21. Volumetric Analysis of the Hypothalamus in Midlife Women with Major Depressive Disorder and Vasomotor Symptoms

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Objective: The menopause transition (MT) and early postmenopausal years have been associated with the occurrence of vasomotor symptoms (VMS) and a heightened risk for the development of depression (MDD) – the latter possibly due to the effects of fluctuating estrogen levels on serotonin synthesis and availability. The medial preoptic nucleus of the anterior hypothalamus is involved in thermoregulation and modulation of changes in core body temperature, controlling sensations associated with VMS such as the initiation and cessation of perspiration and vasodilation. Functional abnormalities of the hypothalamus are thought to be involved in the underlying mechanisms of both VMS and MDD. The present study examined the presence of volumetric hypothalamic differences in midlife women presenting with MDD (untreated, medication-free) with and without concomitant VMS (N=14) and healthy controls (N=18).
P-19.
Effect of testosterone and tibolone on purified STS from human placenta and mammalian gland
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Objective: Hormone therapy affects the mammalian gland with estrogens playing a leading role in the pathogenesis of breast cancer. The mammalian gland possesses the enzymatic systems such as steroid sulfatase (STS) for the biosynthesis of estrogens. The aim of the study was to investigate the effect of testosterone (T) and tibolone (TIB) on purified STS. Design: Human breast tissue from mammoplasties and postpartum placenta were used for enzyme purification. The major steps in the purification procedure included column chromatography and SDS-PAGE gel electrophoresis. STS enzyme activity was obtained by thin layer chromatography without or in presence of T, TIB, and its metabolites Oeg 4094 and OM38 at 10-6M, respectively. Results: All substances investigated displayed an inhibitory effect on mammary and placenta STS. However, the magnitude of inhibition depended on the purification step analyzed. In general, inhibitory effects were less in the microsomal fraction than on the purified enzyme. T displayed an inhibitory effect on purified mammary (63%) and placenta (89%) STS. Similarly, TIB, Oeg 4094 and OM38 had an inhibitory effect on purified placenta STS by 90% and on mammary STS by 79%, 85.5% and 50%, respectively. Conclusion: T and TIB display varying inhibitory effects on STS depending on tissue origin which might be due to different isoformes. Studies in cell cultures and tissues without enzyme purification do not necessarily reflect the true impact of a substance on enzyme activity.

P-20.
EFFECTS OF HYPERPROLACTINEMIA ON THE TIBIAL EPiphySEAL GROWTH PLATE OF OVARIECTOMIZED FEMALE MICE WITH HORMONAL TREATMENT
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Objective: Evaluate the effects of hyperprolactinemia induced by metoclopramide in the tibial epiphyseal plate of normal adult female mice ovariectomized and after treatment with estradiol, progesterone and testosterone. Design: Twelve groups consisting of 10 animals each: control group (GI): 0.2 ml 0.9% NaCl; ovariectomized control group (GII): 0.2 ml 0.9% NaCl; ovariectomized experimental+control group (GV): 0.2 ml of metoclopramide; ovariectomized control+estrusgon group (GVII): 0.2 ml of metoclopramide and 2 mg of estradiol propionate; ovariectomized control+progesterone group (GV): 0.2 ml of metoclopramide and 2 mg of progesterone propionate; ovariectomized control+progestogen group (GVI): 0.2 ml 0.9% NaCl and 2 mg progesterone propionate; ovariectomized experimental+control group (GVIII): 0.2 ml of metoclopramide and 2 mg of estradiol propionate; ovariectomized experimental+estrusgon group (GIX): 0.2 ml 0.9% NaCl and 2 mg of estradiol propionate; ovariectomized experimental+androgen group (GX): 0.2 ml metoclopramide and 90ug testosteron propionate; ovariectomized control+androgen group (GXI): 0.2 ml metoclopramide and 2 mg estradiol propionate; ovariectomized experimental+androgen+progestogen group (GXII): 0.2 ml of metoclopramide and 2 mg estradiol propionate+2 mg progesterone propionate; ovariectomized experimental+estrusgon+androgen group (GXIII): 0.2 ml of metoclopramide and 2 mg estradiol propionate+2 mg progesterone propionate; ovariectomized control+estrusgon+androgen group (GXIV): 0.2 ml of metoclopramide and 90ug testosteron propionate; ovariectomized control+androgen group (GXV): 0.2 ml metoclopramide and 90ug testosteron propionate. All groups were treated for 50 days. After, the animals were sacrificed, the tibiae were removed, fixed in 10% phosphate buffer, decalcified (10% formic acid) and subjected to histological processing for embedding in paraffin. Sections were stained with HE, analyzed morphologically and morphometrically. Results: All substances investigated displayed an inhibitory effect on mammary and placenta STS. However, the magnitude of inhibition depended on the purification step analyzed. In general, inhibitory effects were less in the microsomal fraction than on the purified enzyme. T displayed an inhibitory effect on purified mammary (63%) and placenta (89%) STS. Similarly, TIB, Oeg 4094 and OM38 had an inhibitory effect on purified placenta STS by 90% and on mammary STS by 79%, 85.5% and 50%, respectively. Conclusion: T and TIB display varying inhibitory effects on STS depending on tissue origin which might be due to different isoformes. Studies in cell cultures and tissues without enzyme purification do not necessarily reflect the true impact of a substance on enzyme activity.

P-21.
Long Term Evaluation of the Safety of Ospemifene, on Endometrium and Other Parameters, When Used as Treatment for Vulvar and Vaginal Atrophy (VVA) in Postmenopausal Women
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Objective: Symptoms of vulvar and vaginal atrophy (VVA) vary among women, but all women will experience some degree of vaginal change associated with menopause. Ospemifene, a selective estrogen receptor modulator (SERM), is the first oral non-estrogen-proposed for the treatment of VVA symptoms in postmenopausal women. The objective of this study was to evaluate the long term safety of once daily ospemifene treatment for up to 1 year. Design: A multicenter, randomized, double-blind, long-term (40-week) safety extension study to a 12-week efficacy and safety study conducted in which women with an intact uterus (n=180) received the same blinded treatment that they were randomized to in the initial study (daily oral doses of ospemifene 30 mg, 60 mg, or placebo) for a total of up to 52 weeks. Adverse events were collected throughout the study and long term safety was assessed in endometrial tissue via transvaginal ultrasonography and endometrial biopsy. Additional safety assessments included lipid levels (total cholesterol, LDL-C, HDL-C, and triglycerides), hormone levels (estradiol, FSH, LH, SHBG, and free and total testosterone), and breast evaluation (palpation and mammmography). Results: No cases of endometrial hyperplasia or carcinoma were observed and only 3 ospemifene subjects experienced vaginal bleeding or spotting (2 receiving 30 mg/d and 1 receiving 60 mg/d). There were no cases of endometrial biopsy samples (a 95%) were either negative for endometrial tissue was insufficient for diagnosis, however, there was some evidence of limited, dose related, endometrial thickening. Most treatment-emergent adverse events in subjects treated with ospemifene were mild or moderate. Those events occurring in ≤5% of subjects were nasopharyngitis, urinary tract infection, hypercholesterolemia, dysmenorrhea or pharyngolaryngeal pain, and hot flush. No trends were apparent; there were no TEAEs of pelvic organ prolapse or venous thromboembolism. There were no clinically significant adverse changes seen in lipid parameters or breast palpation and mammography. Two subjects in each of the ospemifene and placebo groups reported severe TEAEs were reported, one with ospemifene (breast prosthesis implantation) and one with PBO (breast cancer in situ). Hormonal changes, consistent with those observed in the initial 12 week study, were decreased LH and FSH levels and increased SHBG and total testosterone levels (in a dose dependent manner). Free testosterone and E2 levels were largely unaffected. Conclusion: Consistent with other studies, this study demonstrated the minimal effect of ospemifene on the endometrium, no negative effect on breast tissue, and lack of effect on laboratory values. Ospemifene was well-tolerated and comparable to PBO across a range of safety parameters including lipid and hormone levels when used for the treatment of vulvar and vaginal atrophy in postmenopausal women with a uterus for up to 1 year. Ospemifene has the potential to be the first oral prescription therapy for this highly prevalent and chronic condition and may provide postmenopausal women with an alternative to estrogen treatment for relief of symptoms related to vulvar and vaginal atrophy.
2 were compared to data from visit 4. Repeated measures ANOVA and Cochrane Q test were used to assess changes in continuous and categorical variables. Results: Participants showed reductions in waist circumference of 1.74 inches (p<0.001) and improvements in self-reported hot flushes by 0.23 on a 3 point scale (p=0.001) after the WAT Points intervention. Diastolic blood pressure decreased by 4 points (p=0.004) and self-reported physical activity levels increased. 72.2% of participants completed the program, despite being responsible for insurance co-payments for each visit. Conclusion: Our findings suggest that WAT Points may serve as an effective office-based clinical method to reduce heart disease risk while reducing menopausal symptoms in women during menopause transition. Further study is planned to evaluate this promising heart healthy method to reduce CVD risk and menopausal symptoms.

P-23.

Intrasphincteric Application of Skeletal Muscle Derived Cells for Stress Urinary Incontinence

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Objective: Stress urinary incontinence (SUI) is a complaint of involuntary leakage of urine on exertion, effort, coughing, or sneezing. The majority of this highly prevalent condition in women arises only after the menopause. Although affected by age-related changes to the pelvic structures, SUI should not be considered as a normal consequence of aging. The integrity of the urethral sphincter complex is necessary to maintain continence, especially that of the external rhabdosphincter, an omega-shaped muscle which compresses the urethra voluntarily. Vaginal delivery, surgical injury, and aging, however, affect the morphologic and functional integrity of this muscle. Methods to treat SUI have long existed, but their limitations have encouraged researchers to investigate new approaches, including within the field of regenerative medicine, in order to preserve or improve tissue function. To avoid the ethical dilemma about the embryonic stem cells, the search has concentrated on the potential use of autologous stem cells from adult tissues. This models pave the way to clinical trials of tissue engineering as a treatment option. One of the first such clinical trials on skeletal muscle derived cells (SMDC) for SUI was conducted between September 2009 and March 2011. For the purposes of this post, results were compared in regard to the menopausal status of the treated patients, although safety, feasibility and efficacy assessment of the ultrasound-guided autologous SMDC injection into the external rhabdosphincter as a possible treatment for SUI were the primary objectives. Design: 38 women were treated. They underwent a small open-cut muscle biopsy of biceps brachii from the upper arm of a non-dominant hand for the isolation and cultivation of autologous SMDC. With a specially designed combined injection-ultrasound device 1x106, 5x107 SMDC were injected into the external rhabdosphincter. The procedure was followed by a cycle of functional electrical stimulation (FES). To ensure safety, vital signs and common laboratory values for urine and blood were monitored. Moreover, particular attention was paid to possible immediate and short-term onset of complications of the muscle tissue harvest and SMDC injections. We first compared the baseline subjective as well as objective measurements associated with SUI evaluation (stress test, pad test urinary incontinence episodes (UIE), the amount of leaked urine measured semi quantitatively (UIS), the number of voids (NOV), the number of pads used, the Incontinence Quality of Life Questionnaire (I-QoL) score, visual analogue scale (VAS), the modified Patient Global Impression of Improvement (PGI-I*) score) with the corresponding measurements obtained after a first, preoperative FES cycle, then, we compared these second measurements with those obtained after completion of treatment at 6 weeks, at 3 and 6 months following the autologous SMDC injection. Results: In all 38 women (35-71 years of age) cell culture was successfully obtained from a biopsy. No serious adverse events or complications were noted. No patients were excluded as well tolerated. Two groups of 19 women were compared for the observed parameters according to their pre- and post- menopausal status. Compared with the objective and subjective measurements collected after the preoperative FES cycle, the corresponding measurements obtained 6 weeks postoperatively, after the completion of a second FES cycle, indicated considerable improvement. Additional improvement was observed over time at 3 and 6 months following implantation. With exceptions of fewer positive results to the stress test at 6 weeks postoperatively and fewer episodes with heavier urine leakage in the group of postmenopausal women, no differences were observed between the groups. Conclusion: Intrasphincteric autologous SMDC injections followed by FES are feasible and well tolerated. This minimally invasive procedure, which safely produced promising initial results, does not seem to be influenced by the menopausal status of the treated population and show at least as good results in post- as in premenopausal women.

P-24.

Effect of estrogen therapy on objective sleep quality in postmenopausal women

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Objective: To determine the effects of transdermal estradiol patch on sleep efficiency in insomniac postmenopausal women with mild to moderate vasomotor symptom without recognition of stress during lesion sleeping. Design: Randomized double-blind, placebo-controlled trial, parallel design (ClinicalTrials.gov: Identifier: NCT01501422) METHODS: The postmenopausal women who visit at Menopause Clinic, King Chulalongkorn Memorial Hospital (KCMH) with insomnia and no severe vasomotor symptom and/or recognized hot flushes during sleep were recruited. They were randomized to 2-month-treatment with 50 micrograms of transdermal estradiol patch or placebo group. They completed two self-administered questionnaires which were Ewprth Sleepiness Scale (ESS) and Insomnia Severity Index (ISI) at baseline and the last visit. The wrist actigraphy was put on their non-dominant wrist for seven days. Sleep quality was determined objectively with wrist actigraphy, sleep efficiency(SE), total sleep time(TST), wake up after sleep onset (WASO) and numbers of awakening (NWAK) were compared before and after treatment. Results: Forty postmenopausal women were recruited. Their average age was 54.4 years and the year since menopause was 4.5 years. The subjective sleep quality assessed by Insomnia severity index (ISI) and Ewprth sleepiness scale (ESS) questionnaires were also not significantly improved after treatment. (Table 1) The baseline sleep efficiency of the placebo and estrogen group was 85.2 and 85.9 %, respectively. After 2-month-treatment, the sleep efficiency of the placebo and estrogen group was 87.1 and 85.7%. (p value = 0.71) The other parameters of sleep detected by actigraphy were not significantly different. (Table 2) estrogen therapy was not significantly improved sleep efficiency in insomniac postmenopausal women with mild-moderate degree of vasomotor symptom and no recognized hot flushes.

Table 1: Sleep quality assessed by self-administered questionnaires

<table>
<thead>
<tr>
<th>ISI</th>
<th>ESS</th>
<th>WASO</th>
<th>NWAK</th>
</tr>
</thead>
<tbody>
<tr>
<td>10.24</td>
<td>5.42</td>
<td>92.1%</td>
<td>3</td>
</tr>
<tr>
<td>7.89</td>
<td>4.11</td>
<td>90.3%</td>
<td>4</td>
</tr>
</tbody>
</table>

*p-Mann-Whitney U test: compare pretreatment and posttreatment between two groups

Data was presented as median (1st Quartile, 3rd Quartile)

Table 2: Parameters of objective sleep quality

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Median (1st Quartile, 3rd Quartile)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep efficiency (SE)</td>
<td>92.1% (87.8%, 96.5%)</td>
<td>0.71</td>
</tr>
<tr>
<td>Total sleep time (TST)</td>
<td>7.89 (7.62, 8.14)</td>
<td>0.72</td>
</tr>
<tr>
<td>Wake up after sleep onset (WASO)</td>
<td>4.11 (3.95, 4.27)</td>
<td>0.91</td>
</tr>
<tr>
<td>Number of awakening (NWAK)</td>
<td>3 (2, 4)</td>
<td>0.45</td>
</tr>
</tbody>
</table>

P-25.

