ABSTRACT PRESENTATIONS

THURSDAY CONCURRENT SESSION #1

S-1. Influence of Reproductive Hormones and Nighttime Hot Flashes on Mood in Depressed Perimenopausal Women Reporting Stressful Life Events
Hadine Joffe, MD, MSC1, Sybil Crawford, PhD, Marlene P. Freeman, M.D.1, Geena Aihuppylll, M.D.1, Wolfe David, MD, MPH2, Semmien Kim2, Thania Galvan2, Julia Cameron2, Freid Cathryn2, Lee S. Cohen, MD, Janet Hall1. 1Psychiatry - Center for Women’s Mental Health, Massachusetts General Hospital, Boston, MA; 2Psychiatry - Women’s Hormones and Aging Research Program, Brigham and Women’s Hospital, Boston, MA; 3School of Medicine, University of Massachusetts, Worcester, MA; 4Reproductive Endocrine Unit, Massachusetts General Hospital, Boston, MA

Objective: The premenopausal period is a time of increased risk for depression. Estradiol variability, hot flashes, and stressful life events each increase the risk for depressive symptoms during this time period. However, the relative contribution of these factors to depressive symptom severity in depressed perimenopausal women is not well understood. We therefore compared perimenopausal participants with high versus low estradiol variability and nighttime hot flashes who independently predict worse mood in depressed perimenopausal women. Design: Perimenopausal women with mild depression (Montgomery-Åsberg Depression Rating Scale [MADRS] score 10–24) completed assessments of mood, serum estradiol and progesterone weekly for 9 weeks, as well as a stressful life event survey and a daily hot flash diary. Repeated-measure regression was used to examine independent associations of mood with the coefficient of estradiol variability in the estradiol, the number of distinct progesterone elevations exceeding 6 n/dl, and hot flashes, while accounting for recent stressful life events. Results: A total of 93,668 women age 50 to 79 years were assessed at baseline for 9 weeks, as well as a stressful life event survey and a daily hot flash diary. Repeated-measure regression was used to examine independent associations of mood with the coefficient of estradiol variability in the estradiol, the number of distinct progesterone elevations exceeding 6 n/dl, and hot flashes, while accounting for recent stressful life events. The response model was used to identify if insomnia symptoms (SL, WASO, A, SQ) change over time by perimenopausal stage (Table 1). Multivariable logistic regression models were used to examine the insomnia trajectory, defined by American Academy of Sleep Medicine (AASM) insomnia criteria. The primary outcome variables were four sleep complaints: difficulty falling asleep (DFA), difficulty maintaining sleep (DMS), waking up feeling unrested (WUFR), and non-restorative sleep (NRS). The prevalence of insomnia (49.7% vs. 53.3%, p-value <0.0001) was used to identify predictors of influence on chronic insomnia. Conclusion: In perimenopausal depressed women, increasing dysregulation of ovarian hormones with greater estradiol variability and loss of ovulation indicated by absence of progesterone production is associated with worse mood. In addition, nighttime hot flashes are associated with higher depression scores among those who are persistently hypo-estrogenic. These menopause-specific correlates of depression are strongly predicted by mood worsening mood after accounting for stressful life events.

S-2. Association of Sleep and Sexual Function in Postmenopausal Women
Julie Tremblay, MD, MPH1, 2, JoAnn E. Manson, MD, MPH1, Michelle Haughton, Ph.D., MPH1, M’hamed Temkit, Ph.D.1, Shannon D. Sullivan, MD, PhD1, Emily W. Gower, Ph.D.1, Lauren Hale, Ph.D.1, Julie C. Weitlauf, Ph.D.1, Sara Nowakowski, Ph.D.1, 2, Carolyn J. Crandall, MD, MS1. 1Department of Internal Medicine, Ohio State University, Columbus, OH; 2Division of Health Sciences Research, Mayo Clinic, Scottsdale, AZ; 3Division of Endocrinology, Medstar Washington Hospital Center and Georgetown University, District of Columbia, DC; 4Department of Epidemiology and Ophthalmology, Wake Forest School of Medicine, Winston-Salem, NC; 5Program in Public Health, Stony Brook University, Stony Brook, NY; 6Department of Medicine, Stanford University School of Medicine, Palo Alto, CA; 7Department of Medicine, David Geffen School of Medicine at University of California, Los Angeles, Los Angeles, CA; 8Department of Medicine, Brigham and Women’s Hospital, Harvard, Boston, MA; 9Department of Obstetrics and Gynecology, University of California Medical Branch, Galveston, TX; 10Department of Medicine, Mayo Clinic, Scottsdale, AZ

Objective: During the menopausal transition, women may report sleep disturbance and decreased sexual function and satisfaction. However, associations between sleep quality and sexual activity have not been fully explored. The aim of this cross-sectional study was to determine whether insomnia and sleep duration using a validated, clinically relevant scale are associated with sexual activity and sexual satisfaction in the Women’s Health Initiative (WHI) Observational Study (OS). Design: Cross-sectional activity questions and self-reported sleep in the past 4 weeks were assessed at baseline for 93,668 women age 50 to 79 years enrolled in the WHI OS. Insomnia was measured using the validated WHI Insomnia Rating Scale (WHIIRS), which includes questions on whether participants had trouble falling asleep, wake up before the alarm, woke up before they had wanted to, woke up before the alarm, woke up after having missed sleep, and overall sleep quality (very sound/restful to very restless). Typical sleep duration (5 hrs or less, 6 hrs, 7, 8, 9 hrs, 9 or more) was also recorded. The primary outcome variables were four sleep complaints: difficulty falling asleep (DFA), difficulty maintaining sleep (DMS), waking up feeling unrested (WUFR), and non-restorative sleep (NRS). The prevalence of insomnia in the WHI OS was 49.7% vs. 53.3%, p-value <0.0001. The prevalence of insomnia (49.7% vs. 53.3%, p-value <0.0001) was used to identify predictors of influence on chronic insomnia. Conclusion: The prevalence of insomnia in perimenopausal women transitioning to menopause was affected by the WHIIRS and self-reported partnered sexual activity and sexual satisfaction. Longitudinal investigation of sleep and its impact on sexual function during menopause would help clarify this relationship further.
Prominent sleep disturbance confirmed with objective polysomnographic recordings in women who develop insomnia in the approach to menopause

Fiona C. Baker, PhD-2, Massimiliano de Zambotti, PhD-1, Adrian R. Willoughby, PhD-1, Stephanie A. Sassoon, Ph.D.-1, Stephanie Claudatos-1, Sarah Inkelis-1, Lena Kardos-1, David Dresser-1, David Sugarbaker-1, Ian M. Colrain, PhD-1,3, Fiona C. Baker, PhD-2,1, SRI International, Menlo Park, CA;1Brain Function Research Group, University of the Witwatersrand, Johannesburg, South Africa;1Melbourne School of Psychological Sciences, The University of Melbourne, Melbourne, VIC, Australia

Objective: The majority of women experience sleep difficulties, particularly night-time awakenings, as they approach menopause, and for about 25% of women, sleep disturbances are severe, causing significant distress and impacting functioning, qualifying them for a diagnosis of insomnia disorder. However, it is unclear whether these sleep disturbances are matched with polysomnographic evidence of poor sleep quality, leading to a lack of clarity about the nature of severe sleep problems in midlife women and how to treat them most effectively. We aimed to determine whether there is physiological evidence of disturbed sleep, based on PSG and spectral electroencephalographic analysis, in women who developed DSM-IV insomnia in the context of the menopause transition (with no past history of insomnia disorder) compared with age-matched women in the menopause transition without insomnia.

Design: Participants were seventy-two women (age range: 43-57 years; 38 meeting DSM-IV criteria for insomnia with an onset proximate to the menopause transition, and 34 controls with no/mild sleep difficulties). They completed sleep diaries for two weeks and came to the laboratory for a clinical PSG screening/ adaptation night to confirm absence of breathing-related or limb movement sleep disorders. They then returned for an additional PSG recording night. Normal skin conductance was measured throughout the night to quantify hot flashes. Results: On their sleep diaries, women with insomnia reported a shorter sleep duration (p=0.04), more wake after sleep onset (p=0.002), more nocturnal awakenings (p=0.050), and more hot flashes (p=0.012) than controls. On the PSG recording night, women with insomnia had a shorter sleep duration (587.5 ± 37.4 min) than controls (606.8 ± 37.2 min, p<0.001), due to a shorter time in bed (p < 0.05) and a higher percentage of PSG-defined wake after sleep onset (p = 0.01). Women with insomnia also had a longer percentage of N2 sleep (insomnia: 46.2 ± 6.7%, control: 49.8 ± 6.7%, p = 0.054) and a lower sleep efficiency (insomnia: 85.6 ± 7.5%, control: 90.1 ± 4.7, p=0.004). More insomniacs (18 of 38) than controls (3 of 34) had a short sleep duration (< 6h) (χ2=12.9, p<0.001). Measures of electroencephalographic activity during sleep did not reveal any group differences although insomniacs tended to have lower delta power during deep sleep than controls (p=0.055). Insomniacs were more likely than controls to have at least one objective hot flash during the PSG recording (χ2=11.07, p=0.001). Conclusion: Women with first-onset insomnia in the approach to menopause have a measurable sleep deficit, with shorter sleep duration, more wake after sleep onset, and lower sleep efficiency, and less delta sleep, compared to women in the menopause transition without insomnia. Nocturnal physiological hot flashes are more common in insomniacs and are likely an important contributor to nocturnal wakefulness in this population. Insomnia in the context of menopause has unique etiological features, such as hot flashes, which should be considered when treating women with menopause-onset insomnia.