Habitual physical activity in pre-, peri- and postmenopause: anthropometrics and cardiovascular risk factors in a cohort of women in São Paulo, Brazil

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Objective: Characterize the status of habitual physical activity (PA) and its effect on climacteric symptoms, anthropometric measures and metabolic parameters in a pre-, peri- and postmenopausal sample women. Design: This study is part of a longitudinal population-based study of menopause status, conducted in Passo Fundo, in southern Brazil. The first cross-sectional study was performed between 1995 and was reconsidered in 2001, (Oppermann K, Fuchs SC, Spritzer PM. Ovarian volume in pre- and perimenopausal women: a population-based study. Menopause 2003;10:209-13). In 2010, it was invited a third follow-up. A sample of 301 women was enrolled. Of those, 9 were excluded due to incomplete data, resulting in a sample of 292 women. Through a standardized questionnaire were collected demographic characteristics, gynecologic data, climacteric symptoms, use of hormone therapy (HT) for menopausal complaints, use of oral contraceptives and habitual PA. Anthropometric measurements were performed in duplicate and included body weight, height, waist circumference and hip circumference. Assessment of habitual PA was performed with a digital pedometer (BP 148, TechLine, São Paulo, Brazil), during 7 days. Subjects were encouraged not to alter their PA habits during the study. The sum of the steps was averaged over the total time period worn. Participants were classified as physically inactive (<6000 steps/day) or active (>6000 steps/day). To compare demography and anthropometric characteristic it was used t test for independent samples or chi square test. Correlations were performed with the Spearman's test. Logistic regression was used to specify the nature of the relation between variables. For menopausal symptoms Poisson Regression Model was used to estimate risk ratio. Results: The mean age was 57.1±5.4 years. The majority of participants were caucasian (83.9%), married (51.4%) and had low school level (51% at 8 years or less of
POSTER PRESENTATIONS (continued)

P-26. Effects of HPO, HPA & ANS Biomarkers on Symptom Severity Clusters and Well-being during the Menopausal Transition and Early Postmenopause
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Objective: In our efforts to extend our understanding of symptom severity clusters women experience throughout the transition through menopause we tested models hypothesizing differential effects of hypothalamic-pituitary-ovarian biomarkers, hypothalamic-pituitary-adrenal biomarkers and hypothalamic-pituitary-adrenergic neurotransmitter biomarkers on symptom clusters and differential relationships of symptom severity clusters to positive well-being. Design: Multilevel latent class analysis with multinomial regression was used to determine the effects of hypothalamic-pituitary-ovarian biomarkers, hypothalamic-pituitary-adrenal biomarkers and hypothalamic-pituitary-adrenergic neurotransmitter biomarkers on PTSD symptom clusters and overall effect of class membership on positive well-being. All models use monthly symptom episodes as the unit of measure and account for the clustering of symptom episodes within individual women. Results: The results consistently find 3 classes of episodes: high hot flash; low hot flash; and all low symptoms. Relative to the low symptom class higher levels of estrogen (OR=0.016) significantly reduces the likelihood of being in the high hot flash class while women with higher levels of FSH (OR=2.870) over hot flush frequency and severity. Searches of the following electronic bibliographic databases were performed to identify relevant randomised controlled trials (RCTs): Cochrane Menstrual Disorders and Subfertility Group Specialised trials register, Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library).
Use of a pragmatic intervention embedded in a randomized trial to study longer-term impact of Tai Chi on multiple fall-related fracture risks in post-menopausal osteopenic women: Insights from qualitative interviews

Gary Elkins, Ph.D., Jim Sliwinski, Aimee K. Johnson, William Fisher, MA. Baylor University, Waco, TX

Objective: Deteriorating bone strength and balance in postmenopausal women underscore the need for accessible and sustainable community-based interventions to prevent fall-related fractures. Tai Chi, a complex multi-component exercise, is a promising intervention but more research is necessary to delineate its effectiveness. Pragmatic clinical trials are useful for studying complex interventions and providing results that can be readily generalized and translated into community programs. Qualitative research may also provide insights into the feasibility and effectiveness of integrative interventions such as Tai Chi. Therefore, we conducted an analysis of qualitative interviews embedded in a larger multiple measures of bone health and balance in osteopenic women to answer the following questions: 1) what factors of a pragmatic approach to studying Tai Chi foster greater participation and post-trial adherence and 2) what are the broader health benefits of participating in community-based Tai Chi programs as described by post-menopausal osteopenic women? Design: Exit interviews were conducted with 43 post-menopausal osteopenic women randomized to the Tai Chi intervention arm of the above study. These women had attended classes at pre-screened community Tai Chi sites in the Greater Boston area. Qualitative Description, a type of naturalistic inquiry useful for addressing questions pertinent to clinical practice or research development, was employed to explore the interview data. This method uses low-inference interpretation to identify themes in the data in comparison to a comprehensive understanding of the views and experience of the participants and expressed in their everyday language. Exit interviews were recorded and transcribed. Transcripts were imported into NVivo, a computer-assisted qualitative data analysis software program. Qualitative content analysis was used to code the data. Patterns emerging from the coded data were further examined and ultimately clustered into themes. Results: Two themes, aligned with the study questions, emerged from the analysis. The first encompasses factors that either facilitated or impeded study participation and post-trial adherence. Facilitators included school location, support from instructors and classmates, social support, health benefits and a desire to improve the health of other women. Barriers consisted primarily of practical issues such as school location, weather, lack of time and the cost of continuing classes after the study ended as well as an uncertainty as to the benefits. The second theme embodies women’s perceptions of the experiences. Majority positive of taking Tai Chi classes. These findings will assist in the design and conduct of future studies exploring the use of Tai Chi in fracture prevention and health-related quality of life in post-menopausal women. Acknowledgements: The pilot study was made possible by grant numbers R21 AT003503 and U19 AT002022 from the National Center for Complementary and Alternative Medicine (NCCAM) at the National Institutes of Health (NIH). Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NCCAM or the NIH.
P-33. Title: the prevalence of hyperinsulinemia or Insulin resistance in women with midlife weight gain: Baseline data from EMPower (Enhance the Metabolic Profile of Women with Insulin Resistance)  

Ruth Freeman, MD1,2, Harriette R. Mogul3, Sheila Farak3, Karen Tananbaum4, Michael Frey5, Gregory Cruikshank6, OB-Gyn and Medicine, Montefiore Medical Center, Bronx, New York, NY; Medicine, New York Medical College, Valhalla, NY; Medicine, Albert Einstein College of Medicine, Bronx, New York, NY.  

Objective: Midlife weight gain has been associated with an increased risk of diabetes (DM)1 and all cause mortality2. The causes of this are unclear. The incidence of diabetes (DM) has been rising, by 2025 estimates suggest that 25% of USA population will have the disease. Prior to developing DM people have weight gain and insulin resistance. These parameters have been rising in the population based on NHANES 1999-2002 for women ages 40-59, 5.7% have known DM, 1.7% have undiagnosed DM, 22.9% have IGF, 3) Hyperinsulinemia precedes these more commonly recognized abnormalities. The objective was to determine the prevalence of hyperinsulinemia and glucose intolerance in women meeting study inclusion criteria. 1) Colditz et al. Ann Intern Med 1995;122:481. 2) Manson JE, etal. N Engl J Med 1995:333:677. 3) Cowe CC et al. Diabetes Care 2009;26:1263 Design: Women aged 35 – 55 were invited to join the EMPower study, a multicenter, placebo controlled, double blind study of metformin or placebo. In addition to a modified diet (clinical trials NCT08619071). Telephone screen excluded women with any major diseases: GI, renal liver and DM by history or medication. At baseline each subject had an oral glucose tolerance test utilizing 75 gm glucose. At times 0, 30, 60, 90, and 120 minutes bloods were drawn for glucose(G) and insulin(I) was measured by glucose oxidase and insulin(1) measured at NYMC by chemiluminescent IRMA, DPC. Results: 109 women mean age 45.9(SE 0.71) were seen for a screening visit and OGTT. Mean BMI was 30.3 (SE 0.3), fasting G 88.3(SE 2.6), fasting Insulin 10.5(0.6) Area under curve (AUC) insulin 157.2 (for 52/109). 16 (19.8%) were of AA background, 10 (12.3%) were Hispanic and 48 (59%). Caucasian, and 3 were Asian/Pacific (3.7%). In this group of asymptomatic women who had gained >20lbs only 23% had normal insulin (and were excluded from actual study).67 (61.5%) had hyperinsulinemia but normal glucose, 11 (10.1%) had IGF or IGT and 4 (3.7%) had DM. 32.8% incomplete data. All had normal BP and none were taking any medications (except thyroxine with normal TSH) or diet pills. Conclusion: We show that in a group of moderately obese midlife women, over 61.5% are hyperinsulinemic. 43.7% had undiagnosed DM. In midlife aged women who have gained >20lbs on OGTT are exceedingly common and are harbingers of DM, increased FFA, inflammation and eventually CAD.  

Glucose and Insulin Status of subjects at baseline  

<table>
<thead>
<tr>
<th>Subject</th>
<th>Normal</th>
<th>Pre-diabetic</th>
<th>Diabetic</th>
<th>IGT or IGT</th>
<th>DM</th>
<th>No data</th>
<th>Missing data</th>
<th>Final data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>67</td>
<td>10</td>
<td>0</td>
<td>11</td>
<td>10</td>
<td>8</td>
<td>0</td>
<td>109</td>
</tr>
<tr>
<td>IGF or IGT</td>
<td>11</td>
<td>80</td>
<td>1</td>
<td>18</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>109</td>
</tr>
<tr>
<td>BMI</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>109</td>
</tr>
<tr>
<td>Systolic</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>109</td>
</tr>
</tbody>
</table>

Total number of subjects 109.

P-34. Symptom reporting among women at midlife in Qatar: the influence of place of birth  

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Objective: The purpose of this study was to examine reported frequencies of menopausal symptoms among Arab women living in Qatar, and to assess if reported frequencies are related to country of birth. Design: This is a cross-sectional study of 737 women aged 40-60 drawn from a general population in Qatar. Face-to-face interviews consisted of demographic and reproductive questions as well as whether, during the past two weeks, women had experienced any symptoms related to menopause. Symptoms reported included vasomotor, cardiovascular and emotional symptoms. Symptom frequencies across place of birth were compared and the significance of differences was assessed by chi-square analysis. Logistic regression analyses were used to evaluate whether associations between place of birth and symptom frequencies persisted after controlling for either menopausal status or age. Results: The frequency of reported symptoms varies across place of birth but many symptoms are frequently considered bothersome by close to 50% of women. Hot flashes were reported less frequently than most other symptoms. Women born in Qatar reported significantly higher frequencies of many symptoms than women born elsewhere. These associations held even after controlling for age or menopause status. Conclusion: These findings indicate that symptoms related to menopause are frequently experienced among women residing in Qatar, with higher frequencies reported among women born in Qatar compared with women from other Arab countries. The results suggest that there may be factors related to place of birth that influence the reporting of menopausal symptoms.

P-35. Prevalence of genital tract malignancies in menopausal and perimenopausal women with abnormal cervical cytology, in a setting of opportunistic cervical screening  

Objective: The Goal1, Moaz Al, Kalbani2, Taimoora Al Sobhi3, Ritu Lakhaitia4, 1obstetrics and gynecology, Sultan Qaboos University, Muscat, Oman; 2OB/GYN, Sultan Qaboos University, Muscat, Oman; 3Intern, Sultan Qaboos University, Muscat, Oman; 4Pathology, Sultan Qaboos University, Muscat Oman.  

Conclusion: To study the prevalence of pelvic malignancies in menopausal and perimenopausal women with abnormal cervical cytology in a tertiary care hospital. Design: A retrospective study of women aged 45 years and above, referred to Colposcopy clinic between June 2006-June 2012 with an abnormal cervical cytology. Results: The prevalence of pelvic malignancies on the cytology reports were 13.2% (13/98). The commonest benign pathology in these women was fibroid uterus (16%) followed by a cervical polyp and endometrial polyp. Two patients had cancer of the uterine cervix and two had endometrial cancer. Conclusion: Borderline atypia was the commonest cytological abnormality in the study group. Though the commonest benign pathology in these women was fibroid uterus (16%) followed by a cervical polyp and endometrial polyp. Two patients had cancer of the uterine cervix and two had endometrial cancer. 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P-37. Oxidative stress contributes to arterial stiffening across the stages of the menopause transition in healthy women

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Objective: Large artery stiffening is a consequence of vascular aging and increases the risk for cardiovascular disease. The age-associated increase in arterial stiffness appears to be augmented in women after menopause, presumably due to estrogen deficiency. However, it is unclear how changes in ovarian hormones during the perimenopausal years contribute to the age-associated increase in arterial stiffness. We evaluated differences in arterial stiffness across the stages of the menopause transition in healthy women. Because oxidative stress is known to contribute to arterial stiffening in estrogen-deficient postmenopausal women, we also determined whether arterial stiffness improved in response to acute antioxidant therapy. Design: Arterial stiffness (carotid artery compliance, ultrasound) was measured during acute intravenous infusions of saline (control) and supraphysiological doses of an antioxidant, ascorbic acid, in 87 healthy women. Participants were examined separately by the frequency of nighttime and then daytime hot flashes to isolate the effects of hot flashes on arterial compliance across the perimenopausal transition. Participants were randomized to receive 0 mg DRSP, 0.5 mg DRSP, 1 mg DRSP or 2 mg DRSP daily at bedtime, and 0.5 mg E2 with DRSP, compared to combinations of 0.5 mg E2 with DRSP. Due to the faster onset of efficacy with Angelici containing 1 mg E2 combined with DRSP there were more responders seen in the higher dose Angelici users compared to women using Angelici containing 0.5 mg E2 in combination with DRSP. The proportion of responders was 75.8% for DRSP 0.5 mg/0.5 mg E2, 65.6% for DRSP 0.5 mg/0.25 mg E2, 56.6% for DRSP 0.25 mg/0.5 mg E2, and 67.2% for the DRSP 0.25 mg/0.25 mg E2 combination. From the groups of Angelici users receiving 1 mg E2, 86.7% of those on the combination with 1 mg E2 DRSP became responders, 100% of those with 2 mg DRSP and 77.7% of those on 5 mg DRSP. In comparison the response rate in the Placebo group was only 27.9%.

Conclusion: The combination of 0.5 mg E2 with DRSP recently approved by the FDA is almost as effective in the reduction of HF as Angelici containing 1 mg E2 in combination with 0.5 mg DRSP. However, there is a slower onset of efficacy with Angelici and the combination containing 1 mg E2. This offers new choices for gynecologists to tailor the treatment of moderate to severe HF better according to the needs of the individual patient.

P-38. Urinary ketones’ positive association with bone metabolism in postmenopausal Korean women

Sang Hyun Je, Dukjoo Lee, Youngseok Kim. Ajou University Hospital, Suwon, Republic of Korea

Objective: The aim of this study is to reveal relationship between bone metabolism and ketogenic ability in women. Design: we investigated the relationship between osteoporosis and its potentially related metabolic parameters in a cross-sectional analysis of 1198 Korean women (492 premenopausal women and 706 postmenopausal women). In our cross-sectional study, we examined body mass index, waist circumference, obesity related factors, urinary ketones, and BMD in Korean women after a fast lasting a minimum of 8 hr (or 6 hr in males). Results: The positive urinary ketONE groups in pre and postmenopausal women showed better BMD than the negative urinary ketONE group. In premenopausal women, body mass index, waist circumference, triglyceride, systolic blood pressure, insulin, HOMA-IR (Homeostasis of measurement assessment-insulin resistance), and alkaline phosphatase were negatively associated with ketonuria after adjusting for age, smoking, and alcohol use. The odds of having ketone decreases in the osteoporosis group, compared to the non-osteoporosis group (OR=0.312, P=0.028 in postmenopausal women). Conclusion: The presence of ketonuria after a fast lasting at least 8 hr may have metabolic benefits on bone metabolism in postmenopausal women.

P-39. Adverse Effects of Induced Nocturnal Hot Flashes on Polysomnography- Measured Sleep, Perceived Sleep Quality, and Mood: A GeNAdron-Releaseing Hormone Agonist Model

Hadhine Joffe, MD, MS1; David White, MD2; Sybil Crawford, PhD; Nicole Economidou, BA3; Semmie Kim, BS3; Susan Regan, PhD3; Lee S. Cohen, MD4; Janet E. Hall5;1Psychiatry, Massachusetts General Hospital, Boston, MA; 2Medicine, Brigham and Women’s Hospital, Boston, MA; 3Medicine, University of Massachusetts Medical School, Worcester, MA; 4Medicine, Massachusetts General Hospital, Boston, MA

Objective: Sleep interruption and mood disturbance are reported commonly by women with hot flashes. The contribution of hot flashes to sleep and mood in healthy women is poorly understood but nocturnal symptoms are thought to play a predominant role. Although hot flashes are associated with perceived sleep disturbance in most studies, the effect of hot flashes on polysomnography (PSG) measured sleep is controversial, with inconsistent evidence about whether hot flashes interrupt sleep. Similarly, results of studies addressing the association between hot flashes and depression are mixed, with depression more likely to precede rather than follow the onset of hot flashes. We used a gonadotropin-releasing hormone agonist (GnRHa) that rapidly induces hypoestrogenism and a wide range of hot flash frequency in two-thirds of those treated to investigate the effect of new-onset hot flashes on sleep and depressive symptoms. The downstream effects of hot flashes were examined separately by the frequency of nighttime and then daytime hot flashes to isolate the effects of hot flashes on sleep and mood.

Design: The GnRHa leuprolide 3.75-mg/day depot was administered during the mid-luteal phase of one menstrual cycle to 29 healthy premenopausal volunteers without hot flashes, sleep disturbance, or psychiatric illness. Hot flashes, serum estradiol, ambulatory PSG’s, sleep diaries, sleep quality through Sleep Quality Index (SFI), and center for Epidemiological Study-åberg Depression Rating Scale (MADRS) were assessed before and during 5 weeks on GnRHa. For each sleep and mood endpoint, differences in symptom levels from pre-treatment to post-treatment were calculated, with PSG measures at each time point calculated using an average of the two PSG studies. Linear regression models were used to investigate whether hot flashes 1) increase PSG-measured awakenings and wake after sleep-onset (WASO), 2) reduce perceived sleep quality, and 3) increase depressive symptoms.

Results: Of 29 women receiving GnRHa, 20 (69%) developed persistent hot flashes, beginning 11.1 ± 5.5 days on GnRHa. Among these 20 women, the median number of nocturnal and daytime hot flashes reported per week was 3.8 (interquartile range [IQR] 2.1–7.5) and 3.3 (IQR 2.2–15.0), respectively. Serum estradiol was suppressed <20 pg/ml in all subjects. Increasing nocturnal hot flash frequency resulted in an increase from baseline to 5 weeks on GnRHa in PSG-measured awakenings (p=0.009) and WASO (p=0.008), an increase in sleep diary reported awakenings (p=0.005) and WASO (p=0.009), as well as an increase in PSQI (p(0.03) and MADRS scores (p=0.006). Among women developing frequent nighttime hot flashes (n=10), the mean increase in awakenings from baseline to follow-up was 5.1 per night on the PSG and 2.2 per night on the sleep diary, and the mean increase in WASO was 21.2 and 25.2 minutes per night on the PSG and sleep diary, respectively. Mean PSQI and MADRS scores in this highly symptomatic group increased from baseline by 1.7 and 5.2 points, respectively. Increasing daytime hot flash frequency was also associated with an increase in WASO (p=0.009) and subjective report (p=0.01) awakenings and not with depressive symptoms or other PSG- or subjectively measured sleep parameters. Conclusion: This GnRHa model of induced hot flashes demonstrates that nocturnal hot flashes increase PSG-measured sleep disruption and WASO, thereby indicating a specific effect of hot flashes on sleep and mood disruption. Nocturnal hot flashes also impaired perceived sleep quality and increased depressive symptoms. The absence of an effect of daytime hot flashes on PSG-measured sleep and mood suggests that nighttime hot flashes specifically play a causative role in the genesis of sleep and mood disturbance in midlife women.
baseline to Week 4 and Week 12. Because data were not normally distributed, medians were compared and P values were generated using a rank-transformed ANCOVA according to the statistical analysis plan. Safety assessments included treatment-emergent adverse drug reactions, laboratory data, vital signs, and clinical laboratory abnormalities. Results: Results: Overall, 614 subjects were randomized, and 549 subjects (271/306 [88.6%] LDM, 278/308 [90.3%] placebo) completed the study. The modified intent-to-treat population comprised 606 subjects (301 subjects [LDM]; 305 subjects [placebo]). Treatment-emergent adverse events were reported in 87.4%: an additional 7 subjects in VMS severity from baseline to Week 4 and until the end of treatment (P < 0.259 for all comparisons). Mean weekly reductions in VMS severity from baseline were significantly greater for LDM than placebo at Week 4 (−85.51 and −60.83 respectively; P = 0.0090). Mean weekly reductions in the frequency of moderate to severe hot flashes were significantly greater for LDM group than placebo at Week 4 (−0.05, respectively; P = 0.0048) but not at Week 12 (−0.10 and −0.09, respectively). (P = 0.2933). Mean percent reductions in VMS hot flash composite scores (moderate and severe) were significantly greater for LDM than placebo at Week 4 (−85.51 and −60.83 respectively; P = 0.0001) and at Week 12 (−111.9 and −96.85 respectively; P = 0.0036). Overall, 44.5 % (134/301) of subjects in the LDM group reported at least one TEAE compared with 42.3% (129/305) in the placebo group. The most frequently reported TEAEs in the LDM group (with at least twice the incidence in the placebo group) were dizziness and fatigue, each reported by 2.7% of subjects in the LDM group and 0.7% of subjects in the placebo group. No clinically meaningful changes were observed in laboratory values, vital signs, or electrocardiograms for either group. Conclusion: Conclusion: LDM was safe, well tolerated, and efficacious in reducing the frequency and severity of moderate to severe VMS associated with menopause at Week 4 and Week 12. Treatment with LDM could represent a nonHRT alternative for women with moderate to severe VMS associated with menopause who cannot or are unable to take HRT.

P-41. Effects of Menopausal Hormone Therapy on Bone Mineral Density and Coronary Artery Calcification in Early Menopause Ann E. Kearns, MD PhD1, Yuko Miyahara, MD2, M. Miller, PhD3. Division of Endocrinology, Mayo Clinic, Rochester, MN; 2Department of Surgery, Mayo Clinic, Rochester, MN; 3Tokyo Women's Hospital, Tokyo, Japan Objective: Cardiovascular disease and osteoporosis are common age-related diseases, and the incidence of both accelerates after the menopause. Estrogen deficiency is thought to be a common mechanism underlying this observation. The Women's Health Initiative demonstrated that menopausal hormone therapy (MHT) in older women did not prevent cardiovascular disease but did lower hip fracture risk. Subset analyses suggested that younger women may experience cardiovascular benefit. The Kronos Early Osteoporosis Prevention Study (KEEPS) is a randomized, double-blind placebo controlled trial to test the hypothesis that early MHT reduces progression of cardiovascular disease as measured by carotid intimal medial thickness and coronary artery calcifications (CAC). We examined changes in CAC and bone mineral density (BMD) in KEEPS participants enrolled at our center. Design: KEEPS participants were healthy menopausal women within 6 months to 3 years from the final menstrual period. They were randomized to oral conjugated equine estrogens (0.45 mg) + oral progesterone (200 mg daily for 12 days each month), 17α-estradiol (0.05 mg) + oral progestin (200 mg daily for 12 days each month), 17α-estradiol (0.05 mg) + oral progesterone (200 mg daily for 12 days each month), and placebo. All were followed for 4 years. CAC was assessed at baseline and year 4 by dual-energy X-ray absorptiometry (DXA) (GE Lunar, Madison, WI). Results: The total number of participants evaluated in this study was 82, 24 oral MHT, 27 transdermal MHT, and 27 placebo. No CAC was detected in 75 individuals (91.5%) at baseline, and 71 (86.6%) at year 4. There were no significant changes of CAC among the groups. Median lumbar spine BMD at baseline was 1.15 (1.05, 1.28) g/cm2. The changes in BMD were significantly different among the groups at year 4: transdermal MHT 0.08 g/cm2, oral MHT 0.02 g/cm2, placebo -0.06 g/cm2 (p=0.05, ANOVA, student's t test). There was no correlation between changes in BMD and changes in CAC among the groups. Conclusion: In this subset of KEEPS participants, a healthy group of early menopausal women, MHT improved BMD and did not affect CAC, which did not change significantly over 4 years in any of the groups.

P-42. Influence of Patient Perceptions and Preferences About Osteoporosis Medication on Adherence in the Denosumab Adherence, Preference, and Satisfaction (DAPS) Study David Kendler1, Michael J. Lilliet, MD2, Alfred H. Moffett, MD3, Sacha Satran-Huang, PhD4, Joice Huang, PharmD5, En-Tzu Tang, PhD6, Primal Kaur, MD5. 1University of British Columbia, Vancouver, BC, Canada; 2Internal Medicine Associates, Fargo, ND; 3Obstetrics and Gynecology, Kansas State University, Manhattan, KS; 4Biostatistics, University of Alabama at Birmingham, Birmingham, AL; 5Biostatistics, University of Alabama at Birmingham, Birmingham, AL. Objective: In women, osteoporosis is a common chronic disease that induces spinal compression and femoral neck fractures, resulting in life-threatening complications. It is very important to identify risk factors in order to prevent this disorder. Bone destruction is a well-recognized complication in a variety of neoplasms without bone metastasis. Invasive cervical cancer is one of the most common gynecological cancers that occurs in patients with cervical cancer without bone metastases. Design: We measured spinal bone mineral densities by dual-photon absorptiometry is 119 patients with invasive uterine cervical cancer and compared them with measurements from 155 control women. Methods: During 2-year bone mineral density (BMD) follow-up, the bone mineral density (BMD) follow-up, patients with uterine cervical cancer was 13.9% lower (p=0.0003) and age-matched percentiles were 9.2% lower (p=0.003) than in control women. The deficits in bone mineral density and age-matched percentiles were confined to the uterine cervical cancer patients in their fifties, ie, less than 5 years’ menopause duration. Conclusion: Our study results suggest that patients with invasive cervical cancer have a lower BMD, resulting in an increased risk of osteoporosis.

P-43. Decreased Bone Mineral Density in Patients With Invasive Cervical Cancer Heung-Yeol Kim, MD, Ph.D. Dept of OB & GYN, Kosin University, Busan, Republic of Korea. Objective: In women, osteoporosis is a common chronic disease that induces spinal compression and femoral neck fractures, resulting in life-threatening complications. It is very important to identify risk factors in order to prevent this disorder. Bone destruction is a well-recognized complication in a variety of neoplasms without bone metastasis. Invasive cervical cancer is one of the most common gynecological cancers that occurs in patients with cervical cancer without bone metastases. Design: We measured spinal bone mineral densities by dual-photon absorptiometry is 119 patients with invasive uterine cervical cancer and compared them with measurements from 155 control women. Methods: During 2-year bone mineral density (BMD) follow-up, the bone mineral density (BMD) follow-up, patients with uterine cervical cancer was 13.9% lower (p=0.0003) and age-matched percentiles were 9.2% lower (p=0.003) than in control women. The deficits in bone mineral density and age-matched percentiles were confined to the uterine cervical cancer patients in their fifties, ie, less than 5 years’ menopause duration. Conclusion: Our study results suggest that patients with invasive cervical cancer have a lower BMD, resulting in an increased risk of osteoporosis.

P-44. The effect of ovariectomy, 17-beta estradiol, and progesterone on the changes of histology and estrogen receptor of bladder in female bladder outlet obstruction rat model Tak Kim, M.D.,Ph.D.,1, 2Bong Kim1, Ki Hoon Ahn1, Byung Koo Yoon3. 1Obstetrics and Gynecology, Korea University Anam Hospital, Seoul, Korea, Seoul, Republic of Korea; 2Obstetrics and Gynecology, Samsung Medical Hospital, Seoul, Korea, Seoul, Republic of Korea. Objective: The aim of this study was to investigate the effect of bilateral ovariectomy, 17-beta estradiol, and progesterone on the change of histology and estrogen expression of bladder in female bladder outlet obstruction rat model Design: A total of 60 female Sprague-Dawley rats were separated into 6 groups of 10 each. Group 1 served as controls. Group 2-F were Bladder outlet obstruction (BOO). Group C-F were ovariectomized (OVX). Group C-F were given 17-beta estradiol (0.1 mg/kg/day). Group P-F were given 17-beta estradiol (0.1 mg/kg/day) and progesterone (0.3 mg/kg/day). Group D-F were given 17-beta estradiol (0.1 mg/kg/day), progesterone (0.3 mg/kg/day), and dehydroepiandrosterone (DHEA) (30ug/kg/day) by Alzet pump. After 4 weeks later, Serum E2 and progesterone levels were evaluated. Each rats was anesthetized and the urinary bladder was removed for bladder weight and histological study. Results: BOO resulted in significant increased bladder weight and thickness of detrusor muscle, whereas 17-beta estradiol or progesterone alone did not show a difference in the treatment group. The estrogen receptor-β (ER-β) density were not significantly different in the control group.
and study groups. BOO increased bladder weight with increased detrusor muscle thickness. OXV had an additive effect to BOO on increased blood vessel density and caliber in the bladder. E2 increased blood vessel density and in contrast P4 supplementation decreased blood vessel density. DHEA did not show a significant effect on blood vessel density. Conclusions: Therapy did not change the expression of estrogen receptors in the bladder outlet obstruction. Estradiol has positive effect but progesterone has negative effect on bladder detrusor. DHEA has no effect on bladder detrusor.

P-45. Treatment of Major Depressive Disorder With Desvenlafaxine 50 mg/d in Perimenopausal and Postmenopausal Women

Suzanne Kornstein, MD 1, Sheryl Kingsberg, PhD 2, Susan Wysocki, NP 3. 1Southern California Perinatal Network, Los Angeles, CA; 2University of Rochester, Rochester, NY; 3Pfizer Inc, Collegeville, PA

Objective: Research has shown that women may be more likely to experience depression during menopausal transition, and menopausal status may influence antidepressant treatment response. Desvenlafaxine (administered as desvenlafaxine succinate) is a serotonin-norepinephrine reuptake inhibitor established with efficacy for major depressive disorder (MDD) in perimenopausal and postmenopausal women at doses of 100 to 200 mg/d. The objective of this randomized, double-blind, placebo-controlled study was to evaluate short-term efficacy and safety of desvenlafaxine 50 mg/d in perimenopausal and postmenopausal women. We report the results of a priori secondary analyses and post hoc analyses evaluating efficacy according to baseline menopausal status and years since last menstrual period.

Design: Perimenopausal and postmenopausal women (40 to 70 years with menstrual cycles intact or had a diagnosis within the past 12 months) were randomized to receive desvenlafaxine 50 mg/d in a 10-week, multicenter, double-blind, placebo-controlled trial. Baseline menopausal status was defined via menstrual history, surgical history, and/or follicle stimulating hormone level. To assess the effect of menopausal status on treatment, the primary endpoint was the first exam score from study day one for efficacy assessments in perimenopausal and postmenopausal groups, using an analysis of covariance with treatment, region, and baseline in the model for the primary efficacy end point (17-item Hamilton Depression Rating Scale [HAM-D17 total score at week 8] and other continuous efficacy variables). Clinical Global Impressions-Improvement was analyzed with a Cochran-Mantel-Haenszel test. Proportion of women achieving response/remission was analyzed using logistic regression with treatment, region, and baseline in the model. Subsequently, treatment by menopausal status interaction was examined in the total population, adding either treatment by menopausal status or treatment by years since last menstrual period to the above models.

Results: A total of 426 patients (desvenlafaxine, n=216; placebo, n=210) were included in this secondary analysis (all randomized patients who took ≥1 dose of study drug, had ≥1 postbaseline HAM-D17 evaluation, and had sufficient data to determine baseline menopausal status): 135 (32%) women were perimenopausal and 291 (68%) were postmenopausal at study baseline. Significant reductions in HAM-D17 total scores for desvenlafaxine 50 mg/d compared with placebo were observed in both perimenopausal and postmenopausal women at week 8. No significant treatment by menopausal status interaction was observed for overall efficacy in improvement of depressive symptoms. In the perimenopausal subgroup, however, desvenlafaxine-treated patients achieved significantly greater functional improvement from baseline compared with placebo based on week 8 Sheehan Disability Scale (SDS) scores (-9.3 vs -5.1; P<0.001). The drug-placebo difference (8.3 vs -8.1) on this measure was not significant in women with MDD, but treatment by menopausal status interaction was significant at week 8 for the perimenopausal group only (P<0.05).

Conclusion: This study suggests that women with MDD are more likely to achieve remission with desvenlafaxine 50 mg/d. In addition, significant functional improvement from baseline was observed in perimenopausal women, with a greater treatment effect being observed in this population compared with postmenopausal women. These findings are consistent with the hypothesis that menopause may play a role in the treatment of depression in perimenopausal and postmenopausal women. Placebo responders were more likely to achieve remission with desvenlafaxine treatment in this population. These findings suggest that desvenlafaxine may be a viable treatment option for women with depression who are perimenopausal or postmenopausal.