S-5. Lower estradiol levels are associated with greater hot flash-related sleep disturbance in women in the menopausal transition

Massimiliano de Zambotti, PhD-1, Sarah Inkelis-1, Stephanie Claudatos-1, David Dresser-1, Lena Sauders-1, David Sugarbaker-1, Ian M. Colrain, PhD-1,3, Fiona C. Baker, PhD-2,1, SRI International, Menlo Park, CA;1Brain Function Research Group, University of the Witwatersrand, Johannesburg, South Africa;1Melbourne School of Psychological Sciences, University of Melbourne, Melbourne, VIC, Australia

Objective: Hot flashes, defined as transient periods of heat, sweating, anxiety, and chills, are reported by about 80% of women in natural menopause. Hot flashes emerge in association with declining estradiol levels and impact quality of life, affecting productivity, mood, social activities, and sleep. We recently showed that a calculation of the amount of time spent awake in association with hot flashes (hot flash-associated wake time) goes beyond hot flash frequency in providing a useful index of the impact of hot flashes on sleep in perimenopausal women (de Zambotti et al., Fertil Steril, 2014 102:1708-15). Hot flash-associated wake time contributes a variable percentage to total in-bed wakefulness, ranging between 0-89%. Reasons for this variable impact of hot flashes on sleep are unknown. Here, we aimed to investigate whether the impact of hot flashes on sleep is associated with circulating reproductive hormones, specifically estradiol in menopausal women, and how cortisol, a stress hormone (cortisol) impacts sleep, along with sleep architecture and sleep efficiency, and hot flash association. Design: Participants were seventy-two women (age: 43-57 years; BMI: 23.5 ± 2.9 Kg.m^-2) in the menopause transition. They completed a clinical polysomnographic (PSG) screening night to confirm absence of breathing-related or periodic limb movement sleep disorders, and then returned for a clinical PSG recording night. Normal skin conductance was measured throughout the night to quantify hot flashes. A blood sample was drawn at their PSG recording night, women with insomnia had a shorter sleep duration (364.3 ± 37.4 min) than controls (406.8 ± 37.2 min, p<0.001), due to a shorter time in bed (p < 0.05) and a higher percentage of PSG-defined wake after sleep onset (p = 0.01). Women with insomnia also had a longer percentage of N2 sleep (insomnia: 46.2 ± 6.7%, control: 49.8 ± 6.7%, p = 0.054) and a lower sleep efficiency (insomnia: 85.6 ± 7.5%, control: 90.1 ± 4.7, p=0.004). More insomniacs (18 of 38) than controls (3 of 34) had a short sleep duration (< 6h) (χ2=12.9, p<0.001). Measures of electroencephalographic activity during sleep did not reveal any group differences although insomniacs tended to have lower delta power during deep sleep than controls (p=0.055). Insomniacs were more likely than controls to have at least one objective hot flash during the PSG recording (χ2=11.07, p=0.001). Conclusion: Women with first-onset insomnia in the approach to menopause have a measurable sleep deficit, with shorter sleep duration, more wake after sleep onset, and lower sleep efficiency, and less delta sleep, compared to women in the menopause transition without insomnia. Nocturnal physiological hot flashes are more common in insomniacs and are likely an important contributor to nocturnal wakefulness in this population. Insomnia in the context of menopause has unique etiological features, such as hot flashes, which should be considered when treating women with menopause-onset insomnia.

S-6. Childhood Physical and Sexual Abuse Predict Menopausal Symptoms among Sexual Minority Women

Bethany Everett, PhD-1, Pauline Maki, Ph.D.-2, Tonda Hughes, PhD-1, Sociology, University of Illinois at Chicago, Chicago, IL;1Psychiatry & Psychology, University of Illinois, Chicago, IL;2Health System Sciences, University of Illinois, Chicago, IL

Objective: Studies of menopause have focused almost exclusively on heterosexual women, despite evidence that sexual minority women report multiple risk factors for more severe menopause symptoms including childhood physical and sexual abuse. Our objective is to examine the association between a history of abuse (i.e., childhood physical and sexual) and menopausal symptoms in a sample of sexual minority women.

Design: Data are from the Chicago Health and Life Experiences of Women (CHLEW) Study, a longitudinal study of sexual minority women in the Chicago area. Participants were initially recruited in 2000-2001, and the third and most recent wave of data was collected in 2010-2012. The sample for this study is restricted to women who reported transitioning through menopause between those two waves (N=112). The mean age of the sample is 59.3. Logistic regression models were used to assess the association between childhood abuse and self-reported menopausal symptoms including vaginal dryness, hot flashes, and psychological symptoms. All models adjust for age, race/ethnicity, education, alcohol and tobacco use, anxiety, and BMI. Results: Eighty percent of the sample reported hot flashes, 33% reported vaginal dryness, and 55% reported nervousness and depression during menopause. Twenty percent of the sample reported childhood physical and sexual abuse and 36% reported childhood sexual abuse. Logistic regression models reveal no significant relationship between childhood abuse and hot flashes, however, women who reported childhood physical abuse were almost 10 times likely to report vaginal dryness (OR=9.77, p<.001) and women who reported childhood sexual abuse were four times as likely to report nervousness and depression (OR=4.21, p<.001) compared to women who did not report abuse (See Table). Conclusion: Rates of hot flashes, vaginal symptoms, and psychological symptoms among sexual minority women were similar to rates observed in epidemiological studies of the menopause, though rates of childhood physical and sexual abuse were higher. Results show an association between childhood sexual and physical abuse and women’s health at midlife. The association between childhood physical abuse and vaginal dryness in menopausal women was particularly strong while the association between childhood sexual abuse and vaginal dryness was not as strong. Although link between childhood sexual abuse and sexual function in adulthood is well established, the current findings did not suggest that this association is particularly pronounced during the menopausal period. The menopausal transition is associated with an elevated risk of depression and anxiety. This suggests that a history of childhood sexual abuse contributes to a worsening of those symptoms in the menopause. Future research should continue to investigate predictors of menopausal symptoms among sexual minority women and their effect on sexual minority women’s health later in life.

S-7. Odds Ratios for effects of childhood abuse on menopausal symptoms among sexual minority women

Sheryl Kingsberg, PhD 1, Julia M. Amadio, MBA 2, Shelli Graham, PhD, 1Department of OB/GYN, Case Western Reserve University School of Medicine, Cleveland, OH;2Psychiatry and Psychology, University of Illinois, Chicago, IL;3Health System Sciences, University of Illinois, Chicago, IL

Objective: To improve understanding of the reasons why women do or do not use prescription (Rx) therapies for VVA and to identify women’s perceptions of VVA.

Notes: N=112; OR=Odds Ratio; CI=Confidence Interval; Adjusted models control for age, race/ethnicity, education, BMI, anxiety, and tobacco use and alcohol use.

The recording with lower estradiol levels (23.3 ± 2.5 pg.ml^-1) and the recording with higher estradiol levels (54.9 ± 35.8 pg.ml^-1) showed that women had more hot flashes (Wilcoxon signed rank test, Z = 2.1, p = 0.036) and tended to have a greater percentage of hot flash-associated wake (Wilcoxon signed rank test, Z = 1.78, p = 0.07) on the night with lower estradiol levels. Conclusion: Lower estradiol levels are associated with a greater impact of hot flashes on sleep, as determined from an objective measure of hot flash-associated wake time, in women in the menopausal transition. Longitudinal data are required to confirm whether hot flashes have an increasingly greater negative impact on sleep as women transition menopause and estradiol levels decline.

THURSDAY CONCURRENT SESSION #2
S-8. Clinician Knowledge, Attitudes, and Barriers to Diagnosis and Treatment of Genitourinary Syndrome of Menopause: Variations in Primary Care and Gynecology

Kimberly Vesco, MD, MPH1,2; Kate Beadle, NP3; Amanda Clark, MD, MCR4; Joanne Bullock, PhD, MPH5; Ashley Stoneburner, MPH6; Michael Leo, PhD, MPhil7; Center for Health Research, Kaiser Permanente Northwest, Portland, OR; Department of Obstetrics and Gynecology, Kaiser Permanente Northwest, Portland, OR

**Objective:** Nearly 50% of postmenopausal women experience symptoms related to genitourinary syndrome of menopause (GSM). However, many clinicians ask about GSM symptoms from circulating but decreasing DHEA activity.

**Methods:** In an effort to improve the diagnosis and management of GSM, we assessed clinician knowledge, attitudes, and barriers regarding its diagnosis and management. **Design:** We developed a survey that included 3 content areas: Knowledge: 8 multiple-choice questions about GSM prevalence, diagnosis and treatment; Attitudes: 3 Likert-scale questions asking clinicians to report their likelihood of assessing for GSM at routine visits and confidence in ability to counsel patients about GSM; and Barriers: a 12-item list with instructions to check all that apply. We conducted the survey on-line using SurveyMonkey. Our health system data showed that most well-care visits for women ≥55 years (82%) are conducted in Primary Care (PC; Family Practice/Internal Medicine); our survey targets both PC and Gynecology (Gyn) clinicians in our health system with valid addresses (363 of 368). We allowed 4 weeks for a response and sent 2 reminder emails. **Results:** The survey response rate was 33% (120/363). The respondents were representative of the overall PC and Gyn clinician population in age (mean 47.8 years, gender (71% female), and clinician type (76% PC). Overall, 67% of knowledge questions were answered correctly, with some variability between Gyn (78% correct, range 37%-97%) and PC clinicians (64% correct, range 18%-97%). Compared to PC, more Gyn clinicians reported being highly likely to assess for GSM at routine visits (78% vs. 62%) and reported being highly or very highly confident in counseling about GSM symptoms (73% vs. 33%) and in advising on risks/benefits of vaginal estrogen (77% vs. 30%). Lack of time was the most commonly reported barrier to GSM diagnosis and treatment (Table). Although PC and Gyn clinicians indicated that patients sometimes felt discomfort discussing GSM, there was a lack of therapeutic options. Some non-users simply refused to consider an Rx therapy and actively sought other options. OTC products helped with milder symptoms but did not moderate to severe pain. Attitudes were very different between Rx users and Rx non-users.

**Conclusion:** Nearly 50% of postmenopausal women experience symptoms related to genitourinary syndrome of menopause (GSM). However, many clinicians ask about GSM symptoms from circulating but decreasing DHEA activity.

S-9. Efficacy of intravaginal dehydroepiandrosterone (DHEA) on dyspareunia and on the FSFI questionnaire in vulvovaginal atrophy due to menopause

Fernand Labrie1, David F. Archer, MD, NCMP2, David J. Portman, MD3, Marlene Montesinos1, Isabelle Côté1, Lyne Laviole1, Celine Martel1, John Balser4, Erick Moyneur5, EndoCetux Inc., Quebec, QC, Canada; 4CONRAD Clinical Research Center, Norfolk, VA; 5Columbus Center for Women’s Health Research, Columbus, OH; 6StatLog Consulting Inc, Ottawa, ON, Canada; 7Veristat, Holliston, MA

**Objective:** The aim of this study was to confirm the beneficial effects of intravaginal dehydroepiandrosterone (DHEA, prasterone) on severe dyspareunia or pain at sexual activity, the most frequent symptom of vulvovaginal atrophy (VVA) or of the genitourinary syndrome of menopause (GSM). **Design:** In a prospective, randomized, double-blind and placebo-controlled phase II clinical trial, the effect of daily intravaginal administration of dehydroepiandrosterone (6.5 mg) (prasterone) was examined in women seeking treatment for dyspareunia or lubrication difficulties, namely percentage of parabasal cells, percentage or superficial cells, vaginal pH and moderate to severe pain at sexual activity (dyspareunia) identified by the women as their most bothersome VVA symptom. **Methods:** The intent-to-treat (ITT) population included 157 and 325 women in the placebo- and DHEA-treated groups, respectively. **Results:** After daily intravaginal administration of 0.50% DHEA for 12 weeks, when compared to baseline the ANCOVA test, the percentage of parabasal cells decreased by 27.7% over placebo (p<0.0001) while the percentage of superficial cells increased by 8.4% over placebo (p=0.0011), vaginal pH decreased by 0.66 pH unit over placebo (p=0.001) and pain at sexual activity decreased by 1.42 severity score unit from baseline 0.36 unit over placebo (p=0.0002). On the other hand, moderate to severe vaginal dryness present in 84.0% of women improved at 12 weeks by 1.44 severity score unit compared to placebo (p=0.0001). The FSFI was observed and confirmed (prasterone vs placebo). A 33.0% ( orgasm, p=0.047) to 56.8% (arousal, p=0.0022) increase over placebo in all the six sexual domains was observed. No adverse events were reported. The safety evaluation showed no significant change in vaginal pH and no change in vaginal flora compared to placebo. A high responder rate of this treatment essentially based upon the novel understanding of the physiology of sex steroids in postmenopausal women when all sex steroids are made locally in pelvic tissues from circulating but decreasing DHEA activity.

S-10. Local Estrogens for Genitourinary Symptoms of Menopause. Does the Method of Treatment (Tablets or Cream) Change the Compliance and Adherence to Treatment?

Israel Yoles, MD1, Tuvia Bayesky, MD1, Alina Weissmann-Brenner, MD2, Clalit Health Services, Central District, Israel; 1The Sheba Medical Center, Ramat Gan, Israel

**Objective:** Prior studies have showed that local estrogens for the treatment of genitourinary symptoms of menopause are well-tolerated and effective. Thus, we hypothesized that the efficacy and adverse effects of both estrogen- containing vaginal tablets (VT) and cream (CV) are comparable. In this study, we gathered real world data of vaginal estrogen treatment in a large cohort of Israeli women, and compared the compliance...
and adherence to treatment with VT vs. VC. **Design:** This study includes data from a large population in the Central District of “Clalit Health Services”, the largest HMO in Israel. All demographic data, as well as treatment utilization, were electronically recorded. Following the approval by the Clalit IRB, we analyzed data on the use of VT and VC over a nine-year period, from January 2006 to December 2014. During the study period, 87,184 women aged 40 and older were registered in this district. Patient age ranged between 40-89 years at entry. “Sporadic” users (patients filling fewer than 4 prescriptions) were not included in the analysis. We defined patients as compliant to treatment if the treatment interval between prescriptions was less than 90 days. Patients were defined as adherent if they followed the treatment regimen over the entire period of estrogen treatment. Student’s t-test was used to compare between treatments. **Results:** 21,674 patients, i.e. 25% of the age-matched women, received at least one local estrogen prescription during the study period, of which 252 were lost to follow-up. Of the remaining 21,422 patients, 17,648 (82%) were sporadic users and were therefore excluded from the study. In total, 3,774 women were eligible for analysis, of which 2,269 (60%) used only one type of treatment (monotherapy), while 1,505 (40%) switched between treatments (switchers). The switchers were not analyzed in the current study. The mean age was 59±9 yrs. In the monotherapy group, 487 (21%) used VT and 1782 (79%) used VC. In the VT group 314/487 (64%) were found to be compliant, as opposed to only 699/1782 (39%) in the VC group. Compliant patients in the VT group adhered to treatment for 1002±38 days as compared to adherence of only 787±25 days in the VC group (significant difference, t-test p<0.010, Fig. 1). **Conclusion:** In the monotherapy group, compliance with vaginal estrogen tablets therapy was higher than with vaginal cream. Additionally, the mean duration of VT usage was significantly longer than with VC. Since the efficacy of VT and VC are considered similar, one possible explanation of these findings may be the difference in the ease of usage between locally applied creams and tablets. In addition, utilization of local estrogens, in general, by postmenopausal women, was extremely low: only one quarter of the population ever used local estrogens, 82% of patients filled prescriptions sporadically and only 5% of the women over 50 years of age repeatedly applied any kind of local estrogen. Since, in some degree, menorrhagia symptoms affect most menopausal women, these findings are a loud call for action.

### Table 1: Genome-wide association study results by study sample and combined in meta-analysis.

<table>
<thead>
<tr>
<th>SNP</th>
<th>Combined Meta-Analysis Odds Ratio</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1.20 (1.10-1.31)</td>
<td>0.003</td>
<td></td>
</tr>
</tbody>
</table>

Carolyn J. Crandall, MD, PhD1, Emma Barinas-Mitchell, PhD2, J. Richard Jennings, PhD3, Nanette Santoro, MD4, Roland von Känel, PhD5, Yuefang Chang6, Doug Landsittel, PhD7, Karen A. Matthews, PhD2. 1Department of Psychiatry, University of Pittsburgh, Pittsburgh, PA; 2Department of Epidemiology, University of Pittsburgh, Pittsburgh, PA; 3Department of Obstetrics and Gynecology, University of Colorado at Denver, Denver, CO; 4Department of Neurology, Inselspital, Bern University Hospital, and University of Bern, Bern, Switzerland; 5Department of Neurosurgery, University of Pittsburgh, Pittsburgh, PA; 6Department of Medicine, University of Pittsburgh, Pittsburgh, PA; 7Department of Obstetrics and Gynecology, University of Pittsburgh, Pittsburgh, PA. **Objective:** Emerging research suggests relations between menopausal hot flashes and subclinical cardiovascular disease (CVD) among midlife women. However, findings have largely been derived from post hoc analyses of studies of brief self-report measures of hot flashes without memory and reporting biases. Here we present data on the first large-scale study designed to test whether physiologically-assessed hot flashes are associated with elevated carotid intima media thickness (IMT), a widely used measure of subclinical CVD, and over and above standard CVD risk factors. **Design:** 255 non-smoking midlife aged 40-46 women free of clinical CVD, 134 who reported having daily hot flashes and 121 who reported no current hot flashes were recruited. No women were taking beta blockers, calcium channel blockers, insulin, or medications known to impact hot flashes. Women underwent 24 hours of physiologic hot flash monitoring to quantify the physiologic frequency of hot flashes over 3 days of electronic diary data. Data were collected and completed at the time of the hot flash to quantify the self-reported frequency, severity, and bother associated with hot flashes. Women also underwent anthropometric measures; a blood draw for assessment of lipids, glucose, insulin, and estradiol (quantified via liquid chromatography-tandem mass spectrometry); and a carotid ultrasound for assessment of IMT. Relations between hot flashes and subclinical CVD indices were examined controlling for age, race, body mass index (BMI), systolic blood pressure (SBP), lipids, the homeostatic model assessment (HOMA), and use of lipid-lowering, anti-hypertensive, and anti-diabetic medications. Estradiol and menopausal stage were also considered as covariates. **Results:** Women were on average 54 years old, overweight (BMI=29), and postmenopausal (83%). 29% were nonwhite. Almost half (n=57, 47%) of the 121 women reporting not having hot flashes at enrollment showed physiologic hot flashes. Women with and without hot flashes were not statistically different on any of the above-mentioned variables (aged 40-46) as determined by a chi-square test on categorical and ANOVA on continuous variables. **Conclusion:** This is the first study to date to test whether physiologically-assessed hot flashes, a greater frequency of waking physiologically-assessed hot flashes, particularly among women showing physiologic hot flashes, was associated with significantly higher mean IMT [β(SE)=0.003 (.001), p=0.004] and maximal IMT [β(SE)=0.004 (.001), p=0.003] as well as individual segments bulb IMT [β(SE)=0.005 (.002), p=0.009] and internal carotid artery IMT [β(SE)=0.003 (.001), p=0.03]. Findings persisted after controlling for estradiol and menopausal stage, neither of which was related to IMT. Greater diary-reported frequency [β(SE)=0.006 (.003), p=0.03] and severity [β(SE)=0.03 (.009), p=0.002], and bother [β(SE)=0.03 (.009), p=0.002] of hot flashes were also associated with higher mean IMT in women reporting hot flashes in multivariable models. Notably, physiologic hot flashes accounted for a comparable or greater amount of variance in IMT in women with hot flashes than standard CVD risk factors including BMI, lipids, HOMA, or SBP. **Conclusion:** This is the first study to date to test whether physiologically-assessed hot flashes were associated with higher IMT. More frequent, severe, or bothersome hot flashes were robustly associated with higher IMT, particularly among women with hot flashes. These associations were not accounted for by traditional CVD risk factors or by endogenous estradiol and were strongest for physiologically-measured hot flashes. The magnitude of the association between physiologic hot flashes and IMT was at least as strong as that of standard CVD risk factors. Research findings support further studies linking hot flashes and CVD risk.

### S-12. Physiologically monitored hot flashes and subclinical cardiovascular disease among midlife women

Rebecca C. Thornton, PhD1,2, Emma Barinas-Mitchell, PhD2, J. Richard Jennings, PhD3, Nanette Santoro, MD4, Roland von Känel, PhD5, Yuefang Chang6, Doug Landsittel, PhD7, Karen A. Matthews, PhD2. 1Department of Psychiatry, University of Pittsburgh, Pittsburgh, PA; 2Department of Epidemiology, University of Pittsburgh, Pittsburgh, PA; 3Department of Obstetrics and Gynecology, University of Colorado at Denver, Denver, CO; 4Department of Neurology, Inselspital, Bern University Hospital, and University of Bern, Bern, Switzerland; 5Department of Neurosurgery, University of Pittsburgh, Pittsburgh, PA; 6Department of Medicine, University of Pittsburgh, Pittsburgh, PA. **Objective:** Emerging research suggests relations between menopausal hot flashes and subclinical cardiovascular disease (CVD) among midlife women. However, findings have largely been derived from post hoc analyses of studies of brief self-report measures of hot flashes without memory and reporting biases. Here we present data on the first large-scale study designed to test whether physiologically-assessed hot flashes are associated with elevated carotid intima media thickness (IMT), a widely used measure of subclinical CVD, and over and above standard CVD risk factors. **Design:** 255 non-smoking midlife aged 40-46 women free of clinical CVD, 134 who reported having daily hot flashes and 121 who reported no current hot flashes were recruited. No women were taking beta blockers, calcium channel blockers, insulin, or medications known to impact hot flashes. Women underwent 24 hours of physiologic hot flash monitoring to quantify the physiologic frequency of hot flashes over 3 days of electronic diary data. Data were collected at the time of the hot flash to quantify the self-reported frequency, severity, and bother associated with hot flashes. Women also underwent anthropometric measures; a blood draw for assessment of lipids, glucose, insulin, and estradiol (quantified via liquid chromatography-tandem mass spectrometry); and a carotid ultrasound for assessment of IMT. Relations between hot flashes and subclinical CVD indices were examined controlling for age, race, body mass index (BMI), systolic blood pressure (SBP), lipids, the homeostatic model assessment (HOMA), and use of lipid-lowering, anti-hypertensive, and anti-diabetic medications. Estradiol and menopausal stage were also considered as covariates. **Results:** Women were on average 54 years old, overweight (BMI=29), and postmenopausal (83%). 29% were nonwhite. Almost half (n=57, 47%) of the 121 women reporting not having hot flashes at enrollment showed physiologic hot flashes. Women with and without hot flashes were not statistically different on any of the above-mentioned variables (aged 40-46) as determined by a chi-square test on categorical and ANOVA on continuous variables. **Conclusion:** This is the first study to date to test whether physiologically-assessed hot flashes were associated with higher IMT. More frequent, severe, or bothersome hot flashes were robustly associated with higher IMT, particularly among women with hot flashes. These associations were not accounted for by traditional CVD risk factors or by endogenous estradiol and were strongest for physiologically-measured hot flashes. The magnitude of the association between physiologic hot flashes and IMT was at least as strong as that of standard CVD risk factors. Research findings support further studies linking hot flashes and CVD risk.