P-47. The Influence on Cardiovascular Mortality of the Metabolic Syndrome in Korean Postmenopausal Women

Sehyoon Kwak, Youn-Jee Chung, Jangheub Kim, Mee-Ran Kim. The catholic university of Korea,Seoul,S.smany's hospital, Seoul, Republic of Korea

Objective: Metabolic syndrome components, insulin resistance and central obesity cause type 2 diabetes and hypertension. This will increase the risk of cardiovascular disease. In women after menopause are at increased risk of metabolic syndrome. Several researchers studied that in menopause, metabolic syndrome increased cardiac mortality. We studied that in menopause, metabolic syndrome increased cardiac mortality. We studied that in menopause, metabolic syndrome increased cardiac mortality. We studied that in menopause, metabolic syndrome increased cardiac mortality.

Design: Twenty thousand and forty postmenopausal women aged 40 years or older were enrolled at health promotion centers of the government hospital located in 18 regions during 1994–2004. Age, weight, height, body mass index(BMI), systolic blood pressure(SBP), diastolic blood pressure(DBP), fasting blood glucose(FBG), cholesterol, triglyceride(TG), high-density lipoprotein were evaluated and history taking about alcohol consumption, smoking and exercise was performed. In addition, subjects who died of cardiac disease were analyzed from January 1995 to December 2009.

Results: Metabolic syndrome was higher in postmenopausal women with increased in age, BMI, blood pressure(BP), FGB, cholesterol, TG. Thirty cardiac deaths occurred during the observation period. Factors affecting cardiac death were age, smoking, FBG and when age and smoking were controlled. FBG was an important factor affecting cardiovascular mortality in our study. When controlling age, smoking, and alcohol consumption, metabolic syndrome caused an increased relative risk of cardiovascular mortality. Survival rate was much lower in postmenopausal women with metabolic syndrome than those without metabolic syndrome.

Conclusion: Metabolic syndrome in Korean postmenopausal women increase cardiovascular mortality.
and hormones, topical corticosteroids, vaginal dilators, and intercourse. Surgery was reserved for severe cases. In our centre, seven patients have been followed. Common complaints at presentation included vaginal dryness (n=4, 57.1%), dyspareunia (n=5, 71.4%), and difficulty inserting a tampon (n=6, 85.7%). Common examination findings were narrowed vault (n=4, 57.1%), vaginal adhesions (n=4, 57.1%), and vaginal stenosis (n=4, 57.1%). One patient had complete vaginal obstruction and was referred for surgery. One patient has been treated successfully with hormone replacement therapy, dilators, and topical estrogens, and has regular intercourse. Conclusion: Female genital GVHD remains under-recognized and poorly understood. Education of patients and clinicians is crucial. An effective therapy needs to be elucidated in virginal patents. We are currently establishing a dedicated clinic for these patients to be seen 3-3 months after transplant in hopes of preventing the sequela of this disease, with an estimated 50 patients referred annually.

### Literature Review

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### Patient Demographics

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### Agglutination of clitoral hood, vulvovaginal erythema and scarring

#### P-49

**Subclinical cardiovascular disease in non-smoker, non-diabetic, postmenopausal women with low to medium Framingham Risk Score**

Maria A. Maturana, PhD1, Roberta F. Franz1, Marcela Metzdorf1, Thais Rasia da Silva1, Poli M. Spritzer 1,2. 1Gynecological Endocrinology Unit, Division of Endocrinology, Hospital de Clínicas de Porto Alegre/Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil; 2Department of Molecular Diagnostics, Institute of Oncology Ljubljana, Ljubljana, Slovenia; 3Hospital for Gynecology and Obstetrics Kranj, Kranj, Slovenia

**Objective:** The present study aimed to evaluate the presence of subclinical cardiovascular disease (CVD) in postmenopausal women with no evidence of clinical disease and its association with anthropometric and metabolic parameters. Design: Ninety-two postmenopausal women with low to medium Framingham Risk Score (FRS) were included in this cross-sectional study. None were smoker, diabetic or user of hormone therapy during the 3 months preceding the study. Clinical and laboratory evaluation was obtained. Coronary artery calcification (CAC) was assessed by electron-beam computed tomography. IMT as well as the presence of atheromatous plaques were assessed using B-mode ultrasound imaging. IMT was measured at three paired segments, in the right and left common, bulb and internal carotid. Then we also used maximum IMT (IMTmax), and the mean of the mean values of the 3 measured segments in each side, right and left (RC and LC). We defined presence of subclinical CVD: presence of plaque and/or IMT ≥0.9 mm. Results: The mean age was 55 (±5) yr and the median age at menopause was 49 yr (IQR: 46-51). Waist circumference was 87 cm (s11), BMI 27 (±4.5), cholesteral 216 mg/dl (±46) and HDL- C 54 mg/dl (±12). Hypertension was present in 30 %, impaired glucose tolerance in 15% and 63% was dyslipidemic. Thirty-four % (n=32) of patients had subclinical atherosclerosis at carotid ultrasound evaluation, from these 24.5 % (n=23) had the presence of plaque. From the 19 patients classified as medium FRS, 47% had IMT ≥0.9 mm and 42% had plaque. Age (p=0.021) and CAC score (p=0.035) were higher in patients with subclinical atherosclerosis. Positive correlations were found between age and RC (r=0.348 p=0.001) and LC (r=0.311 p=0.002). Also, CAC score was correlated with RC (r=0.369 p=0.021) and LC (r=0.362 p=0.0024). When only women with subclinical atherosclerosis were considered, internal carotid IMT was negatively correlated with HDL-C (r= -0.445 p=0.011). In patients with no subclinical disease only HDL-C showed negative correlation with common carotid IMT (r= -0.357 p=0.005). Conclusion: Subclinical atherosclerosis was prevalent in this sample of postmenopausal women with low to medium FRS and age were highly associated with altered IMT.

#### P-50

**Telomere length, anti-Müllerian hormone and follicle stimulating hormone in women with premature ovarian failure compared to healthy women**

Renata Kosić Pogačnik1,2, Helena Meden-Vrtovec, PhD1, Srdjan Novakovic1, Petra Costaković1. 1Department of Obstetrics and Gynecology, University Medical Centre Ljubljana, Ljubljana, Slovenia; 2Department of Molecular Diagnostics, Institute of Oncology Ljubljana, Ljubljana, Slovenia; 3Hospital for Gynecology and Obstetrics Kranj, Kranj, Slovenia

**Objective:** Telomeres are regions of repetitive nucleotide sequences at the end of chromosomes, which protect the end of chromosomes from deterioration which occurs during chromosome replication. Over time, due to each cell division, the telomere ends become shorter. Determination of telomere length could be a diagnoic tool distinguishing premature ovarian failure as an isolated biological process caused by reduced ovarian reserve from the possibility of generalized premature aging of the whole body. Design: Our study was designed as a cross-sectional survey with a study group of 30 patients with premature ovarian failure, matched by age with the control group of 30 healthy women. In both groups we performed targeted personal, family and reproductive history, gynecological examination and vaginal ultrasound examination. Telomere length was determined in peripheral blood lymphocytes using the telomere-specific quantitative polymerase chain reaction and then the telomere to singe copy gene (T/S) ratio was calculated. From the T/S ratio we calculated the length of the telomere in kilobase with a specific formula. Measurements of anti-Müllerian hormone (ELISA technique), follicle stimulating hormone (FSH), luteningize hormone (LH), estradiol, thyrotropic hormone (TSH) and prolactin in peripheral blood and karyotyping with screening for fragile X chromosomes, which protect the end of chromosomes from deterioration which occurs during chromosome replication. Over time, due to each cell division, the telomere ends become shorter. Determination of telomere length could be a diagnostic tool distinguishing premature ovarian failure as an isolated biological process caused by reduced ovarian reserve from the possibility of generalized premature aging of the whole body. Results: The mean patient age was 31.08 ± 6.69 years in the study group and 29.4 ± 4.1 years in the control group, they all had a normal 46, XX karyotype. The mean lymphocyte telomere length in the study group was significantly longer being 6.9 ± 0.74 kb (P < 0.001), lymphocyte telomere length in the control group was 5.98 ± 0.26 kb. The mean FSH level in the study group was 100.82 ± 42.92 IU/L and it was significantly higher than in the control group being 7.03 ± 3.24 IU/L (P < 0.001). The mean LH level in the study group was 40.18 ± 16.93 IU/L and was significantly higher than in the control group being 6.49 ± 3.77 IU/L (P < 0.001). Levels of anti-Müllerian hormone in the study group were undetectable, the mean level being significantly lower than in the control group (3.89 ± 2.61 mg/L, P < 0.001). Conclusion: Although according to physiology of cell senescence shorter telomere length should be expected in women with premature ovarian failure, longer telomeres exhibit the possibility of isolated non physiologic, intrinsic intraovarian process, confirmed also by anti-Müllerian hormone and FSH levels. Further studies should be performed in order to identify pathology within the ovaries in women with premature ovarian failure.

#### P-51

**Subjective sleep disturbance and correlates in Colombian women around the menopause (*)**

Alvaro Monterroza-Castro1, Marta Marrugo-Florez1, Ivette Romero-Pérez1, Ana M Fernández-Alonso2, Peter Chedraui2, Faustino R Pérez-López2. 1Ginecologia, Universidad de Cartagena, Cartagena, Colombia; 2Servicio de Obstetricia y Ginecología, Hospital Torrecardenas, Almeria, Spain; 3Universidad Católica de Guayaquil, Guayaquil, Ecuador; 4Universidad de Zaragoza, Zaragoza, Spain

**Objective:** To examine the relationship between self-reported sleep quality and menopausal symptoms, and quality of life (QoL) in mid-aged Colombian women. Design: This cross-sectional study included 1,078 women aged 40 to 59 who were requested to fill out the Pittsburgh Sleep Quality Index (PSQI), the Menopausal Rating Scale (MRS) and a general questionnaire exploring socio-demographic characteristics. Results: Median age of the sample was 49.0 (100) years. A 45.4% were postmenopausal, 57.2% had increased body mass index (BMI) values, 86.1% were mestizo, 20.7% had hypertension, 74.1% had a stable partner, and 3.8% used hormone therapy. The prevalence of insomnia was 57.1% (PSQI score ≥5). Significant correlations were found between PSQI and MRS total and sub-scales scores. Multivariate analysis found that higher PSQI scores (lower quality of sleep) correlated with MRS psychological and somatic scores (lower QoL in these sub-scales), smoking habit and hypertension. Mild correlations were also detected between PSQI score and parity and BMI. Conclusion: Low quality of sleep was highly prevalent in this mid-aged Colombian women.
P-52. Quality of life and sexual dysfunction in climacteric women living in a Colombian Caribbean region (*)
Alvaro Monterrosa-Castro, Jhonner Marquez-Vega, Cindy Arteta-Acosta. Ginecologia, Universidad de Cartagena, Cartagena, Colombia

Objective: BACKGROUND: Prevalence of hot flashes and poor quality of life are high in postmenopausal women. Studies elsewhere have noted a correlation of these conditions with further deterioration in quality of life. OBJECTIVE: To establish whether overweight and obese Colombian climacteric women have worse quality of life and sexual function compared to normal weight women.

Methods: We conducted a cross-sectional study of 445 women, healthy Zenu indigenous descendants, in a certain way, between 40 and 59 years old, natives and residents in the Colombian Caribbean. Results: 208 women studied. 100 (48%) premenopausal and 108 (52%) postmenopausal women, average age of last period: 44.8±4.5, the entire population was MRS total score: 15.9±6.9, much higher than in other Colombian and Latin American populations. The most prevalent symptoms were: sleep disturbance (91.3%), physical-fatigue (91.3%), and muscle-joint discomfort (89.9%). Urogenital domain deterioration was high. 50% of women had severely impaired quality of life. The demonstrations, highly prevalent in premenopausal women, increase with the transition to menopause. 77% of the population suffers from sexual dysfunction, increased prevalence in postmenopausal women. The most impaired domain: pain coital penetration.

Conclusion: There is consistency between sexual dysfunction and deterioration urogenital observed in women breast cancer survivors. It is a part of the CAVIMEC (Calidad de Vida en la Menopausia y Etnias Colombianas) Research Program.

P-53. Overweight and obese Colombian climacteric women have high prevalence of hot flashes and poor quality of life (*)
Alvaro Monterrosa-Castro, Ivette Romero-Pérez, Angel Paternina-Caicedo. Ginecologia, Universidad de Cartagena, Cartagena, Colombia

Objective: BACKGROUND: Prevalence of overweight and obesity are rising and they are common in menopausal women. Studies elsewhere have noted a correlation of these conditions with further deterioration in quality of life. OBJECTIVE: To establish whether overweight and obese Colombian climacteric women have worse quality of life and sexual function compared to normal weight women.

Methods: We conducted a cross-sectional study of 445 women, healthy Zenu indigenous descendants, in a certain way, between 40 and 59 years old, natives and residents in the Colombian Caribbean. Results: 208 women studied. 100 (48%) premenopausal and 108 (52%) postmenopausal women, average age of last period: 44.8±4.5, the entire population was MRS total score: 15.9±6.9, much higher than in other Colombian and Latin American populations. The most prevalent symptoms were: sleep disturbance (91.3%), physical-fatigue (91.3%), and muscle-joint discomfort (89.9%). Urogenital domain deterioration was high. 50% of women had severely impaired quality of life. The demonstrations, highly prevalent in premenopausal women, increase with the transition to menopause. 77% of the population suffers from sexual dysfunction, increased prevalence in postmenopausal women. The most impaired domain: pain coital penetration.

Conclusion: There is consistency between sexual dysfunction and deterioration urogenital observed in women breast cancer survivors. It is a part of the CAVIMEC (Calidad de Vida en la Menopausia y Etnias Colombianas) Research Program.

P-54. Evaluation of risk factors for the metabolic syndrome in postmenopausal women breast cancer survivors
Daniel Buttros, MD, Eliana A. Nahas, MD, Helsa 1. Vespoli, MD, Gilberto Uemura, MD, Bruno R. Almeida, student, Jorge Nahas-Neto, MD. Gynecology and Obstetrics, Botucatu Medical School-Sao Paulo State University, Botucatu, Brazil

Objective: Women breast cancer survivors are at risk for cardiovascular disease due to the high rate of cancer-uncorrelated comorbidities, such as obesity, hypertension and diabetes.

The purpose of study was to assess risk for the metabolic syndrome (MetS) in postmenopausal women breast cancer survivors as compared to postmenopausal women without breast cancer. Design: In a cross-sectional study of 104 postmenopausal breast cancer survivors were compared with 208 postmenopausal women (control) attended to at a University Hospital. Eligibility criteria included women with amenorrhea ≥12 months and age ≥45 years without breast cancer and matched by age, in a proportion of 1:2, as sample calculation. Clinical and anthropometric data were collected by means of interviews. Biochemical data, including total cholesterol, HDL, LDL, triglycerides, glucose and C-reactive protein (CRP), were measured. Women showing three or more diagnostic criteria were diagnosed with MetS: waist circumference (WC) ≥88cm, blood pressure ≥130/85mmHg, triglycerides ≥150mg/dL, HDL <50mg/dL and fasting glucose ≥100mg/dL. For statistical analysis, Student’s t-test, the chi-square test and logistic regression were conducted at the University Hospital, Passo Fundo, Brazil. "Financial support by FAPESP; process number 2009/14884-2."
levels were determined in all women and the sample was stratified according to free androgen index (FAI) > or ≤ percentile 75 (75%). Clinical characteristics and ovarian volume were compared between the baseline and the second follow-up. Results: Mean age of the participants was 52.6 ± 6.0 years at baseline and 52.0 ± 6.0 years at the second follow-up. In baseline, 59% of participants were pre- and 41% were in the menopausal transition and in the second follow-up, 29% maintained the pre-menopause status, 37% were in the menopause transition and 41% were in the menopause. Participants in the second follow-up presented higher glucose (p=0.035), total- (p=0.046) and LDL-cholesterol levels (p=0.024), diastolic blood pressure (p=0.074), BMI (p=0.062), waist circumference (p=0.020) and lower SHBG levels (p=0.001). In addition, women in the superior quartile of calcium intake showed higher testosterone levels and lower estradiol levels (p=0.042). Conclusion: The pre-, menopause transition and post-menopause women who had higher androgenic androgen levels presented worst metabolic profile and higher ovarian volume. Further follow-ups are needed to confirm the clinical relevance of these data.

P-57. The effect of equol, a phytoestrogen, on endothelium-independent vascular reactivity of human uterine artery
Hyoung Moo Park, Ph.D., Hoon Choi1, Obstetrics & Gynecology, Chung-Ang University, Seoul, Republic of Korea; Obstetrics & Gynecology, Inje University Sanggye Paik Hospital, Seoul, Republic of Korea

Objective: Equol, one class of the phytoestrogen as a metabolite of daidzein is natural nonsteroidal polyphenols of plant origin. Equol has highest binding affinity to estrogen receptor and antioxidant properties among all isoflavones. Therefore equal may have a promising role as an alternative remedy to HRT for the management of postmenopausal estrogen deficient symptoms & conditions. The purpose of present study is to investigate, 1) whether equal has the direct modulation on vascular tone of endothelium-dependent and 2) if present, which level of equol affects vascular tone. Results: Phenylephrine, receptor-dependent Ca channel agonist & high concentrated potassium chloride solution, voltage-dependent Ca channel agonist were used. The uterine smooth muscles were pretreated with phenylephrine, 10^-6 & high concentrated potassium chloride solution 70mM. After pretreatment by equal 10^-6 for 30 min, phenylephrine induced contraction from 10^-3 to 10^-4M concentration was compared with the results without equal pretreatment. To investigate the effect of equal on potassium channel in vascular smooth muscle, 2 kinds of K channel antagonist, tetrodotoxinn & 4-aminopyridine were used. After pretreatment by these 2 drugs for 30 minutes, the relaxatory concentrations of equal were determined on phenylephrine-induced contractions and compared with the results without pretreatment. Results: Equal 10^-4M to 10^-2M in concentration showed relaxation effect on vascular smooth muscle contraction which was induced by phenylephrine receptor-dependent Ca channel, but not for voltage-dependent Ca channel in vascular smooth muscle. Vascular relaxatory effect of equal may be induced by non-K channel calcium channel on this relaxation action. As far as we know, this is the first report of phytoestrogen on vascular reactivity of human vessels.

P-58. The effect of a soy-based dietary supplement on the vaginal epithelium and endometrium in postmenopause: a randomized double blind, controlled clinical trial
Adriana O. Chaves-Paixao, MD, Carmen Giagnoni, MA, Azara M. Pinto-Neto, MD, PhD, Lucia S. Costa-Paiva, MD, PhD. Obstetrics and Gynecology, UNICAMP, Campinas, Brazil

Objective: To compare the effects of a soy-based dietary supplement, low-dose hormone therapy (HT) and placebo on the vaginal epithelium and endometrium in postmenopausal women with comprehensive armamentarium. Design: Sixty participants were recruited from two postmenopause outpatient clinics at the Center for Women’s Integrated Healthcare of the State 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 1 mg of estradiol and 0.5 mg 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. It was evaluated symptoms of estrogen deficiency, vaginal cytology and endometrial histology according to menopause rating scale. Vaginal cytological maturation value and vaginal pH were evaluated to determine hormonal action on the vaginal cells. Genital bleeding pattern was assessed. Transvaginal sonography was performed to evaluate endometrial thickness. Patients with endometrium thickness ≥ 5mm underwent to diagnosis of endometrial hyperplasia. For statistical analysis, the chi-square test, Fisher’s exact test and Kruskal-Wallis test were used. Results: The mean age of the patients was 52.4 years (SD 3.9). There was a significant improvement in vaginal dryness in the soy group and in the HT group (p=0.04). Urinary symptoms did not change with treatment in the three groups. After 6 weeks of treatment there was a significantly increased in maturation value only in the HT group. There was a significantly decrease in vaginal pH only in the HT group. There were no statistically significant differences in endometrial thickness between the three groups. None of the groups evidenced significant genital bleeding. Conclusion: This study showed that soy-based dietary supplement used during 16 weeks did not exert estrogenic action on the vaginal epithelium assessed by maturation value and vaginal pH. HT proved to improving vaginal trophism. However, it did not increase the incidence of genital bleeding or cause a significant change in endometrial thickness. Financial Support: FAPESP 03/44644-0.

P-59. Multimorbidity and associated factors in women aged 50 year old or more : a population-based study
Vanessa Machado, Ana Valadares, MD, PhD, Lucia S. Costa-Paiva, MD, PhD, Maria Delio M. Conde, MD, PhD1, Érika P de Sousa, MD1, Lucia S. Costa-Paiva, MD, PhD, Edson Z. Martinez, PhD,1 Azara M. Pinto-Neto, MD, PhD1, Breast Service, Hospital of Women and Child Healthcare, Goiania, Brazil; 2Gynecology and Obstetrics, Universidade Estadual de Campinas, Campinas, Brazil; 3Social Medicine, Universidade de São Paulo, Ribeirão Preto, Brazil

Objective: To investigate the prevalence of dyslipidemia, the risk of cardiovascular disease (CVD) risk factors and the agreement between CVD risk models in breast cancer survivors. Design: A cross-sectional study was conducted, including 67 breast cancer survivors, ranging in age from 45-65 years, who underwent complete oncologic treatment and were not users of hormone replacement therapy or tamoxifen in the last six months. Lipid profile was evaluated. The risk of CVD was estimated according to the Framingham and Systematic Coronary Risk Evaluation (SCORE) models. The risk of CVD was classified as low (<10%), moderate (10-20%) and high (>20%), according to the SCORE model. A descriptive analysis with absolute and relative frequencies was carried out. To investigate the agreement between both risk models, the kappa coefficient was calculated. Results: The mean age of the participants was 53.2±6.0 years and body mass index (BMI) was 27.8±5.7 kg/m2. Ninety percent of participants had at least one type of dyslipidemia. The median total cholesterol levels (≥200mg/dl) in 40% of the participants, respectively (Table 1). The risk of CVD, according to the Framingham model, was classified as low (45%), moderate (33%) and high (22%); and low (9%) and moderate (4%) according to the SCORE equation. The agreement between Framingham and SCORE models showed a kappa coefficient of 0.073 (95% CI -0.008 to 0.155). Conclusion: Dyslipidemia was common in this cohort. The majority of participants had low to moderate cardiovascular risk. The between both risk models were low. These data indicate that CVD in middle-aged breast cancer survivors is necessary and close attention should be focused on adequate control of serum lipid levels.
P-61. Bone Mineral Density in Postmenopausal Women with and without Breast Cancer
Delio M. Conde, MD, PhD1; Aarao M. Pinto-Neto, MD, PhD2; Lucia S. Costa-Paiva, MD, PhD3; Edson Z. Martinez, PhD1; Breast Service, Hospital for Maternal and Child Healthcare, Goiania, Brazil; 2Gynecology and Obstetrics, Universidade Estadual de Campinas, Campinas, Brazil; 3Social Medicine, Universidade de São Paulo, Ribeirão Preto, Brazil
Objectives: We compared bone mineral density (BMD) values in postmenopausal women with and without breast cancer. Design: A cross-sectional study was conducted including 51 breast cancer survivors (BCS) and 71 women without breast cancer, non-users of hormone therapy, tamoxifen or aromatase inhibitors. BMD T-scores and measurements in grams per centimeter squared (g/cm²) were obtained at the femoral neck, trochanter, Ward’s triangle, and lumbar spine. Osteopenia and osteoporosis were grouped and categorized as abnormal BMD. Unconditional logistic regression analysis was used to estimate the odds ratios (OR) of abnormal BMD values as measures of association, with 95% confidence intervals (CIs), adjusting for age, years since menopause, parity and body mass index (BMI). Results: The mean age of the women with and without breast cancer was 54.7±5.8 years and 58.2±4.8 years (p<0.01, respectively). After adjusting for age, parity and BMI, abnormal BMD at the femoral neck (OR adjusted: 4.8; 95% CI 1.5-15.4), trochanter (OR adjusted: 4.6; 95% CI 1.4-15.5) and Ward’s triangle (OR adjusted: 4.5; 95% CI 1.5-12.9) was significantly more frequent in postmenopausal BCS than in women without breast cancer. Postmenopausal BCS had a significantly lower mean BMD at the trochanter (0.719 vs 0.809 g/cm², p<0.01) and Ward’s triangle (0.751 vs 0.805 g/cm², p<0.05). Conclusion: The prevalence of abnormal BMD was higher in postmenopausal women with breast cancer. Bone health requires special vigilance and the adoption of interventions should be instituted early to minimize bone loss in survivors of breast cancer.

P-62. Comparative Long-Term Safety and Efficacy in Pre- and Post-Menopausal Women with Hypoactive Sexual Desire Disorder (HSDD) Receiving Flibanserin Treatment
James P. Symons, Ph.D.1; James A. Simon, MD2; David Portman, MD2; Clinical Research, Sprout Pharmaceuticals, Inc., Raleigh, NC; 2Women’s Health and Research, Columbus, OH
Objectives: Primary objective was to generate additional long-term safety and efficacy data in pre- and naturally post-menopausal women with HSDD during 28 weeks of treatment. Primary safety endpoint was frequency of adverse events. Efficacy endpoints included total FSFI (Female Sexual Function Index) and FSDS-R. Design: Study was a prospective, multi-center, 28-week, open-label extension study in premenopausal and naturally postmenopausal women with HSDD. Premenopausal and postmenopausal patients were enrolled after completing treatment in 24-week, double-blind, placebo controlled trials (parent trials). The parent trials were separate double-blind, placebo controlled trials for pre- and post-menopausal women with HSDD. Patients were to enroll in this study within 7 days of the final visit of their parent trial. After completing the 24-week parent trials and a Screen period of up to 2 weeks for this trial, eligible patients were enrolled into the 28-week treatment portion during which they all received 100 mg flibanserin qhs. Results: A total of 708 patients were screened and 595 were enrolled and treated. The study was discontinued early by original sponsor because they elected to partner the compound. However, sufficient data are available to draw conclusions regarding longer term safety and efficacy. While no patient completed 28-weeks of treatment, 73 (12.3%) were treated for up to 167 days excluding the duration of treatment in the parent trial. The most frequent AEAs (occurring in ≥5% of patients) were dizziness, somnolence, insomnia and nausea all reported with comparable frequencies in pre- and post-menopausal patients. These were expected events and were reported in previous flibanserin trials as well as with other 5-HT1A agonists and 5-HT2A antagonists. No deaths were reported. Four patients reported 5 serious adverse events during treatment and none of the events were considered related to flibanserin treatment. The SAEs reported were cellulitis, animal bite, basal cell carcinoma, irritable bowel syndrome and cholelithiasis. A total of 22 (3.7%) of patients reported severe AE while most AEs were of mild (32.8%) or of moderate (22.7%) severity. The most frequently reported severe AEs were dizziness (3 patients), headache (2 patients), and insomnia (2 patients). While the primary purpose of this study was safety, efficacy, and measures were an obtained identical to those in the parent studies. The major differences between the parent studies and this study with regard to baseline outcome measures was the prior 24-week exposure to flibanserin. While some of the patients enrolled in this longer term study would have only been exposed to placebo in the parent study, many would have received flibanserin treatment. Partly this study is reflected in the different baseline scores for the efficacy measures between the parent studies and the long-term extension study and is summarized Table 1. All of the baseline scores for this long-term study reflect improvement from the baseline scores in the parent studies and there was continued improvement with continued treatment in this study. Conclusions: Safety results from this long-term extension study indicated no safety concerns for longer term exposure to flibanserin. Flibanserin treatment was well tolerated in this population of pre- and post-menopausal women with HSDD. Flibanserin treatment continued to be efficacious with continued exposure in both pre- and post-menopausal women.

P-63. Dietary pattern and physical activity in postmenopausal women: associations with body composition, metabolic and hormonal variables and cardiovascular risk factors
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Objectives: The aim of this study was to characterize dietary composition and to assess whether habitual physical activity is associated with dietary variables, hormonal and metabolic profile and cardiovascular risk markers in postmenopausal women. Design: A hundred and five postmenopausal women were included, smokers, diabetics and users of hormone therapy were excluded. Anthropometric and clinical variables were measured and a validated food frequency questionnaire was applied. Participants were stratified into active and inactive according to the mean step/day obtained by pedometer (≥6000 and <6000, respectively). Results: The mean age was 55.2 ± 4.9 years, the mean years since menopause was 6.8 ± 1.0, the body mass index (BMI) was 27.0 ± 4.7 Kg/m2 and more than half of the sample (58%) was classified as sedentary. Active women had higher protein (P=0.004), fat (P=0.017), cholesterol (P=0.047), iron (P=0.016), zinc (P=0.009), calcium (P=0.045) and selenium (P=0.017) intake. Active participants had lower waist circumference, BMI, % body fat, trunk fat mass and diastolic blood pressure compared with inactive participants (P<0.05). SHBG (P=0.011) was higher and high-sensitivity C-reactive protein (P=0.011), fasting glucose (P=0.003), fasting insulin (P=0.019), and HOMA-IR (P=0.017) were lower in active women in comparison to inactive ones.
Conclusions: Data of the present study indicates that active postmenopausal women present more adequate dietary consumption, especially important antioxidant micronutrients, such as zinc and selenium. Both physical activity and dietary choices may have contributed towards a healthier anthropometric and metabolic profile.

P-64. Impact of a 12-month exercise program and hormone therapy (HT) on the body composition of postmenopausal women
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Objectives: To determine the impact of a 12-month exercise program and hormone therapy (HT) on the body composition of postmenopausal women. Design: Methods: A total of 169 healthy postmenopausal women participated in a randomized controlled trial. They were assigned to an exercise (EG, n = 91) or control group (CG, n = 78). Body composition and basal metabolic rate were evaluated by octopolar segmental bioelectrical impedance (SIBI) and helium dilution methods. All the sample elements completed a 3-day food intake questionnaire, and the EG performed 60 minutes of exercise, 3 times a week, involving body step, resistance and flexibility training. Results: There were no statistically significant differences between means of variables in both groups at baseline except for age. With the exception of weight and fat mass (kg), percentual changes in all measurements favored the exercisers compared to the control group. A 1-year exercise program resulted in an improvement of height, visceral fat area, skeletal muscle mass (SM) and soft lean mass (total, trunk and arms), regardless of HT. In relation to the women who performed HT use, the EG displayed a better percent change of SM (absolute and relative), height and soft lean mass (arms and total) when compared to those of the CG. This was only verified in the SM of non-users of HT. Conclusion: The results suggest that the exercise program attenuated the increase in the levels of total and central adiposity and preserved muscle condition, regardless of the usage of hormone therapy.

Table 1. Prevalence of dyslipidemia.

<table>
<thead>
<tr>
<th>Lipid</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol</td>
<td>40</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>30</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>20</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>10</td>
</tr>
</tbody>
</table>

Table 1. Mean (SD) Baseline Scores for the Parent and Long-Term Extension Studies

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Total Score</th>
<th>Desire Domain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flibanserin</td>
<td>6.5 (2.3)</td>
<td>5.8 (2.1)</td>
</tr>
<tr>
<td>Placebo</td>
<td>5.2 (1.8)</td>
<td>4.9 (2.2)</td>
</tr>
</tbody>
</table>

Conclusion: Safety results from this long-term extension study indicated no safety concerns for longer term exposure to flibanserin. Flibanserin treatment continued to be efficacious with continued exposure in both pre- and post-menopausal women.

Impact of a 12-month exercise program and hormone therapy (HT) on the body composition of postmenopausal women.
Objective: The purpose of this study was to compare maximal oxygen uptake (VO2max) and variables of body composition basal metabolic rate and characteristics of menopause in non-obese and obese postmenopausal women. Design: The sample was composed by 208 postmenopausal women (55.57 ± 6.62 years), 56% (75.5%) with a time of menopause inferior to 10 years, 55% non-users of hormone therapy and 74% obese. Visceral fat area (VFA), skeletal muscle mass (SM) and regional soft lean mass (arms, trunk and legs) were evaluated by octopolar biotimpedance InBody 720 (Biospace) and the basal metabolic rate (BMR) was appreciated resorting to the use of the equation of Cunningham (1991). Skeletal muscle mass index (SMI) was calculated by the formula SMI = SM/W and VFA (39.37 cm²) and minor values of SMI (-6.42%), VO2max (-4.77 ml/kg/min), compare to non-obese women, not being identified differences on BMR, SM and absolute values of regional SLM. The increase in VFA committed to women’s aerobic fitness (p<0.01), more strongly in obese than in non-obese (r=0.43 e r= -0.36, respectively). In the obese the highest correlations with VO2max was SLM (r=0.38, p≤ 0.01) of SMI (r=0.39, p≤ 0.01).