### S-13. Effect of Postmenopausal Hormone Therapy on the Severity of Myocardial Infarction

Pauliina Tuomikoski, Adjunct Professor1, Aki Havalimaa1, Veikko Salomaa1, Tomi Mikkola1,2. 1Department of Obstetrics and Gynecology, Helsinki University Hospital, HUS Helsinki, Finland; 2Tikkurila Research Center, Helsinki, Finland; 3THL-National Institute for Health and Welfare, Helsinki, Finland. **Objective:** Acute myocardial infarction (MI) is still the leading cause of death in women. In general, pre-hospital case-fatality in women is 25-30%, and 1-year case-fatality as high as 50%. Luckily total mortality to coronary heart disease is declining due to an increase in...
survival after MI. Postmenopausal hormone therapy (HT) confers cardiovascular benefits in terms of reduced coronary heart disease, if treatment is initiated to a healthy woman who is younger than 60 years, or less than 10 years postmenopausal. Less is known about the outcomes of myocardial infarction (MI) in HT users. Design: Register-based cohort study of 64,698 women aged 40 years who started HT in the years 1994-1996, registered in the Reimbursement Database. Data on HT purchases are available from 1994 onwards. In Finland HT regimens require a doctor’s prescription and they can be bought only for a 3-months need at time. Therefore repeat entries into the Reimbursement register confirm that the woman continued HT once prescribed. SAMI is a registry-based, longitudinal study on all acute coronary events on four regions in Finland. The FINAMI data also include information about the patients previous MIs, smoking status, levels of lipids and cardiac enzymes, treatment of the coronary event in question and case fatality. By comparing these databases we studied the association between the incidence of MI and the possible impact of continued/discontinued HT use and the risk of reinfarction. Results: We acquired data on MIs in 12 483 women during 1995 to 2005. Overall, in women with acute MI, the use of HT was associated with a 31% (p=0.001) reduced risk of death within 28 days from the MI, as compared with non-users. The use of systemic HT was associated with a 44% (p<0.001) lower risk of 28-day case-fatality, whereas the use of vaginal estrogen use did not confer a significant reduction in this mortality risk (OR 0.80, p=0.053). Conclusion: Our preliminary data imply that systemic HT use is associated with a decreased risk of death due to MI. Further analyses on the association between various lengths of HT use and the severity of MI, immediate, 28-day, and 1-year case-fatality, will be completed in the coming months. Interesting data is pointing on the possible impact of HT discontinuation on the risk of reinfarction will also be investigated.

S-14. Endometrial effects of lasofoxifene: Results from two phase 3 osteoporosis prevention trials
Steven R. Goldstein, MD1, David Portman, MD2, James Symons, MS, PhD3. 1NYU School of Medicine, New York, NY; 2Merck Serono, New Jersey, NJ; 3Sankyo Pharmaceutical, Columbus, OH

Objective: Unopposed estrogens and tamoxifen confer an increased incidence of endometrial hyperplasia and endometrial cancer in a dose- and duration-dependent manner. Several selective estrogen receptor modulators (SERMs) halded in development have also been associated with similar unfavorable endometrial effects. An extensive endometrial effect analyses included postmenopausal women without prior hysterectomy (n=21). For all lasofoxifene treatment groups after 24 months, endometrial thickness ≥8 mm occurred in approximately 1.7% of lasofoxifene subjects compared with 0.8% (2/243) in placebo- group (n=475).

Conclusion: The incidence of vaginal bleeding was comparable between lasofoxifene and placebo. For all lasofoxifene treatment groups after 24 months, endometrial thickness ≥8 mm occurred in approximately 10% of lasofoxifene subjects in a non-dose dependent manner and approximately 3% of placebo subjects. All histopathological assessments from these subjects were benign. The incidence of vaginal bleeding (preferred term: vaginal hemorrhage) in the lasofoxifene treatment groups (n=1419) ranged from 1.5% to 1.7% compared with 1.9% in the placebo group (n=475). Lasofoxifene in postmenopausal non-Mayan women was not associated with an increase in endometrial hyperplasia or carcinoma. After 24 months, the incidence of endometrial hyperplasia or carcinoma was 0.4% (3/773) for all lasofoxifene-treated subjects compared with 0.8% (2/243) in placebo-treated subjects. Sub-endometrial cystic ectopy was observed in the lasofoxifene treatment groups (1.7%) and the placebo group (0.8%). The incidence of vaginal bleeding was comparable between the lasofoxifene groups and the placebo group. Lasofoxifene for the prevention of osteoporosis has a safe endometrial profile out to 24 months. Published gynecologic effects included endometrial thickening, which was observed in natural menopause and postmenopausal non-Mayan women.

S-15. Objective and subjective hot flashes in the city of Campeche, Mexico
Lynnette L. Sievert, PhD1, Laura Huicochea Gomez, PhD2, Diana Cahuich Campos, PhD2, Daniel E. Brown, PhD1. 1Anthropology, Univ. of Mass. Amherst, Amherst, MA; 2Area de Sociologia, Cultura y Salud, El Colegio de la Frontera Sur, Campeche, Mexico

Objective: Hot flashes associated with the hormonal changes of menopause can cause considerable discomfort, and can last for 10 years or longer. Human biologists have shown population differences in heat dissipation responses, e.g., the number and location of sweat glands, and the quantity of sweat produced. These differences may impact the experience of hot flashes. We report on an analysis of the incidence of hot flashes. Previous research found that women in Mexico described hot flashes on the back of the neck, in addition to the more common U.S. pattern of hot flashes on the face and upper chest. The purpose of this study was to document the experience of hot flashes in Campeche, Mexico, and whether ambulatory hot flashes measured across the sternum and back of the neck correspond with subjective report. Ethnicity was examined in relation to hot flashes, with the expectation that Mayan women would be less likely to report and demonstrate hot flashes. Design: Women aged 40 to 55 were recruited throughout the city of Campeche by opportunity sampling and snowball techniques. Mayan and non-Mayan ancestry was defined by birth place, last names, and language spoken by the participant, her parents, and her grandparents. Women participated in face-to-face interviews with structured questionnaires that queried symptom frequencies during the past 2 weeks. A body diagram was used to show where women felt the heat of hot flashes and the sweating associated with hot flashes. Women who were peri-menopausal (with irregular periods) or early post-menopausal (up to 2 years after the final menstrual period) were invited to wear a 2-channel Biolomab ambulatory hot flash monitor for 24 hours. Electrodes were placed 4” apart on the sternum and back of the neck. To date, 187 women have participated in interviews. Of those, 53 women were a hot flash monitor. Results: The sample consists of women of Mayan ancestry (n=59), non-Mayan ancestry (n=55), and women for whom we were unable to classify ancestry (n=17). Among the first 20 women who reported at least one subjective hot flash, frequency of concordance was very similar occurring on the upper chest (73%), face (69%), front of neck (69%), and back of neck (58%). Sweating was described most often on the face (56%), upper chest (49%), front of neck (38%), back (40%), and back of neck (33%). Mayan women and women not classified by ancestry reported hot flashes on the face and upper chest more frequently than non-Mayan women (50%, p<0.01). The same pattern was true for the front of the neck (p=0.06), with no other significant differences in where hot flashes occurred. Hot flash monitors were worn for an average of 2.1 hours (s.d., 0.4 hours). Among the first 27 women who wore the monitors, the number of objective sternal hot flashes ranged from 0 to 22, with a mean of 5.2 (s.d., 5.3), and nuchal hot flashes ranged from 0 to 14, with a mean of 5.9 (s.d., 4.0). The number of subjective hot flashes ranged from 0 to 6 with a mean of 1.3 (s.d., 1.6). There was no significant difference between Mayan women and non-Mayan women in the number of objective or subjective hot flashes. Among women who reported at least one subjective hot flash, frequency of concordance was very similar between sternal (1.1, s.d. 1.9, range 0 to 3) and nuchal (1.2, s.d. 1.2, range 0 to 4). The frequency of subjective/objective concordance did not differ by ethnicity. Conclusion: About half of women experienced vasomotor symptoms around the time of menopause, without variation by ethnicity. Subjective, but not objective, patterns of heat dissipation differed by ethnicity. Rates of concordance were similar between subjective and objective sternal vs. nuchal measures. This study is on-going, with data collection in rural communities as well as the city of Campeche. Funding: NSF Grant #BCS-1156368

S-16. Baseline Anti-Mullerian hormone (AMH) is associated with incident natural menopause in the CARDIA Women’s Study (CWS)
Sangeeta Nair1, James Terry1, Chris Slaughter2, Duke Appiah1, Imo Ebong3, Cora Lewis4, Pamela Schreiner2, David Siscovick1, Erica Wang1, Edmond Kabagambe1, Melissa Wellons, MD, MHS1. 1Vanderbilt University, Nashville, TN; 2University of Minnesota, Minneapolis, MN; 3Loma Linda University, Loma Linda, CA; 4University of California, Birmingham, Birmingham, AL; 5The New York Academy of Medicine, New York, NY; 6Cedars-Sinai, Los Angeles, CA