Conclusion: The study suggests Obesity tends to be related with a high VFA and a low SMI e SLM regional. The cardiorespiratory fitness is committed to high levels of AAV in obese and non-obese postmenopausal women. In non-obese women was observed an increase in levels of VO2max about 3.30 ml/kg/min in the presence of an elevated central adiposity. In the obese, the mean difference of VO2max between women with high VFA (Between 100 and 150 cm²) and very high (top to 150 cm²) was 3.72 ml/kg/min

P-66. Incident detection of HPV in older women: contributions of recent and past sexual partnerships and implications for HPV vaccination

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Objective: Human papillomavirus (HPV) infection, the primary cause of cervical cancer, is strongly associated with recent sexual exposure in women of all ages; however, risk factors for incident HPV among women who report sexual abstinence or long-term monogamous partnership are largely unknown. Using data from a cohort of middle-aged women, we aimed to estimate the incidence and potential fraction of HPV infections that are associated with recent new sexual partnerships and to determine factors associated with the infections not linked to new sexual partners. Design: Information on lifetime and recent sexual activity were collected biannually for up to two years from women age 35-60 years who were enrolled in the Baltimore-based HPV in Perimenopause (HIP) cohort. Cervico-vaginal samples for HPV DNA detection using the Roche Linear Array (LAAS) assay were also collected at 6 month intervals. Incidence rate ratios were calculated using Poisson models comparing different categories of recent sexual behavior and number of lifetime sexual partners. Results were based on these rate ratios, and odds of incident infection attributed to both exposures were calculated. Cox proportional hazards frailty models were used to estimate hazard ratios (HR) and 95% confidence intervals (CI) for new HPV DNA detection by recent and lifetime sexual behavior and other potential risk factors.

Results: Among 701 women, with a median age of 47 years, incident HPV detection among women with ≤5 vs. >5 lifetime partners (incidence ratio (IRR) of 5.1 (95% confidence interval (CI): 2.2, 8.1)) was almost identical to the relative rate of incident HPV detection in women who reported new sex partners compared to women reporting no sex in the previous 6 months (IRR: 5.6, 95% CI: 3.6, 8.7). However, since the average prevalence of new partners (4%) was relatively low, only 3% of incident infections could be attributed to new sexual partners, whereas 72% could be attributed to a higher number of lifetime sexual partners. Conclusion: 155 incident HPV infections were detected during periods of sexual abstinence or monogamy, and were strongly associated with cumulative lifetime sexual exposure (HR: 4.1, 95% CI: 2.0, 8.4). Furthermore, the effect of lifetime sexual partners on incident detection increased with increasing age. These data suggest that previous HPV infections may become newly detectable as women age and transition through menopause. Understanding the sources of newly detected infection in older women has important implications on HPV vaccination and screening strategies and how the research community conceptualizes the natural history of HPV in aging women.

P-67. Correlation between HPV positivity and abnormal cervical cytology differs by age among perimenopausal women

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Objective: We explored the age-stratified correlates and correlations between high-risk (HR) human papillomavirus (HPV) infection and cervical abnormalities in perimenopausal women. HPV testing and Pap smear screening were performed at baseline on 841 routinely screened women age 35-60 years in the HPV in Perimenopause (HIP) cohort. Demographic, behavioral and medical information was collected through telephone administered questionnaires. Design: Logistic regression was used to determine correlates of HPV and abnormalities in women under and over 45 years of age. Descriptive analyses were used to examine the correlation between HR-HPV infection and cervical abnormalities by age. Among women who had discordant Pap smear and HPV test results, we analyzed and compared their combined test status at the next available clinic visit to determine whether it was consistent with their previous Pap smear or HPV test result. Results: Among 781 women, the prevalence of HPV, HR-HPV and cervical abnormalities decreased significantly with increasing age, as did the correlation between HR-HPV and cervical abnormalities. The prevalence of HR-HPV was 50% among younger women with abnormalities but this decreased steadily to 20% HR-HPV detection among 50-54 year old, and no abnormalities were detected in 55-60 year old women. Different correlates of HR-HPV infection and abnormalities were observed in women a≥45 years, a pattern not seen in the younger women. Although the relative proportion of low and high-grade abnormalities did not change with age, we saw a loss of concordance between HR-HPV detection and cytological abnormalities with increasing age. At follow-up, only a small fraction of women who were Pap+/HPV− at baseline were still Pap− (16%), whereas a large fraction of Pap+/HPV+ women were still HPV+ (62%). Conclusion: Current guidelines for cervical cancer screening group together all women age 30 and above. Our data raise important questions about the interpretation of HPV and Pap test results in this age group and suggest that ongoing surveillance of HPV and cytology in cervical cancer screening programs consider a third age stratification among older women.

P-68. Timing of Menopausal Hormone Therapy and Carotid Intima Media Thickness: Who May Benefit?

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Objective: Menopausal hormone therapy (HT) may have variable atherosclerotic effects depending on its timing. While menopause is associated with a shift in cardiovascular risk factors, the progression of atherosclerosis related to HT timing has been inadequately explored. We studied the relationship between HT timing and carotid intima media thickness (cIMT). Design: The Los Angeles Atherosclerosis Study (LAAS) was a prospective cohort study of 576 men and women who were utility company employees without diagnosed cardiovascular disease at study entry. We studied 246 women aged 44 - 61 with cIMT at baseline, 1.5, 3, and 6 years follow up. Menopausal status was classified at each visit by the LAAS Hormone Committee, based on menstrual status and hormone levels. cIMT was measured with B-mode ultrasound using automated edge-tracking software. Mixed model regression analysis was performed using observations as unit of analysis. Results: Mean age of the women was 51.9 ± 4.3yrs. Over the study period, 11 women remained PERI and 167 remained POST; 14 women transitioned from PRE to PERI, 27 from PRE to POST, and 27 from PERI to POST. HT was associated with a statistically lower cIMT levels only in the PERI to POST group (Figure), even after adjusting for risk factors such as age, ethnicity, BMI, smoking, and C-reactive protein. Conclusion: Among women without diagnosed cardiovascular disease undergoing repeated cIMT measurements in the LAAS, HT predicted lower cIMT only in women in the later phase of the menopausal transition. These findings support the HT timing hypothesis, and suggest that HT used during the perimenopausal transition may be useful for atherosclerosis prevention in healthy women.
A comparison of salivary cortisol levels between symptomatic and non-symptomatic women at midlife

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Objective: There is a potential relationship between hot flashes and biomarkers of stress. Hot flashes can be experienced as stressful in the sense that they are uncontrollable and socially embarrassing events. Hot flashes have been shown to precede an increase in ambulatory systolic BP. Serum cortisol levels have been shown to increase with hot flashes in laboratory studies. Elevated urinary cortisol levels have been associated with greater hot flash severity. The purpose of this study was to test a hypothesized relationship between salivary cortisol levels measured at 4 points in time and diurnal change in cortisol levels in relation to reported hot flash experience and number of symptoms. Design: This is a cross-sectional analysis of 139 women aged 40 to 60. White or Black, free of CVD and diabetes, enrolled from 4 NYC hospitals in the Neighborhood Study of Blood Pressure and Sleep. Salivary samples were collected at waking, 30 minutes after waking, 1 hour before bedtime, and at bedtime. For each of 23 symptoms, women were asked to report whether or not they were bothered during the past 2 weeks. Cortisol awakening response (CAR), cortisol daily decline (CDD), and log transformed cortisol levels were examined in relation to hot flashes (yes/no) during the past 2 weeks by t-test analyses. Nonparametric median tests of untransformed cortisol levels were also carried out. Symptoms were summed and examined for correlation with cortisol measures. CAR and CDD were each categorized into positive change versus negative/no change and examined in relation to symptom experience. Linear regressions were also carried out to control for age, race/ethnicity, BMI, smoking status, menopausal status, HT use, and socioeconomic status. Results: The expected pattern of diurnal variation in salivary cortisol levels was demonstrated; however, there were no significant differences in salivary cortisol levels at any point in time across the course of the day between women who were symptomatic or non-symptomatic for hot flashes. Neither were there significant differences in median cortisol levels in relation to hot flash report. Sum of symptoms was not significantly correlated with any of the measures of salivary cortisol. Women for whom CAR remained relatively flat or decreased did not differ by hot flash report compared to women with a rise in CAR. Conclusion: Although we had expected symptomatic women to have higher cortisol levels, our findings do not demonstrate a relationship between salivary cortisol levels and symptom experience during the two weeks (or more) prior to the day of sample collection.

P-71 Efficacy and safety of daily ospemifene 60 mg for up to 1 year when used in the treatment of vulvar and vaginal atrophy in postmenopausal women

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Objective: Currently, the only prescription options for postmenopausal women who require treatment for vulvar and vaginal atrophy (VVA) are estrogen-based systemic or topical preparations. Development of tissue-selective non-estrogen therapies to treat VVA in order to avoid the possible undesired effects of estrogen is warranted and may also provide a treatment option for women who are unable to use estrogen containing preparations. Ospemifene, a selective estrogen receptor modulator (SERM), is differentiated from other SERMs by its positive estrogenic action in the vaginal epithelium with minimal effect on the endometrium and no effect on breast tissue. Ospemifene is under investigation for use in postmenopausal women with symptoms of VVA; this study evaluated the efficacy and long term safety of once daily ospemifene treatment for up to 1 year. Design: A 52-wk, 6:1 randomized, double-blind, placebo-controlled, parallel-group study was conducted comparing 60 mg/d of oral ospemifene (n=363) with PBO (n=63) in postmenopausal women (aged 40 to 80 years) with VVA and an intact uterus. Primary efficacy endpoints measured change from Baseline to Wk 12 in the percent (%) of superficial cells, the percent of parabasal cells, and vaginal pH. Endometrial thickness, area, and safety endpoints, was measured for all subjects by transvaginal ultrasound (TVU) at Baseline and Wks 12, 26, and 52 and by endometrial histology (biopsy) at Baseline and Wk 52. Additional safety assessments for all subjects included mammography (at Screening and Wk 52), breast exam, serum lipid levels, and ECG (at Screening and Wks 12, 26, 52). Results: A statistically significant change from Baseline to Wk 12 (LOCF) (all P values <0.0001) was seen for all primary efficacy endpoints. In the ospemifene 60 mg/day group, mean (SD) endometrial thickness as measured by TVU increased from Baseline to Wk 52 (LOCF) by 0.68 (1.62) mm; endometrial biopsy found 3 (1.0%) cases of active proliferation (1 (0.3%) of these subjects was diagnosed with endometrial hyperplasia (simple hyperplasia without atypia) 88 days after last dose of study drug). All events subsequently resolved. Mammography and breast exam produced no clinically significant changes from Baseline to Wk 52 or at any point during the study. There were no cases of breast or endometrial cancer. There were no meaningful differences between ospemifene 60 mg/day or PBO in the percentage of subjects with a normal to abnormal value shift from Baseline to Wk 52 for Triglycerides, HDL, LDL, and Total Cholesterol. One nonfatal thrombotic stroke (CVA) was reported in a subject with hypercholesterolemia. No subjects showed abnormal, clinically significant findings on locally assessed ECGs or summary ECG values from Baseline to Wk 52. In the ospemifene group, 1 (0.3%) subject, who was on thrombosis prophylaxis therapy prior to entering the study, was diagnosed with a deep vein thrombosis, which resolved. No cases of uterine leiomyomas, endometrial, salpingeal, or ovarian, or myocarcial infarction were reported. Conclusion: Ospemifene was found to be efficacious in relieving signs of VVA, and its safety is consistent with other studies in demonstrating minimal endometrial effect. It was well-tolerated and comparable to PBO across a range of safety parameters, including mammography and breast exam, lipid profile and cardiac events, when compared to placebo. There were no cases of breast or endometrial cancer, vulvar and vaginal atrophy in postmenopausal women with a uterus for up to 1 year. Ospemifene has the potential to be the first non-estrogen oral prescription therapy for this highly prevalent and chronic condition.
restitution of elevator therapy, or a serious chronic, physical or psychological illness. The final sample had a mean age of 52.5 years, with 76% of respondents being Caucasian, 60% being peri-menopausal (periods had become irregular or ceased within the last 12 months) and 30% being post-menopausal. The survey had 40% being greater than 50 years. The survey used the Climacteric Scale (21 items) to measure the severity of the psychological, somatic and vasomotor menopause symptoms; the Perceived Stress Scale (10 items) to measure stress; and the Kaiser Physical Activity Scale (75 items) to assess household duties, active living activities and exercise behavior. Several items surveying activity avoidance due to menopause symptoms were also used. Data was assessed for normality and descriptive statistics were analysed according to menopausal status. Stepwise linear regressions were used to assess differences in activity based on the severity of menopausal symptoms and perceived stress. Results: The menopause symptoms for each category were strongly correlated with each other and with perceived stress (r = .35; p < .001). Regression analyses revealed that menopause symptoms were associated with reduced participation in moderate intensity sport/ exercise (R2change = .04; Fchange = 2.98; p = .032) and reduced household duties engagement (R2change = .06; Fchange = 5.28; p = .002). The effects were observed after controlling reductions in activity associated with age, menopausal status and stress. Twenty per cent of women reported avoiding activity purely due to menopausal symptoms. These symptoms included tiredness, heavy sweating, weight gain, irregular and heavy bleeding and a general lack of motivation. Activities avoided included household chores, gardening, structured exercise classes and other self-initiated forms of exercise (e.g., walking and running). Conclusion: The severity of menopausal symptoms can have a significant influence on the amount of self-reported activity women engage in and is associated with avoidance of physical activities ranging from household duties to moderate and vigorous exercise pursuits.

P-75. Associations among Depression, Anxiety, and Somatic Symptoms in Peri- and Postmenopausal Women

Masakazu Terauchi, MD, PhD,1 Shiro Hiramitsu, MD,2 Mihoko Akiyoshi,2 Yoko Owa1,2, Kiyoko Kato2, Satoshi Obayashi, MD, PhD,2 Eisuke Matsushima, MD, PhD,2 Toshio Kubota, MD, PhD,2 1Department of Women’s Health, Tokyo Medical and Dental University, Tokyo, Japan; 2Department of Obstetrics and Gynecology, Tokyo Medical and Dental University, Tokyo, Japan; 3Department of Psychosomatics, Tokyo Medical and Dental University, Tokyo, Japan Objective: To investigate the associations among depression, anxiety, and physical symptoms in peri- and postmenopausal women in a clinical setting. Design: Two hundred and thirty-seven peri- and postmenopausal women enrolled in the Systematic Health and Nutrition Education Program at the Menopause Clinic of the Tokyo Medical and Dental University Hospital. Their responses to the Menopause Health-Related Quality of Life (MHR-QOL) and Hospital Anxiety and Depression Scale (HADS) questionnaires were subjected to a cross-sectional analysis. The study focused on the relationship between the scores for HADS depression (HADS-D) and anxiety (HADS-A) subscales and those for somatic (nausea, dizziness, numbness, muscle and joint pains, tiredness, headaches), urinary (frequent urination), and vasomotor symptoms (hot flashes, night sweats) in the MHR-QOL questionnaire. Results: The correlations among the scores for the 6 somatic symptoms and HADS-D and HADS-A were stronger than those for urinary or vasomotor symptoms. Multiple logistic regression analysis revealed that the score for headaches and the score for HADS-A were significantly associated with severe depression after adjustment (odds ratio (OR) [95% confidence interval (CI)]: 1.45 [1.01-2.09] and 1.57 [1.36-1.81], respectively), whereas the scores for nausea and numbness, as well as HADS-D, were significantly associated with severe anxiety (OR [95% CI]: 1.51 [1.02-2.23], 1.36 [1.02-1.84], respectively). However, the score for HADS-A was associated with depression, whereas nausea and numbness were associated with anxiety in peri- and postmenopausal women. The assessment of underlying mood disorders is required for the management of middle-aged women presenting with these somatic symptoms.