Objective: The timing of menopause is associated with future risk of cardiovascular disease, cancer and osteoporosis. Previously in CWS, we have shown that ultrasound-measured antral follicle count (AFC) can predict incident menopause up to 7 years later, and AFC measured after menopause is a biomarker of the time to menopause. Anti-Mullerian Hormone (AMH) is a more readily obtained serum biomarker of incident menopause. In cross-sectional studies, AMH appears to peak in women around 25 years of age and then gradually declines, disappearing by age 50, near the average age for many events across a lifetime. AMH has been implicated in the reproductive age span of women, and US women, AMH is associated with the timing of menopause. In one Dutch study (n=257) that also investigated AFC, AMH was the only biomarker associated with menopause after adjustment for age. Our aim here is to establish AMH’s age-independent association with natural menopause and examine any incremental value of AFC. The Coronary Artery Risk Development in Young Adults Study (CARDIA) is a longitudinal population-based study (Chicago, IL; Birmingham, AL; Minneapolis, MN; and Oakland, CA) that recruited 18-30 year olds when it began in 1985-86. In 2002-2003, a subset of CARDIA women, the CARDIA Women’s Study (CWS), had biologic samples collected from 1995 to 1996 and AMH was measured by ELISA.
ultrasonography performed with AFC measured (2-10 mm follicles on both ovaries) and serum collected and stored for potential future use. In 2014, we measured AMH in stored samples from all CWS women with serum available. AMH was measured using the Aush ultrasensitive method ELISA kit (ReproSource Laboratory (Boston, MA)) with a detection limit of 0.08 ng/mL. Follicle stimulating hormone (FSH) and estradiol were also measured. Demographic information, smoking history, and reproductive characteristics were obtained from self-report. BMI was calculated from measured height and weight in kg/m². Incident natural menopause was determined by self-report through the Year 25 CARDIA exam (2010-2011). We analyzed the crude and adjusted associations of serum AMH with incident natural menopause using logistic regression analysis. Women self-reporting prevalent natural menopause, prevalent hysterectomy, or incident hysterectomy were excluded from analyses. Models included age (years), race (black vs. white), CARDIA site, smoking history (never vs. current, past), education (at least some college vs. >high school), menopausal characteristic (stable menses vs. all other answers), FSH (ng/dL), estradiol (ng/dL) and BMI. Results: In our sample of initially premenopausal women with measured AMH (n=34-49) who completed the Year 25 CARDIA survey on menopause and denied hysterectomy (n=703), 195 women reported natural menopause, 9 years after initial AMH measurement. Among all women in our sample, the median AMH was 0.76 ng/dL and the 25% to 75% interquartile range/IQR was 0.22-1.98 ng/dL. Fifteen percent (n=105/703) had AMH below the limit of detection of the assay (0.08 ng/mL). Associations of serum AMH with incident menopause over 9 years were measured for a 0.5 ng/dL lower AMH had a 3-fold higher crude odds of experiencing menopause over 9 years of follow-up (OR 3.19; 95% CI, 2.49-4.10) and 2-fold higher odds after adjustment for all covariates (OR 2.22; 95% CI, 1.76-2.86). Conclusion: Baseline AMH is inversely associated with natural menopause over 9 years of follow-up, controlling for demographic information and clinical markers of ovarian aging. We are currently comparing the utility of AMH, AFC, and FSH as biomarkers of the timing of future natural menopause. These analyses are needed to establish the most useful biomarker, or combination of biomarkers, to predict the timing of natural menopause in CARDIA women.

S-17. The association between menopausal hormone therapy and coronary heart disease depends on timing of initiation in relation to menopause onset. Results based on pooled individual participant data from The Combined Cohorts of Menopausal Women – Studies of Register Based Health Outcomes in Relation to Hormonal Drugs (COMPREHEND) study.

German D. Carraquilla, PhD student1, Chiara Chiavenna1, Matteo Bottai2, Patrik K. Magnusson1, Michele Santacattarina1, Alicia Wolk1, Göran Hallmans3, Jan-Håkan Jarvholm4, Göran Engström5, Christo Borgfeldt6, Nancy L. Pederson7, Mats Eliasson8, Anita Berglund2, Karin Leander1. 1Inst. of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden; 2Dept. of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden; 3Dept. of Biobank Research, Umeå University, Umeå, Sweden; 4Dept. of Clinical Sciences, Lund University, Lund, Sweden; 5Dept. of Clinical Sciences, Lund University, Lund, Sweden

Objective: Menopausal hormone therapy (MHT) use has been intensely debated since menopause onset) was associated with a shorter time period free from CHD events: 0.07 years (95% CI -0.13, 0.27) in the unadjusted model, 0.09 years (95% CI -0.10, 0.27) in the multivariable model, and 0.07 years (95% CI -0.10, 0.22) in the model adjusted for smoking, BMI, and educational level. In logistic regression models, baseline AMH, age, and race were independently associated with incident natural menopause over 9 years. Adjustments were made for age (years), education (< high school, Menstrual characteristic (stable menses vs. all other answers), race (black vs. white), CARDIA site, smoking history (never vs. current, past), education (at least some college vs. >high school), and BMI. Results: In our sample of initially premenopausal women with measured AMH (n=34-49) who completed the Year 25 CARDIA survey on menopause and denied hysterectomy (n=703), 195 women reported natural menopause, 9 years after initial AMH measurement. Among all women in our sample, the median AMH was 0.76 ng/dL and the 25% to 75% interquartile range/IQR was 0.22-1.98 ng/dL. Fifteen percent (n=105/703) had AMH below the limit of detection of the assay (0.08 ng/mL). Associations of serum AMH with incident menopause over 9 years were measured for a 0.5 ng/dL lower AMH had a 3-fold higher crude odds of experiencing menopause over 9 years of follow-up (OR 3.19; 95% CI, 2.49-4.10) and 2-fold higher odds after adjustment for all covariates (OR 2.22; 95% CI, 1.76-2.86). Conclusion: Baseline AMH is inversely associated with natural menopause over 9 years of follow-up, controlling for demographic information and clinical markers of ovarian aging. We are currently comparing the utility of AMH, AFC, and FSH as biomarkers of the timing of future natural menopause. These analyses are needed to establish the most useful biomarker, or combination of biomarkers, to predict the timing of natural menopause in CARDIA women.

S-18. Increases in High Density Lipoprotein-Cholesterol Levels are Associated with Greater Intima-Media Thickness Progression over The Menopausal Transition: The Study of Women’s Health Across the Nation (SWAN)

Samar R. El Khoudary, PhD, MPH1, Lin Wang2, Maria M. Brooks3, Rebecca C. Thurston, PhD1, Carol Derby1, Karen A. Matthews1. University of Pittsburgh, Pittsburgh, PA; 2Albert Einstein College of Medicine, Bronx, NY

Objective: Experimental and observational evidence demonstrates that high density lipoprotein (HDL) can lose its well-documented atheroprotective functions and adopt a paradoxically proinflammatory nature in certain conditions. Hormonal alterations, especially estradiol reduction, influence the accumulation of risk factors that could potentially impair the quality of HDL as women transitioning through menopause. Limited data exist to evaluate the relationship between changes in high density lipoprotein cholesterol (HDL-C) over the menopausal transition and the progression of atherosclerosis in women. We evaluated the association between changes in HDL-C and progression of carotid intima-media thickness (cIMT) since the final menstrual period (FMP) in a sample of midlife women. Design: Participants were from the Study of Women’s Health Across the Nation (SWAN) Pittsburgh site, who had up to 5 measures of cIMT over a maximum of 9 years of follow-up. Women were free of cardiovascular disease (CVD) at the baseline scan. Time points at which women were on hormone therapy or lipid lowering medications were excluded. Linear mixed effects models with a random intercept were used to model longitudinal measures of cIMT. Repeated measures of cIMT-C were coded using separate interactions between time since FMP and HDL-C at baseline and, and between time since FMP and change in HDL-C since baseline to assess the cross-sectional and the longitudinal effects of HDL-C on cIMT progression, respectively. Final models included age at baseline, time since FMP, race, education, and time-varying covariates: systolic blood pressure (SBP), body mass index (BMI), low density lipoprotein cholesterol (LDL-C), menopausal status, and use of CVD medications. Results: The study included 225 women (28% Black, 72% White), who had up to 5 measures of cIMT-C over a maximum of 9 years of follow-up. Women were free of cardiovascular disease (CVD) at the baseline scan. Time points at which women were on hormone therapy or lipid lowering medications were excluded. Linear mixed effects models with a random intercept were used to model longitudinal measures of cIMT. Repeated measures of cIMT-C were coded using separate interactions between time since FMP and HDL-C at baseline and, and between time since FMP and change in HDL-C since baseline to assess the cross-sectional and the longitudinal effects of HDL-C on cIMT progression, respectively. Final models included age at baseline, time since FMP, race, education, and time-varying covariates: systolic blood pressure (SBP), body mass index (BMI), low density lipoprotein cholesterol (LDL-C), menopausal status, and use of CVD medications. Conclusion: These findings are needed to establish the most useful biomarker, or combination of biomarkers, to predict the timing of natural menopause in CARDIA women.

S-19. Gamma-oryzanol increases NO production of carotid artery in ovariectomized rats

Makoto Iizuka, M.D.1,2, Satoshi Obayashi, M.D., Ph.D.1, Ayumi Yamaguchi, M.S.1, Yoshimichi Okuura, M.D., Ph.D.1, Shuichi Sakamoto, M.D., Ph.D.1, Toshio Kubota, M.D., Ph.D.1. 1Department of Comprehensive Reproductive Medicine, Tokyo Medical & Dental University, Bunkyo-ku, Japan; 2Obstetrics and Gynecology, Dokkyo Medical University Koshigaya Hospital, Koshigaya, Japan

Objective: Loss of ovarian hormones has impairment on endothelial function and results in cardiovascular disease. In Japanese traditional foods, rice bran oil has been used to improve the effect of menopausal symptom and to prevent cardiovascular diseases, but...
its precise mechanism was not clarified. Gamma-oryzanol (gamma-ORZ) is a mixture of phytoestrogen ferulates purified from rice bran oil and we examined whether gamma-ORZ represents some direct effects on the endothelial function including nitric oxide (NO) production. The aim of this study was to determine the bioavailability of gamma-ORZ and possible involvement in arterial function. Design: Twelve weeks female Sprague-Dawley rats underwent abdominal ovariectomy and fed by soy-bean free diet, AIN-93G for 2 months in order to eliminate the effect of endogenous estrogen and phytoestrogens. After 16th week, rats were divided into 3 groups and given the following diets: Group (n=6), AIN-93G; Group 1% gamma-ORZ mixed with AIN-93G; Group 3% gamma-ORZ mixed with AIN-93G. At 18th week, the left carotid arteries were denuded with 2 Fr forgaty balloon catheter to induce intimal hyperplasia and all rats were sacrificed at 20th week. The effect of gamma-ORZ (1% or 3%) on formation of intimal hyperplasia was analyzed with microscopic examination and the effect of gamma-ORZ on NO release function including endothelial NO release in carotid artery were evaluated with isometric tension change. Acetylsalicylic acid (ACh: 10(-9) to 3x10(-6) M) was used as a receptor-mediated endothelium-dependent agonist and A23187 (10(-6) to 3x10(-3) M) was used as a receptor-non-mediated, endothelium-dependent agonist. Two of these agonists induced relaxation with or without NO synthase inhibitor (N^O nitro-L-arginine: LNA: 10(-4) M) under U66619 (10(-7) M) evoked contraction, was recognized as NO release marker. Sodium nitroprusside (SNP; 10(-10) to 3x10(-5) M) as an NO donor was used to evaluate NO sensitivity of smooth muscle. The plasma ferrate acid (FA) concentration as the metabololite of gamma-ORZ was also assessed by high performance liquid chromatography (HPLC). All results are expressed as mean ± S.D. Statistical analysis were performed with t-test or two-way ANOVA with Stat View J 5.0 program and values of p<0.05 were considered as statistically significant. All studies compiled with the Animal Welfare Regulations of the Tokyo Medical and Dental University. Results: There were no significant differences in body weights among 3 groups. In gamma-ORZ groups, the plasma concentration of FA were significantly higher (1% group, 70.1±11.9 (ng/ml) ; 3% group, 70.9±10.2) compared with control group (CON: 53.3±3.0). Plasma glucose levels for gamma-ORZ groups indicated higher reduction in intima/media ratio (0.63±0.59 and 0.66±0.53, respectively) than control group (1.30±0.61). The relaxation response induced by ACh (3x10(-6) M) was significantly higher in 3% group (71.6±5.1 (%) ) than control group (CON: 53.3%). However, no significant differences were observed compared with 1% group (57.9±8.4 (%)). And these relaxations were significantly inhibited by NLA pretreatment (CON: 9.3±5.9(%) ; 1% group, 8.4±6.0 ; 3% group,5.1±3.5). On the other hand, no significant differences were observed in both A23187 (3x10(-6) M) and SNP (10(-6) M) induced relaxation responses among 3 groups which suggested the remaining post receptor signal transduction in these groups. Conclusion: In isoflavone free condition, gamma-ORZ administration enhanced ACh stimulated vasodilation through ACh membrane receptor level or post receptor level modification. Gamma-ORZ demonstrates some direct effects on the endothelial function including nitric oxide (NO) production and possible involvement in arterial function.

FRIDAY CONCURRENCE SESSION #2

S-20. Lasofoxifene prevents postmenopausal bone loss: Pooled data from two pivotal 24 month osteoporosis prevention trials

Risa Kagan, MD1, James Symons, MS, PhD, David Portman, MD2. 1University of California, San Diego and Sutter East Bay Medical Foundation, Berkeley, CA; 2Sermonix Pharmaceuticals, Columbus, OH

Objective: Rapid onset of bone loss in menopause predisposes women to lower bone mass and to an ultimate 50% lifetime risk of fragility fracture. Early intervention may help prevent this bone mass and trauma, and estrogenic effects on the vagina, and antagonistic effects on breast tissue. The impact of lasofoxifene on bone mineral density(BMD) and bone turnover markers (BTMs) were the subject of 2 randomized placebo controlled studies in postmenopausal women. Design: Screened postmenopausal women 40-74 years of age with normal or low spinal bone mass were given 1000 mg calcium and 200-500 IU of vitamin D daily during a 6 to 8-week pre-randomization period. A total of 1,907 women (mean age 58.6) were randomized in two trials, approximately 475 each to one of 4 treatment groups: lasofoxifene 0.025mg, 0.25mg, 0.5mg, or placebo. At baseline, the subjects were a mean 10.1 years postmenopausal with an average BMD T-score -1.36 at the lumbar spine (LS: L 1–L4) with no significant baseline demographic differences between treatment groups. 88% remained in the trial for the planned 24 months. 90% had a baseline and at least one on-study lumbar spine BMD and were analyzed for the primary endpoint of percent change from baseline to two years in BMD of the LS. Secondary endpoints included percent change from baseline to months 6, 12, and 24, in BMD for total hip, femoral neck, intertrochanteric area, greater trochanter, and Ward’s triangle and percent change from baseline in BTMs osteocalcin and C-telopeptide (CTX)at Months 6 and 24, and at all timepoints and placebo. The landmark model was used for analysis. Results: Changes from baseline in LS and non-lumbar BMD included treatment group and baseline BMD as covariates. Serum BTMs were rank-transformed and analyzed using linear models. Results: Lasofoxifene, at all doses, and at all time points significantly (p<0.001) increased lumbar spine BMD compared with placebo. At 24 months, lasofoxifene increased mean lumbar spine BMD by 1.5%, 2.2%, and 2.3% for the 0.025mg, 0.25mg, and 0.5mg doses respectively, compared to a 0.7% loss in placebo. The 0.25mg and 0.5mg lasofoxifene groups produced significantly superior BMD responses as early as 6 months when compared to the 0.025mg dose. At 24 months, lasofoxifene increased total hip BMD by 1.4%, 2.0%, and 2.1% in the 0.025mg, 0.25mg and 0.5mg doses respectively, compared to a 0.3% loss in the placebo group. The 0.25mg and 0.5mg doses produced significantly better BMD responses as early as 6 months when compared to the 0.025mg dose. Lasofoxifene at all doses showed significant improvement (p<0.021) to 0.5mg doses and non-vertebral fracture reduction at 5 years with 0.5mg. The present pivotal phase 3 studies identify lasofoxifene in doses of 0.25mg and 0.5mg as an effective option for the prevention of osteoporosis in women seeking the tissue selective benefits of the SERM lasofoxifene.

S-21. Lasofoxifene, an estrogen agonist/antagonist favorably impacts lipid parameters: Results from the Osteoporosis and Lipid Lowering (OPAL) Study

David J. Portman, MD1, James A. Simon, MD, CCD, NCMP, FACOG2, James Symons, MS, PhD1, 1Sermonix Pharmaceuticals, Columbus, OH, 2George Washington, Washington, DC

Objective: Some of the beneficial effects of estrogen on the cardiovascular system in early menopause may be attributable to a favorable impact on lipids, however the traditional cardiovascular risk events trial demonstrated reduced reduction in vertebral fractures at 3 years with the 0.25mg and 0.5mg doses and non-vertebral fracture reduction at 5 years with 0.5mg. The present pivotal phase 3 studies identify lasofoxifene in doses of 0.25mg and 0.5mg as an effective option for the prevention of osteoporosis in women seeking the tissue selective benefits of the SERM lasofoxifene.

Effects of Ospemifene on Lipid and Coagulation Parameters in Postmenopausal Women

David F. Archer1, Corrado Altomare, MD2, Wei Jiang2, Susannah Cort2. 1Eastern Virginia Medical School, Norfolk, VA; 2Shionogi Inc., Florham Park, NJ

Objective: The 24 month OPAL trial randomized 1,907 women (mean age 58.6 years). Approximately 575 were assigned to one of four treatment arms: lasofoxifene 0.025, 0.25, or 0.5mg, or placebo. The two co-primary endpoints of this study were percent change from baseline to 24 months in serum LDL-C (baseline to 6 months, measured by direct assay) in a pre-specified subgroup. This designated Lipid Analysis Subgroup of 575 women required a stable baseline serum LDL-C between 130 and 190 mg/dl after a 6 week, low-fat diet, run-in period and who did not use lipid-lowering medications during the 90 days preceding the trial. The study population at large was also evaluated for lipid effects and safety. Rank-transformed percent change from baseline in LDL-C was analyzed by means of linear models and tests and were done on least square means. Results: Lasofoxifene in the Lipid Analysis Subgroup, at all doses, and at all timepoints (1.5, 3 and 6 months) significantly (p<0.001) reduced serum LDL-C compared to placebo. Lasofoxifene at 0.25mg and 0.5mg decreased LDL-C by 16% and 17% respectively, compared to a 9% reduction with 0.025mg. The difference between 0.025 mg lasofoxifene and the two higher doses were statistically significant (p<0.001). LDL-C was measured for the placebo group. In the overall OPAL cohort, multiple lipid parameters were also evaluated at 12 months. Lasofoxifene at all doses showed significant (p<0.001) reductions in total cholesterol, LDL-C, Apo B-100 and Lp(a). Similar LDL-C reductions of approximately 10% were observed in both this general study population (median at 12 months) and the lipid subgroup (mean at 6 months) for the 0.25mg and 0.5mg lasofoxifene doses.

Conclusion: In the placebo-controlled OPAL study of women with elevated baseline LDL-C as well as in the larger osteoporosis prevention cohort, lasofoxifene had significant beneficial lipid-lowering effects. Additionally, in the lasofoxifene Phase 3 program, CRP was lowered by 13-16%. Of note, in the published 5 year PEARL study of over 8,500 women 67 years of age on average, lasofoxifene was associated with a reduction in coronary heart disease and stroke. The 0.5mg dose statistically reduced major coronary heart events by 32% (primarily coronary revascularization). This differs from the increase in early harm cardiovascular events seen in the Women’s Health Initiative when estrogen-progesterin was initiated later in menopause. The favorable effects of lasofoxifene on lipid parameters and inflammatory markers may help explain its beneficial impact on coronary heart disease reduction in postmenopausal women with osteoporosis. Lasofoxifene offers women a SERM alternative to estrogen, with extraskelatal benefits on the cardiovascular system in addition to its demonstrated favorable effects on breast and vulvo-vaginal health.
controlled clinical trials of ospemifene in postmenopausal women were included. Lipid and coagulation parameters were measured at baseline, and at 12 weeks, 6 months, and 12 months. Lipid parameters included total cholesterol (TC), high density lipoproteins (HDL), low density lipoproteins (LDL), and triglycerides (TG). Coagulation parameters included activated partial thromboplastin time (aPTT), fibrinogen, antithrombin antigen, protein C Ag, and protein S Ag free. Mean±SD percent changes from baseline were calculated. Welch’s t-test was used to compare ospemifene 60 mg/day versus placebo. Subgroup analyses based on age, BMI, and baseline TG level were also conducted. Results: A total of 2,166 participants were randomized in the 6 trials to receive oral daily ospemifene 60 mg (N=1,242) or placebo (N=924). Similar percentages of women completed the studies in the ospemifene (85.4%) and placebo groups (86.8%). Baseline characteristics (age, race, BMI, gynecological history) were similar between groups; the majority of the women were Caucasians with mean age 59 years and mean BMI 26 kg/m². Ospemifene significantly increased HDL and decreased LDL levels, compared with placebo, at 12, 6 months, and 12 months (Table 1). TG and TC levels were not significantly different between the ospemifene and placebo groups, except for TC at 6 months (Table 1). Similar effects on the lipid factors were observed across subgroups based on age, BMI, and baseline TG level. The coagulation parameters, fibrinogen and protein C Ag, significantly decreased from baseline with ospemifene versus placebo at all time points (Table 2). The post-baseline levels of those two factors remained within the normal range in more than 90% of women throughout the study. Conclusion: In this pooled, post-hoc analysis, ospemifene 60 mg/day significantly increased HDL and decreased LDL levels, while having little effect on TG levels, compared with placebo. Such effect of ospemifene on lipids appears to be similar to that of other SERMs. The decreases in fibrinogen and protein C Ag levels in ospemifene-treated women are considered unlikely to have clinical consequences.