P-76. A population-based study of self classification of sexual life and associated factors in a cohort of Brazilian women aged 50 or more years

Ana Valadares, MD, PhD, Aarão M. Pinto-Neto, MD, PhD, Lícia Costa-Paiva, Vanessa Machado, Maria Helena Souza, Maria Jose Osis. Gynecology and obstetrics, UNICAMP, Campinas, Brazil Objective: To evaluate self classification of sexual life of women aged 50 or more years and associated factors. Design: Cross-sectional, population-based self-report household survey. A total of 622 Brazilian-born women, aged 50 or more were included. Self classification of sexual life was assessed as very good, good, fair, poor or very poor. Sociodemographic, clinical and behavioral factors were evaluated. Data were analyzed using the chi squared and Fisher exact tests and Poisson multiple regression analysis. Prevalence ratios (PRs) and their 95% CIs were calculated. Results: Of the sample 394 (63.3%) of women were excluded because they had told not to have sexual life. From the other 228 women on this sample, 53.5% classified their sexual life as very good, good or very good and 46.5% as fair, poor or very poor. Bivariate analysis indicated that being post menopausal (p=0.025) and being on treatment with natural remedies (p=0.035) were associated with a fair, poor or very poor self classification of sexual life. Multiple regression analysis showed that the prevalence of fair, poor or very poor self classification of sexual life was higher in women that had said to use natural medicines. Conclusion: More than half of women aged 50 or more didn’t have sexual life. A worse self classification of sexual life was associated with treatment with natural remedies. It may indicate the need of a better evaluation and treatment of these women.
P-77.
Self-perception of health and associated factors in Brazilian women aged 50 years or older: population-based study
Vanessa Machado, Ana Valadares, MD, PhD, Luiza S. Costa-Paiva, MD, PhD, Aaro M. Pinho-Neto, MD, PhD, Maria Helena Souza. Gynecology and obstetrics, UNICAMP, Campinas, Brazil
Objective: To evaluate self-perception of health among women aged 50 or more years and associated factors. Design: Cross-sectional, population-based, self-report household survey. A total of 6,556 Brazilian-born women aged 50 or more were included. Self classification of health was assessed as very good, good, fair, poor or very poor. Sociodemographic, clinical and behavioral factors were evaluated. Data were analyzed using the chi squared and Fisher exact tests and Poisson multiple regression analysis. Results: 4,243 (71.1%) women were aged 50 to 69 years and 1,813 (28.9%) had 70 or more. Of the sample 58.7% of women rated their health as very good or good and 41.3% as fair, poor or very poor. Multiple analysis showed that increasing weight after 50 years of age (PR=1.02, CI 1.01-1.04) and reporting multimorbidities (> 2 morbidities) PR= 1.97 (CI=1.48-2.63) was associated with a health self perception fair, poor or very poor. Conclusion: Multimorbidities and increase of weight increased the likelihood of experiencing a worse self health perception. Practicing physical activity, having a better education and medical insurance decreased the chance of a bad self perception of health.

P-78.
Sexuality in HIV soropositive women aged 40 to 60 years
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Objective: To evaluate sexuality in HIV soropositive women. Design: A cross-sectional study was described out using interviews with a questionnaire including Short Personal Experiences Questionnaire (SPEQ) and questions about condom use and sexual repertoire. Study was carried out using interviews with a questionnaire including Short Personal Experiences Questionnaire (SPEQ) and questions about condom use and sexual repertoire, completed by 213 soropositive women and 195 controls aged 40 to 60 years old, attending a menopause or an infectology center. Sociodemographic, clinical, behavioral and reproductive factors were evaluated. Data were analyzed using the chi-squared and Fisher exact tests and Poisson multiple regression analysis. Results: 442 (71.1%) women were aged 50 to 69 years and 180 (28.9%) had 70 or more. Of the sample 58.7% of women rated their health as very good or good and 41.3% as fair, poor or very poor. Multiple analysis showed that increasing weight after 50 years of age (PR=1.02, CI 1.01-1.04) and reporting multimorbidities (> 2 morbidities) PR= 1.97 (CI=1.48-2.63) was associated with a health self perception fair, poor or very poor. Schooling (≥8 years) PR=0.50 (CI=0.36-0.70), having health insurance: PR=0.75 (95% CI = 0.59-0.86) and practicing physical activity weekly: PR=0.68 (IC=0.54-0.86) were factors indicative of a protective effect against health self perception fair, poor or very poor. Conclusion: Multimorbidities and increase of weight increased the likelihood of experiencing a worse self health perception. Practicing physical activity, having a better education and medical insurance decreased the chance of a bad self perception of health.

P-79.
Estetrol for HRT with Special Emphasis on Breast Cancer
Monique Visser, PhD, Herjan JT Coelingh Bennink, Prof.Dr., Pantarhei Bioscience, Zeist, the Netherlands
Objective: To investigate the possible role of the fetal estrogen Estetrol (E4) in the treatment of menopausal complaints in women, with special emphasis on the treatment of women who have or have had breast cancer. Design: The effects of E4 on the vagina, uterus, bone and breast were investigated in several animal models and several clinical studies in women. Results: Pharmacology: The fetal estrogen Estetrol (E4) alleviates hot flashes in an experimental rat model and has estrogenic effects on the vagina, the uterus and bone in ovariectomised (OVX) rats. In MCF7 and T47D breast tumor cell lines E4 alone acts as a weak estrogen agonist, but as an estrogen antagonist in the presence of estradiol (E2). In the rat DMBA tumor model E4 prevents and treats breast tumors with a potency comparable to tamoxifen and ovariecatomy. Studies in women: In the human E4 is orally bioavailable with an elimination half life of 28 hrs. Multiple dose studies were performed in early postmenopausal women for 28-day treatment periods with doses up to 40 mg E4 per day. The effect of a single daily dose of 2 mg E4 on vaginal cytology was comparable to 2 mg E2-valerate. A daily dose of 10 mg E4 in women with frequent hot flashes showed efficacy. Biochemical bone formation and resorption parameters demonstrated a significant and dose-dependent decrease of bone turn-over, even during short treatment periods of 4 weeks. In contraceptive studies, a monophasic 24/4 day regimen of E4 combined with several progestogens inhibited follicular development and ovulation and had significantly fewer side effects on liver function compared to E2, including a favourable effect on coagulation parameters. Bleeding patterns were superior to an E2 contraceptive. Study in women with breast cancer: A prospective, randomised double-blind, placebo-controlled, two-week, pre-operative, neo-adjuvant study was performed in 50 women with estrogen-receptor (ER) positive breast cancer. The results showed no stimulation of the proliferation marker Ki67 and a significant increase of the apoptosis index by E4. Estetrol induced a significant decrease of ER-alpha receptors in the tumor cells and a trend to increase ER-beta receptors, which may offer an explanation for the unexpected estrogenic effect of E4. Conclusion: Estetrol may become an alternative for the symptomatic treatment of menopausal complaints such as hot flushes and vaginal dryness in early postmenopausal women. Estetrol may also be suitable for the prevention of osteoporosis in the same population. Due to its estrogen antagonistic effect on the breast, E4 may be suitable for HRT in women who have or have had breast cancer or who are treated with aromatase inhibitors.

P-80.
Women's Health Fellowship Awareness
Lauren Weber, DO, Judith Volkart, MD. Women's Health Institute, Cleveland Clinic, Cleveland, OH
Objective: Women’s Health Fellowships (WHF) were developed to create a more standardized curriculum to train Women’s Health Specialists in interdisciplinary Women’s Health. Most WHF in the United States started between 1995 and 2002. Cleveland established its fellowship in 1997 as a two-year curriculum that is designed for Family Practice (FP) or Internal Medicine (IM) trained physicians to further develop their clinical skills to provide comprehensive and optimal care for Women’s Health needs. The core areas of training include but are not limited to, comprehensive care-health maintenance and disease prevention, breast diseases, menopause, outpatient gynecology, osteoporosis evaluation and treatment, mood disorders, cardiovascular risk assessment, and common endocrine abnormalities. Focused research is also a part of the training program. Locally, the WHF at the Cleveland Clinic is well respected. However, WHF is not yet an accredited ACGME fellowship. Our belief was that knowledge of the existence of WHF, in general, is limited. This study was conducted to evaluate the national level of awareness of WHF by FP and IM residents, as well as their respective program directors. An expected additional benefit of the survey was that its very existence would increase awareness.
Design: A letter introducing the survey and the 9-question survey (tables 1 and 2) was sent to 452 FP and 381 IM program directors in the United States in February of 2012. The list of program directors and residency programs was derived from the Accreditation Council for Graduate Medical Education (ACGME) website. The letter asked the program directors to distribute the included survey to their medical residents. The residents were to complete the anonymous surveys and send them back to our office at the Cleveland Clinic in the included return envelope with paid postage. Six months was allowed for return of the surveys. The respondent’s information was tallied and placed into an excel spreadsheet. Data collection and analysis was then evaluated and is listed in tables 1 and 2 below. IRB approval was not necessary for this survey. Results: 833 surveys were mailed to the program directors and were to be distributed to the individual FP and IM residents. 99 surveys were collected. Forty-six men and fifty-three women returned their surveys, representing a 12% response rate. Only a few of the questions (n=7) were not answered. The affected questions on the incomplete surveys were utilized. The responses for questions 1 and 2 are presented in table 1, questions 3 through 8 are presented in table 2. In regards to question 9, respondents stated that they became aware of WHF through a number of means: people were aged 50, internet, colleagues, brochures, websites, the present survey, medical journals, personal research and through the AAP.org. Conclusion: This survey was, to our knowledge, the first assessment of the awareness of Women’s Health graduate education. Although improvement has been seen in the awareness of Women’s Health curricula since the 1990s, it is evident that there is much room for improvement. The lack of Women’s Health training in many medical schools and residency programs impacts not only how female patients are treated medically, but may impact the amount of physicians that want to further specialize in gender specific medicine due to lack of exposure to a formal curriculum. Women’s Health Fellowship programs could benefit from a more active recruitment effort by their programs. Additionally, formal accreditation by the ACGME would make this a more attractive fellowship. Finally, more efforts by national Women’s Health organizations, such as North American Menopause Society (NAMS), are needed to increase the awareness of this field and the important role it has in the health of women.

Table 1: Questions 1-2

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
<th>FP</th>
<th>IM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1</td>
<td>60%</td>
<td>55%</td>
<td>55%</td>
<td>60%</td>
</tr>
<tr>
<td>Q2</td>
<td>65%</td>
<td>60%</td>
<td>60%</td>
<td>65%</td>
</tr>
</tbody>
</table>

Table 2: Questions 3-8 reported by percentage

<table>
<thead>
<tr>
<th>Question</th>
<th>YES</th>
<th>NO</th>
</tr>
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<tbody>
<tr>
<td>Are you aware that there are fellowships specifically dedicated to the care of Women’s Health?</td>
<td>60%</td>
<td>40%</td>
</tr>
<tr>
<td>Are you aware that there are fellowships that focus on the surgical aspects of Women’s Health?</td>
<td>55%</td>
<td>45%</td>
</tr>
<tr>
<td>Are you aware that there are fellowships that focus on the medical aspects of Women’s Health?</td>
<td>45%</td>
<td>55%</td>
</tr>
<tr>
<td>Would you be interested in doing a Women’s Health Fellowship?</td>
<td>70%</td>
<td>30%</td>
</tr>
<tr>
<td>Do you think your medical school has a Women’s Health Curriculum?</td>
<td>35%</td>
<td>65%</td>
</tr>
<tr>
<td>Do you currently feel that Women’s Health is on an ACGME accredited fellowship?</td>
<td>40%</td>
<td>60%</td>
</tr>
</tbody>
</table>

P-81.
The effect of reproductive aging stage on cognitive function in midlife women
Miriam Weaber, Ph.D.,1 Pauline Maki, Ph.D. 2. 1Department of Neurology, University of Rochester, Rochester, NY; 2Departments of Psychiatry and Psychology, University of Illinois, Chicago, IL
Objective: Our understanding of the impact of menopausal stage on cognitive performance has been significantly advanced in recent years due to findings from large-scale studies of the menopausal transition. Findings from both the Kinmen-Women Health Investigation (KWII) and the Study of Women’s Health Across the Nation (SWAN) indicate that there are small but measurable negative outcomes in cognitive function during the perimenopause. Findings from studies with smaller numbers of perimenopausal women, however, including those of the Melbourne Women’s Midlife Health Project, show no impact of perimenopausal stage on cognitive function. These discrepancies may

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be due to differing criteria used to stage the menopausal transition and different tests used to measure cognitive function. Recently, an expert group convened to revise the criteria for the onset of late reproductive life and early menopausal transition. The aim of this cross-sectional and longitudinal study was to determine if cognitive function differs across these new stages of reproductive aging and to evaluate whether hormone levels or menopausal symptoms predicted cognitive function in the perimenopause. Design: One hundred and seventeen middle aged women were categorized into late reproductive, early transition, late transition, and early postmenopause stage according to these new criteria from the STRAW+10 workshop. We administered a comprehensive neuropsychological battery assessing six domains of cognition: attention, executive function, visuospatial function, verbal learning and verbal memory and motor function. We also administered inventories of menopausal symptoms and collected serum levels of estradiol and follicle stimulating hormone. Multivariate analyses were conducted to compare groups on cognitive performance. Correlational analyses were conducted to determine predictors of cognitive function. Results: The cognitive domain of verbal memory was most sensitive to reproductive aging; however, significant changes were seen in the early postmenopause stage. Women in the late reproductive and the late transition stages on measures of verbal memory. The groups did not differ in symptoms of depression or anxiety or other menopausal symptoms. Cognitive performance was not related to depression, anxiety, vasomotor symptoms or sleep disturbance. Conclusion: Cognitive function does not appear to change linearly across perimenopausal stages. Instead, there appear to be domain specific vulnerabilities. Decreases in verbal memory may be most evident in the first year after the final menstrual period. Mood symptoms, sleep disturbance and vasomotor symptoms did not account for these differences.

P.82. Toward Therapeutics for Syndrome Clusters during the Menopause Transition and Early Postmenopause: A Systematic Review

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Objective: Although most women experience clusters of symptoms during the menopausal transition, most investigations focus on a single symptom: the hot flash. The objective of this research was to systematically review clinical trials of acupuncture, soy and isoflavone preparations, black cohosh preparations, and body-mind therapies for managing symptoms of hot flashes and at least one additional symptom, including mood, sleep, pain, and cognitive symptoms. Design: An experienced reference librarian searched PubMed/Medline, CINAHL Plus, PsycInfo, Cochrane Database of Systematic Reviews, Cochran Central Register of Controlled Trials, Web of Science, AMED, and Alt-Health Watch for randomized controlled trials reported in English between 2004 and 2012. Of 1193 abstracts identified, 59 trials examining effectiveness of therapies on hot flashes and at least one additional symptom of interest were identified. Objective sample sizes, <10. Nine systematic reviews of studies of Traditional East Asian Medicine, including acupuncture (13), herbs including black cohosh (20), soy and isoflavone preparations (17), and body-mind therapies (9) reported significant effects on multiple symptoms. Thirteen trials examined acupuncture (9), Chinese herbal medicines (2), or moxibustion (1). Seven acupuncture trials reported significantly reduced hot flash frequency, intensity or bother, along with improved mood (2) and sleep (1). CHM significantly decreased HF frequency (3 trials), mood (1), sleep (1) and pain (1). Moxibustion (heat therapy) significantly decreased HF frequency (8). All the acupuncture studies were placebo controlled trials and other herbal (9) hypericum perforatum and vitex agnus-castus, French maritime pine bark extract, herbal formula phyto-female complex, diascorea, pollen extracts, rheum rhaponticum, and pueraria mirifica. Most herbs improved hot flashes, except pueraria mirifica and half of black cohosh studies demonstrated treatment effects. Rheum rhaponticum, French maritime pine bark extract, and over half of black cohosh studies resulted in significantly improved sleep and mood. Black cohosh and French maritime pine bark extract significantly improved cognitive symptoms. Only black cohosh, pollen extracts, and rheum rhaponticum significantly reduced pain. Eleven trials used soy preparations and nine decreased hot flashes (45-80%). Two trials recommending at least 60-70 mg of isoflavones daily significantly reduced vasomotor, sleep, cognitive and pain symptoms. Equol supplements of 30 mg/d for Non-Equal producing women significantly reduced HF frequency (7) and sleep (1). Exercise trials (6) yielded mixed results; 3 significantly reduced hot flash frequency, intensity or bother, along with improved mood and sleep; cognitive symptoms (1) but amnino acids yielded no significant results. Nine trials examined relaxation, yoga, or exercise. Two relaxation therapy trials (mindfulness and relaxation) significantly reduced hot flash frequency, intensity or bother; mindfulness improved sleep symptoms. Yoga (1 trial) significantly reduced hot flashes and improved cognitive symptoms, but not mood or somatic symptoms. Exercise trials (6) yielded mixed results; 3 significantly reduced hot flashes and cognitive symptoms (1), but increased pain in exercisers (1). Conclusion: Although investigators study multiple symptoms, few report treatment effects in ways that allow clinicians to consider symptom clusters when prescribing therapies. Recommendations include use of standardized multiple-symptom instruments to report results and analysis of multiple symptom effects in future research.