### Table 1. Changes in serum lipid levels from baseline to 12 weeks, 6 months, and 12 months with ospemifene 60 mg.

<table>
<thead>
<tr>
<th>Time Points (months)</th>
<th>Mean Percent Change from Baseline (%)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ospemifene 60 mg (N=1,242)</td>
<td>Placebo (N=942)</td>
</tr>
<tr>
<td>TC</td>
<td>-1.07 (977)</td>
<td>-0.16 (715)</td>
</tr>
<tr>
<td>6</td>
<td>-1.06 (974)</td>
<td>-1.65 (954)</td>
</tr>
<tr>
<td>12</td>
<td>-2.98 (342)</td>
<td>-1.56 (88)</td>
</tr>
<tr>
<td>HDL</td>
<td>3.49 (977)</td>
<td>0.23 (715)</td>
</tr>
<tr>
<td>6</td>
<td>5.10 (374)</td>
<td>1.52 (954)</td>
</tr>
<tr>
<td>12</td>
<td>2.28 (342)</td>
<td>-1.91 (88)</td>
</tr>
<tr>
<td>LDL</td>
<td>-5.16 (564)</td>
<td>2.42 (308)</td>
</tr>
<tr>
<td>6</td>
<td>-6.37 (372)</td>
<td>2.37 (954)</td>
</tr>
<tr>
<td>12</td>
<td>-6.90 (340)</td>
<td>-2.13 (88)</td>
</tr>
<tr>
<td>TG</td>
<td>3.93 (977)</td>
<td>6.60 (715)</td>
</tr>
<tr>
<td>6</td>
<td>14.99 (374)</td>
<td>19.15 (954)</td>
</tr>
<tr>
<td>12</td>
<td>13.30 (342)</td>
<td>17.63 (88)</td>
</tr>
</tbody>
</table>

### Table 2. Changes in coagulation parameters from baseline to 12 weeks, 6 months, and 12 months with ospemifene 60 mg.

<table>
<thead>
<tr>
<th>Time Point (months)</th>
<th>Mean Percent Change from Baseline (%)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ospemifene 60 mg (N=1,242)</td>
<td>Placebo (N=942)</td>
</tr>
<tr>
<td>oPTT</td>
<td>-1.95 (617)</td>
<td>0.74 (614)</td>
</tr>
<tr>
<td>6</td>
<td>-1.87 (653)</td>
<td>1.74 (38)</td>
</tr>
<tr>
<td>12</td>
<td>2.04 (57)</td>
<td>5.33 (34)</td>
</tr>
<tr>
<td>Antithrombin antigen</td>
<td>-2.87 (930)</td>
<td>-0.83 (672)</td>
</tr>
<tr>
<td>6</td>
<td>-2.60 (370)</td>
<td>0.64 (94)</td>
</tr>
<tr>
<td>12</td>
<td>10.06 (351)</td>
<td>10.65 (89)</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>-8.65 (655)</td>
<td>-0.76 (650)</td>
</tr>
<tr>
<td>6</td>
<td>-5.96 (63)</td>
<td>6.68 (38)</td>
</tr>
<tr>
<td>12</td>
<td>8.66 (57)</td>
<td>7.29 (34)</td>
</tr>
<tr>
<td>Protein C Ag</td>
<td>-2.65 (931)</td>
<td>0.54 (670)</td>
</tr>
<tr>
<td>6</td>
<td>-3.61 (370)</td>
<td>0.01 (94)</td>
</tr>
<tr>
<td>12</td>
<td>12.51 (352)</td>
<td>6.58 (89)</td>
</tr>
<tr>
<td>Protein S Ag free</td>
<td>5.82 (614)</td>
<td>1.55 (612)</td>
</tr>
<tr>
<td>6</td>
<td>6.06 (63)</td>
<td>5.07 (38)</td>
</tr>
<tr>
<td>12</td>
<td>11.45 (356)</td>
<td>8.48 (34)</td>
</tr>
</tbody>
</table>

### S-23. Time to Transient and Stable Reductions in Hot Flush (HF) Frequency in Postmenopausal Women Using CE/BZA

- **Objective:** Phase 3 trials of conjugated estrogens/bazedoxifene (CE/BZA) reported reductions in HF frequency at 12 wk and beyond, but time to various degrees of improvement is unknown. To help clinicians set patient expectations regarding onset of benefit, this post hoc analysis estimates median time to transient and stable reductions in HF frequency in postmenopausal women using CE/BZA.
- **Design:** In the 12-wk SMART-2 trial of CE0.45mg/BZA20mg and CE0.625mg/BZA20mg, women with ≥7 moderate/severe HF or ≥50% at screening recorded frequency of moderate/severe HF in diaries. We used nonparametric models to estimate median times to transient improvement (first postbaseline day with improvement) and stable improvement (first postbaseline day with improvement maintained for the remainder of the study). Improvement was defined based on reduction in HF frequency. The SAS Proc Lifetest was used. Results: CE/BZA produced transient HF frequency reductions of 40%–100% and stable reductions of 30%–100% significantly faster than PBO (Fig). Median time to a transient 50% reduction was 8 d for CE0.45mg/BZA20 mg, 9.5 d for CE0.625 mg/BZA20mg, and 10 for PBO.
- **Conclusion:** Median time to a stable 50% reduction was 9, 10, and 38 respectively. Median time to a transient 90% reduction was 32 d for CE0.45mg/BZA20mg and 22.5 d for CE0.625mg/BZA20mg vs >12 wk (not reached) for PBO. Median time to a stable 90% reduction was 83 and 29 d, vs >12 wk (not reached). Conclusion: Although women using CE/BZA may not achieve permanent elimination of HFs, HF frequency is likely to be substantially reduced during the first week to month of use. Women can expect ~50% reduction in HF frequency after about 8–10 d; once achieved, this improvement is likely to be sustained quickly with continued treatment. Improvement may vary for individual women. Women should be encouraged on the rapidity of response but cautioned against discontinuing CE/BZA prematurely as greater reductions in HF frequency are expected as treatment continues.

**Fig. Time to (A) Transient and (B) Stable Events**

---

**S-24. Time to First Occurrence of Breast Pain/Tenderness and Vaginal Bleeding in Phase 3 Trials of CE/BZA**

- **Objective:** Breast pain/tenderness (BPT) and vaginal bleeding. In clinical trials of a menopausal therapy combining conjugated estrogens (CE) with the selective estrogen receptor modulator bazedoxifene (BZA), BPT and vaginal bleeding rates were comparable to PBO and lower vs CE-mediated progesterone acetate (CEMPA). This post hoc analysis determined median time to first occurrence of BPT and vaginal bleeding with CE/BZA, PBO, and CEMP.
- **Design:** In phase 3 CE/BZA trials, postmenopausal women recorded the presence of BPT and/or vaginal bleeding. In the SMART-1, -2, and -5 trials, ospemifene 60 mg/day was not significantly different from CE/BZA and PBO. Median time to vaginal bleeding was 314, 341, 357, and 362 d respectively. Survival curves (Fig) were not significantly different for CE/BZA and PBO (P = 0.001). Analyses used log-rank tests. Results: In SMART-5, median time to onset of breast tenderness was 299 d for CE/BZA and PBO, while median time to first occurrence of vaginal bleeding was 314, 341, 357, and 362 d respectively. Survival curves (Fig) were not significantly different for CE/BZA and PBO (P = 0.05), but were not significant when CEMP was added to the sample. Breast pain survival curves in SMART-1 and -2 were not significantly different for CE/BZA and PBO. Breast pain occurred at a median of >730 d with CE/BZA and PBO in SMART-1 or -2, and not reached for CE0.45mg/BZA20mg and CE0.625mg/BZA20mg.
Simões, PhD1, Paulo Cerri, Dr 2. 1Morfologia e Genética, Universidade Federal de São Paulo, São Paulo, Brazil; 2Unesp-Araraquara, Araraquara, Brazil

Objective: To evaluate the HMGB1 (a chromatin nuclear associated protein) immunoexpression pattern in osteocytes and a possible association with alveolar bone resorption in ovariectomized rats. Design: Immunohistochemistry for detection of HMGB1. The number of TUNEL-positive osteocytes was evaluated using qRT-PCR from 24, 48, 72 hrs groups. Results: In vitro proliferative activity of HESCs was decreased in response to gonadotropin treatment, however, significant dose dependent response was not observed. Expression of cell cycle-related gene expression was altered in all treated groups. Conclusion: Taken together, gonadotropin-induced suppression of proliferation in addition to depletion of estrogen may explain the atrophy of postmenopausal endometrium. (H114C2289 and H114C2259).

BASIC SCIENCE POSTER PRESENTATIONS

P-1. A possible participation of HMGB1 in the recruitment of osteoclasts in the alveolar bone of estrogen deficient female rats.
Rinaldo Florencio-Silva, Dr1, Gisela R. Sassó1, Estela Sasso-Cerri, Dr2, Manuel J. Simões, PhD2, Paulo Cerri, Dr3, 1Morfologia e Genética, Universidade Federal de São Paulo, São Paulo, Brazil; 2Unesp-Araraquara, Araraquara, Brazil

Objective: To evaluate the HMGB1 (a chromatin nuclear associated protein) immunoexpression pattern in osteocytes and a possible association with alveolar bone resorption in ovariectomized rats. Design: Eighteen adult female rats were sham-operated (SHAMG) or ovariectomized (OVXG). After 21 days, the rats received daily subcutaneous injection of 30εg/Kg of body weight of estrogen (OVXEG) or vehicle solution (OVXG) for 30 days. The rats were euthanized and the fragments of maxilla containing the alveolar bone of the first molars were fixed and embedded in paraffin. Sections were subjected to the TRAP method (osteoclast marker) for osteoclast quantification and TUNEL method for apoptosis detection. Sections were also subjected to immunohistochemistry for detection of HMGB1. The number of TUNEL-positive osteocytes and the percentage of HMGB1 immunolabeled cytoplasm and nuclei in osteocytes were computed. Statistical analyses were performed using Tukey test and the significance level was 5%. Results: OVXG group showed a significant increase in the number of osteoclasts and TUNEL-positive osteocytes in comparison to SHAMG and OVXEG groups. In addition, a high percentage of HMGB1-positive nuclei in osteocytes were seen in the OVXG group in comparison with the SHAMG and OVXEG groups. Conclusion: The estrogen withdrawal-induced osteocytes apoptosis may be related to changes in the HMGB1 immunoexpression pattern in these cells. These findings point to a possible role of HMGB1 in the recruitment of osteoclasts culminating in bone resorption in estrogen deficient female rats.