P.83. Urinary Incontinence during the Menopausal Transition and Early Postmenopause

Nancy F. Woods, PhD, RN, Ellen S. Mitchell, PhD. Biobehavioral Nursing, University of Washington, Seattle, WA

Objective: Urinary Incontinence (UI) becomes more prevalent as women age, but little is known about symptomatic trends and UI and their relationship to endocrine changes associated with menopause. The objective was to determine the influence of age and menopause transition factors (menopausal transition stages, FSH, E1G, hormone therapy use), health history (perceived health, smoking, BMI, hypertension, diabetes), and reproductive history (live births, fibroids) on the experience of UI among middle women during the menopausal transition and early postmenopause. Design: A subset of Seattle Midlife Women’s Health Study for participants (n=303 with up to 2452 observations) who provided data during the late reproductive, early, and late menopausal transition stages and early postmenopause, including menstrual calendars, annual health updates since 1990, and provided symptom diaries and urine specimens assayed for hormones several times per year provided data.
Multilevel modeling (r program) was used to test models accounting for UI. **Results:** We tested a model predicting any urinary incontinence that included age, the menopausal transition, health, personal resources, stress and social factors. Significant predictors tested included smoking, number of live births, BMI, HT status, FSH, years of education, social self consciousness, ethnicity, amount of income, if partnered, and perceived stress level. When these variables were included in the model with age, significant predictors were the menopausal transition (being in late stage, \( p < 0.02 \)), being partnered (\( p < 0.02 \)) and having 3 or more live births (\( p < 0.02 \)). When only UI was considered as an outcome, the model included age (\( p < 0.0001 \)), number of live births (\( p < 0.0001 \)), and BMI (\( p < 0.004 \)). **Conclusion:** The late stage of the menopausal transition appears to be a time of vulnerability for any UI, but is not specifically for SUI. Instead, aging seems more strongly related to SUI. BMI and parity and BMI were associated significantly with both any type of UI and SUI. Further exploration of incontinence during the menopausal transition is needed to articulate a lifespan view of UI and its types.

P-86. A Content Analysis of Bioidentical Hormone Therapy Blog Posts

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**Objective:** It is estimated that 75% of all users search the internet to look for health information. With the recent controversy surrounding the term “bioidentical hormone therapy” (BHT), women may be turning to internet blogs as a source of health information on this topic. The objectives of this study were to analyze the content of the information in BHT blogs and to describe the perspectives on BHT presented in these blogs. **Design:** Blogs were identified using the search engine Google Blog Search®. Inclusion criteria included blogs that had been developed or updated between September, 2011 to February, 2012, and not more than three clicks from the top 200 search results. Video or discussion forum blogs, as well as those requiring password access were excluded. A quantitative content analysis was performed on 30 blogs meeting study criteria. Emerging themes were identified through thematic analysis. Blogs were reviewed by two investigators and agreement reached by consensus. **Results:** The author was indicated in 70% of blogs, with equal representation between male and female. Only 17% of blogs were from health care professionals, however, 68% did not indicate the profession. Provision of health information was the predominant purpose of the blogs (99%), with 73% also promoting a product or service. None of the blogs were from a professional organization. A quarter of blogs mentioned evidence (23%) with 13% providing references. Majority of blogs defined BHT as custom-compounded formulations (73%), while only 3% indicated that BHT is also commercially available. Bioidentical hormones were categorized as estradiol (43%), estranol (33%), estrone (30%) and natural progesterone (80%). In addition, testosterone (70%) and dehydroepiandrosterone (DHEA) (40%) were frequently mentioned. Over 90% of blogs portrayed BHT positively, and 67% relayed negative perspectives on conventional hormone therapy (HT). Majority of blogs made safety claims regarding the use of BHT related to breast cancer (70%) and associated cardiovascular risk (70%) in comparison to conventional HT. Salivary testing of hormones was mentioned in 30% of blogs. General themes included “hormone balance”, “natural”, and “lack of side effects”. **Conclusion:** Individuals seeking health information on BHT on the internet may encounter information presented in blogs. Claims made on BHT blogs presented perspectives that were largely promotional in nature and were not consistent with evidence-based recommendations supported by professional organizations.

P-87. Antioxidant effect of one year hormone therapy on oxidative stress in postmenopausal women

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**Objective:** To determine the effect of one year hormone therapy (HT) on oxidative stress (OS) in postmenopausal women (POS). **Design:** A randomized, double blind controlled trial was carried out in 60 women: 1) control, 20 postmenopausal [PRE] (45±3.3 years, estradiol (E2) 107±81 pg/mL, FSH 16±9 mIU/mL); 2) HT (0.625 mg/d of synthetic conjugated estrogens [estradiol] 5 mg/g of medroxyprogesterone [MPA]); 20 POS (51±3.1 years, E2 16±8 pg/mL, FSH 6±4±3 mIU/mL); 3) placebo [P]; 20 POS (52±3.2 years, E2 14±6 pg/mL, FSH 6±2±3 mIU/mL). We measured lipoperoxides ([LPO]) by TBARS assay as oxidative stress biomarker. The test was carried out at the beginning, 6 and 12 months of treatment. An alternative cut-off value of LPO ≥ 320 μmol/L was defined on the basis of the 90th percentile of young healthy subjects. **Results:** Of the 60 participants enrolled, 15 dropped out in different time, leaving 45 subjects who completed 3 assessments. In PRE group, 5 women left the study because they stop attending. In HT group, 4 participant discontinued intervention: 3 due to bleeding and one moved to another city. In P group, 6 women discontinued treatment: 2 due headaches, one by discomfort, 2 by family problems and other did not come back. At basal time, LPO levels were similar in the three groups. LPO levels decreased after 6 mo. in PRE (0.334±0.05 to 0.293±0.05 μmol/L, p<0.05), also in HT (0.359±0.06 to 0.311±0.07 μmol/L, not significant); in P were similar to basal. After 12 months, LPO levels continued decreased in HT (0.292±0.04 μmol/L, p<0.01, compared basal vs. 12 mo.); in PRE and P groups LPO no change (Figure). We found that women with high LPO in HT diminished after 6 mo. and continued until 12 mo.: basal 9 (56%), 6 mo. and 12 mo. 4 (25%); in PRE also decrease: basal 8 (53%), 6 mo. and 12 mo. 5 (33%); in P, 10 (71%) women had high LPO and they were maintained. **Conclusion:** Our findings suggest that HT decreases LPO as OS biomarker after 12 months. This work was supported by DGAIP-UNAM IN30611L and sponsored by Laboratorios Senosiain SA de CV. Trial registration: C0000120.

P-88. Oral Estrogen vs. Transdermal Estrogen Effects on Lipids and Lipoproteins in Recently Menopausal Women: the Kronos Early Estrogen Prevention Study (KEEPS)

Eliot Brinton, MD1, Nazeem Nanjee, PhD2, Paul N. Hopkins1, Nanette Santoro, MD2. 1Pharmaceutical Sciences, University of Alberta, Edmonton, AB, Canada

**Objective:** Dyslipidemia is one of the most common treatable risk factors for cardiovascular disease (CVD), affecting nearly half of all US adults. Higher estrogen levels appear to be the main factor accounting for the lower prevalence of dyslipidemia among premenopausal women, particularly the significantly higher levels of high-density lipoprotein-cholesterol (HDL-C) usually seen in premenopausal women vs men of comparable age. This, in turn may account for a large fraction of the relative protection against CVD enjoyed by premenopausal women. The loss of endogenous estrogen at the menopause is believed to account for the rapid increase in CVD risk in postmenopausal women. Menopausal hormone therapy (MHT) is designed to replace the striking loss of endogenous estrogen in postmenopausal women, and most observational studies and some clinical trial data suggest that MHT may help prevent the increase in atherosclerosis and rise in CVD incidence after the menopause. A very few randomized controlled trials have tested the lipid effects of oral vs transdermal MHT, but these have tended to be relatively short-term or to include relatively few subjects, and generally have not evaluated the lower doses of MHT frequently used in contemporary clinical practice. **Design:** The Kronos Early Estrogen Prevention Study (KEEPS) is a multicenter, foundation-sponsored trial designed to test a wide array of effects of 4 years of randomized, double-blind MHT in 727 women recruited within 3 years of the menopause, who were without prior CVD events, severe dyslipidemia or other major CVD risk factors. MHT was tested in 3 study arms: low-dose (0.45 mg/d oral conjugated equine estrogen (CEE) vs transdermal 17β estradiol (50 mcg/d)—both combined with cyclic oral micronized progesterone—as matching placebos. The primary endpoint was subclinical atherosclerosis, measured as the slope of change over time in carotid artery intima-media thickness (CIMT) by ultrasound. Secondary endpoints included lipid levels and changes in coronary artery atherosclerosis, measured as the Agatston coronary artery calcium (CAC) score by chest CT. **Results:** We performed standard lipid panel analyses in KEEPS subjects at baseline and at 12, 36, and 48 months during the study and will present the effects over time of low-dose oral CEE vs transdermal estradiol vs placebo on the major lipoproteins. In addition, to evaluate lipid levels as potential determinants of atherosclerosis during MHT, we will also present the interrelationships between baseline and/or on-study lipids with changes in subclinical atherosclerosis by CIMT and CAC. **Conclusion:** Lipid changes with early postmenopausal MHT may alter the progression of atherosclerosis and differing routes of MHT may differ in their effects on lipids and atherosclerosis.
P-99. White Matter Hyperintensities Correlate with Platelet-derived and Prothrombotic Microvesicles in Women of the Kronos Early Estrogen Prevention Study (KEEPS)

**Objective:** White matter hyperintensities (WMH) detected on T2-weighted brain magnetic resonance imaging (MRI) are prevalent with increasing age and known to associate with a higher risk of stroke. Previous studies have reported a correlation between WMH prevalence with conventional cardiovascular (CV) risk factors in older, gender mixed cohorts. WMH etiology and histopathophysics in younger, recently menopausal women remain to be elucidated. The objective of this study was to determine the relationship between the load and progression of WMH with conventional and non-conventional CV risk factors found within the peripheral circulation in a population of healthy, recently menopausal women.

**Design:** WMH volumes were quantified in women enrolled in Kronos Early Estrogen Prevention Study (KEEPS) at Mayo Clinic (n=953) using a semi-automated segmentation algorithm based on fluid attenuated inversion recovery (FLAIR). MRI. Changes in WMH volumes were calculated as the change in volume from that obtained prior to randomization (baseline) and that obtained at 18, 36 and 48 months (mo) after randomization to treatment. Changes in WMH were correlated with traditional conventional CV risk factors, outcomes (carotid intima-media thickness, CIMT; coronary arterial calcification, CAC), markers of platelet activation and prothrombotic microvesicles (MV) measured in peripheral blood. Longitudinal changes in WMH were adjusted for age, time since last menstruation, Apolipoprotein E e4 and treatment assignment (oral conjugated estrogens or transdermal estradiol plus oral micronized progesterone).

**Conclusion:** Activated platelets and thrombogenic membrane-derived MV assessed in peripheral blood are associated with increases in WMH load, in this cohort of healthy postmenopausal women. Supported by the Aurora Found, NIH HL90639, NS066147, HD65987 and the Mayo Found.

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P-98. Effects of Oral Conjugated Estrogen or Transdermal Estradiol Plus Oral Progestrone Treatment on Breast Outcomes among menopausal women in the Kronos Early Estrogen Prevention Study (KEEPS)

**Objective:** Combined standard dose estrogen and progestin therapy in the WHI randomized trials was shown to affect breast outcomes, including increased rates of additional radiologic imaging, mammographic density, and incidence of breast cancer. Lower dose hormone therapy regimens are now advocated, but the effects of these lower dose hormone therapy regimens on breast outcomes are relatively unknown.

**Design:** The Kronos Early Estrogen Prevention Study (KEEPS) is a randomized clinical trial of 727 women ages 42-58 years with a primary goal of examining the effects of low-dose transdermal versus oral estrogen combined with cyclic micronized progesterone on progression of subclinical atherosclerosis in recently menopausal women. Women were assigned to oral conjugated estradiol (0.45 mg/d) or transdermal estradiol (50 mg/d), or placebo, with cyclic micronized progesterone (200 mg for 12 days) for active hormonal therapy groups. An separate ancillary study on breast outcomes was funded by the National Cancer Institute. Mammmogram reports from KEEPS participants who provided consent for the ancillary study were obtained from baseline to year 4 of KEEPS study follow-up. For each participant, a dichotomous outcome variable was created indicating breast outcome (additional imaging, short interval follow-up or breast biopsy required) versus usual imaging. Breast Imaging Reporting and Data System (BI RADS) mammographic density categories were used. Change in BIRADS category from baseline to year 1, and from baseline to year 4 was calculated for each participant.

**Results:** A total of 618 KEEPS participants were eligible for the breast outcomes ancillary study, and of these, 521 women (84.3%) consented for the breast outcomes study. Rates of breast outcomes were compared for each randomized treatment group compared with placebo from baseline to year 1, and from baseline to study completion (year 4). In addition, change in BIRADS mammographic density categories from baseline to year 1 and from baseline to study
P-93. Change Over Time in Menopausal Symptoms in Women Randomized to Oral Conjugated Estrogen or Transdermal Estradiol Plus Micronized Progesterone Versus Placebo: the Kronos Early Estrogen Prevention Study (KEEPS)

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Objective: To examine the course of menopausal symptoms in a community-based cohort of recently menopausal women randomized to receive menopausal hormone therapy compared to a placebo control group. Design: 727 menopausal women who were within 3 years of their final menstrual period were randomized to either: oral conjugated estrogen 0.45mg/d (n=230) or transdermal estradiol 50mcg/d (n=225), both with oral micronized progesterone 200mg qhs for 12 days each month, versus a placebo control group (n=275). Nine recruitment sites from across the USA participated in the KEEPS trial. All women completed a symptom checklist at screening and again at 6, 12, 24, 36 and 48 months. Each of the two treatment arms will be compared to placebo. The proportion of women reporting any or moderate-severe symptoms will be assessed and compared across groups.

Results: Among screening, hot flashes (85.7% of women reported any; 43.7% reported moderate-severe) and night sweats (67.7% reported any and 34.9% reported moderate-severe) were the most common symptoms, followed by insomnia (65.8% reported any, and 32.6% reported moderate-severe), vaginal dryness (59.8% with any and 26.6% moderate-severe), irritability (58.1% with any and 16.9% moderate-severe), adverse mood (56.7% with any, and 15.8% with moderate severe disruption), depression (37.0% reported any and 8.8% reported moderate-severe), palpitations (28.2% reported any and 5.6% reported moderate-severe), and dyspareunia (30.7% reported any and 13.9% reported moderate-severe). Over time, all of these symptoms decreased in the two hormone treatment groups. Comparisons between hormone groups and placebo will be shown.

Conclusion: Women in this community based sample had a high prevalence of self-reported menopausal symptoms at screening. These symptoms, including palpitations (not usually reported in studies of menopausal symptoms), decreased with hormone therapy.