P-2. Altered short-term in vitro proliferative activity of human endometrial stromal cells by high-concentration gonadotropins
Yoon Young Kim, PhD, Hye Min Kim, Seung-Yup Ku, MD,PhD, Chang Suk Suh, MD, PhD, Seok Hyun Kim, Young Min Choi. OB/GYN, Seoul Natl Univ Hospital, Seoul, Korea (the Republic of)

Objective: Menopause is accompanied by high FSH and LH levels. Recently, FSH receptors as well as LH receptors were found on the endometrium. However, direct effects of gonadotropins on the endometrium is rarely elucidated to date. We tried to evaluate the effects of FSH, LH and hMG on the in vitro proliferative activity of human endometrial stromal cells. Design: A human endometrial stromal cell (HESC) line was purchased from ATCC. Cells were plated at a concentration of 1.5 x 10^5 cells/plate, and treated with 0, 15, 30, 150 μIU/mL of urinary and recombinant FSH, LH and hMG for up to 72 hrs. Proliferative activity was measured by BrdU assay. Expression of cell cycle-related genes, cyclin A1, cyclin D1 and cyclin E1 was evaluated using qRT-PCR from 24, 48, 72 hrs groups. Results: In vitro proliferative activity of HESCs was decreased in response to gonadotropin treatment, however, significant dose dependent response was not observed. Expression of cell cycle-related gene expression was altered in all treated groups. Conclusion: Taken together, gonadotropin-induced suppression of proliferation in addition to depletion of estrogen may explain the atrophy of postmenopausal endometrium. (H114C2289 and H114C2259).

P-3. Imbalance between the apoptotic cell death (caspase-3 cleaved) and the cellular proliferation (PCNA) in liral gland of female mice of hyperprolactinemic female mice
Ariadne S. Leal, Ms1,2, Manuel J. Simões, PhD2, José M. Soares Junior, MD, Ph.D2, Carina Verna, Dr1, Regina C. Teixeira Gomes, PhD2, 1Department of Morphology, Federal University of São Paulo, São Paulo, Brazil; 2Morphology, Federal University of São Paulo, São Paulo, Brazil; 3Obstetrics and Gynecology, Faculty of Medicine University of São Paulo, São Paulo, Brazil

Objective: To investigate expression of cleaved caspase-3 and PCNA in the in the lacrimal glands of female mice of hyperprolactinemic mice female. Design: 20 female/groups: control group (non pregnant, Ctr1): 0.2 mL of saline (vehicle) and the experimental group (non pregnant, HPV1): 200 μg/day of metoclopramide, dissolved in vehicle. After 50 days 10 females of each group were placed for mating with males and continued to receive treatment. The females non pregnant were euthanased on 50th day (experimental I) and the females pregnant were euthanased on 5.5th to 6.5th post-coital day (Ctr2: control group and HPV2: experimental group). The blood samples were collected for hormone measurements. The uterus was processed for immunohistochemistry. The results were subjected to statistical test (p <0.05). Results: The decreased immunoexpression of caspase 3 in the non pregnant controls compared to non-experimental group (p <0.05). And increased cell proliferation (PCNA) in the pregnant control group compared to pregnant experimental group (p <0.05). Serum prolactin levels were higher whereas the levels of estradiol and progesterone were lower in the animals that received metoclopramide compared to controls. Conclusion: The metoclopramide-induced hyperprolactinemia altered the cellular activity in liral gland in non pregnancy and pregnancy as a consequence of the imbalance between the apoptotic cellular death (caspase-3 cleaved) and the cellular proliferation (PCNA). It is hypothesized that this effect might be related with decrease in the hormonal production of estrogen and progesterone.

P-4. Expression and influence ovarian function by the upregulation and downregulation of steroidogenesis related genes in ovaries of pinealectomized rats in proestrous phase: Folistatin and Inhibin-βA
Carla C. Maganhin, post doctoral 1, Luiz F. Fuchs 1, Ricardo S. Simões, Dr 1, Gisela R. Sassó1, Edurned C. Baracat 1, José Maria Soares- Jr. 1, Obstetrics and Gynecology, University São Paulo, FMUSP/USP, São Paulo, Brazil, 2Gynecology and Reproduction, Federal University of São Paulo, São Paulo, Brazil

Objective: To analyze the immunoexpression of estrogen receptors in ovaries of pinealectomized or melatonin-treated pinealectomized rats. Design: Thirty adult female rats were randomly divided into three groups of 10 animals each: Group I – Control; Group II – pinealectomized (Px), and Group III – Px treated with melatonin (10μg/night, per animal). After two months’ treatment, the ovaries were collected, fixed in 10% buffered formaldehyde and processed for paraffin embedding. Sections were then subjected to immunohistochemical detection of estrogen receptors. Under 400× magnification, the analyses were carried out according to the color intensity, which varied from weak to strong immunoreactivity. Results: The Px (GI) group showed a higher immunoreactivity of estrogen receptors in the granulosa and interstitial cells, as compared to the control (GI) and melatonin treated (GIH) groups, whereas a similar weak immunoreactivity was found in the outer and inner theca cells in all groups. Conclusion: Melatonin may decrease estrogen receptors immunoreexpression in ovarian follicles of pinealectomized rats.<![-[fi'supportLineBreakNewLine]-><!-[endif]-->
P-5

Immunoeexpression of estrogen receptors may decrease produce melatonin in ovaries of pinealectomized female rats

Carla C. Magahan, post doctoral1, Luiz F. Fuchs1, Gisela R. Sasso3, Ricardo S. Simões, Dr1, Edmund C. Baracat1, José M. Soares Júnior, MD, Ph.D1. 1Obstetrics and Gynecology, University of São Paulo, São Paulo, Brazil; 2Evolutionary Medicine, Federal University of São Paulo, São Paulo, Brazil; 3Institute of Pathology and Genetics, Federal University of São Paulo, São Paulo, Brazil

Objective: To analyze the immunoeexpression of estrogen receptors in ovaries of pinealectomized or melatonin-treated pinealectomized rats. Design: Thirty adult female rats were randomly assigned to 4 groups each: Group Control; Group II - pinealectomized (Px), and Group III - Px + treated with melatonin (10μg/night, per animal). After two months’ treatment, the ovaries were collected, fixed in 10% buffered formaldehyde and processed for paraffin embedding. Sections were then analyzed using immunohistochemical detection of estrogen receptors. As a result of magnification, the analyses were carried out according to the color intensity, which varied from weak to strong immunoreactivity. Results: The Px (GII) group showed a higher immunoreactivity of estrogen receptors in the granulosa and interstitial cells, as compared to the control (GI) and melatonin treated (GIII) groups, whereas a similar weak immunostaining was found in the outer and inner theca cells in all groups. Conclusion: Melatonin may decrease estrogen receptors immunoeexpression in ovarian follicles of pinealectomized rats.

P-6

Preventive application of high-frequency mechanical vibration is better than its treatment in bone of osteopenic rats

Gisela R. Sasso, Rinaldo Florencio-Silva, Miriam A. Santos, Cristiane D. Teixeira, Dr, Manuel J. Simões, PhD. Federal University of São Paulo, São Paulo, Brazil

Objective: Low-intensity, high-frequency mechanical vibration (LHMV) has shown to increase bone mass. However, studies comparing the effectiveness of preventive and pre-treatments of LHMV to counteract bone loss have not been documented. This study was designed to compare the effects of preventive and pre-treatments of LHMV (at 30 Hz/0.6g, 20 min per day/5 days per week, for 12 weeks) on bone parameters in ovariectomized rats. Design: Thirty adult female rats were randomly divided into four groups: GI (preventive control group); GII treated with LHMV three days per week for 8 days after Ovx (preventive treatment); GI (late control group) and GIV treated with LHMV three weeks after Ovx (late treatment). Bone mineral density (BMD) was analyzed before Ovx and after treatments. Animals were killed, the femurs collected and their length and diameter measurement were measured; the distal femurs were processed for histomorphometry and polarized light microscopy for collagen fibers analysis or subjected to immunohistochemistry of cleaved caspase-3 in osteocytes. Statistical analysis: ANOVA and Bonferroni post hoc test (P<0.05). Results: BMD was similar among the groups before Ovx, but after treatments, it was significantly higher in GII and GIV compared with their control groups (P<0.05). Femur length and cortical bone thickness was similar among the groups, but the diaphysis diameter of GII was higher compared to GI. Trabecular bone area was higher in the vibrated bones, but was greater in GIV (P<0.05). Also, GII showed the higher presence of mature collagen fibers and lower percentage of apoptotic osteocytes (positive caspase-3 immunoreactivity) when compared to GI (P<0.05). Conclusions: This results suggest that both preventive- and pre-treatments with LHMV counteract bone loss and improve bone parameters in Ovx rats, being the preventive treatment was more effective than the late treatment.

P-7

Transdermal Progesterone Opposes the Effects of 17-beta Estradiol on the Uterus of the Female Rat

Ginger D. Constantine, MD1, Richard Winneker, PhD1, Lawrence de Garavilla, PhD1, Brian Bernick, MD1, James H. Pickard, MD1, Annette M. Shaadick, PhD2. 1TherapeuticsMD, Boca Raton, FL; 2EndoRheum Consulting LLC, Makvern, PA

Objective: To demonstrate that transdermally delivered progesterone can inhibit estrogenic effects on the endometrium and vagina in oophorectomized rats. Design: Thirty-two 8-week-old, female, Crl:CDB rats underwent oophorectomy 2 weeks prior to study start. Rats were randomly assigned to 4 groups of 8 rats each. Three of the groups received 3 mg/kg/day 17 beta-estradiol, (E2) subcutaneously (SC), for 8 days as well as one of the following: (a) placebo cream, (b) 10 μg/kg/day progesterone, SC, or (c) 3.125 mg/day progesterone transdermally beginning on Day 4. A fourth group received the E2 vehicle (corn oil), SC for 8 days and placebo cream beginning on Day 4. Two hours post the final dose (Day 8), the rats were euthanized and the vagina and uteri were dissected. Results: Mean (±SD) progesterone levels in the salivary glands and log-transformed means (lower, upper) estradiol levels in the plasma were ~12-times higher with SC administration compared to topical. Furthermore, the sum of the levels of these metabolites in the plasma was ~2-times the levels of progesterone after SC dosing as compared to equivalent levels after topical dosing. Conclusion: Transdermal delivery of progesterone cream resulted in similar progesterone levels in the uterus compared with SC delivery; however, lower plasma levels of progesterone and ALLO were reported. These data suggest that this formulation of topical progesterone may provide protective endometrial effects from estradiol while limiting systemic exposure.

P-8

Exposure, Tissue Distribution, and Metabolite Profile of Transdermal Progesterone in the Female Rat

Ginger D. Constantine, MD1, PhD, Insuk Lee, PhD2, Richard Winneker, PhD, Lawrence de Garavilla, PhD1, Brian Bernick, MD1, James H. Pickard, MD1, Annette M. Shaadick, PhD2. 1TherapeuticsMD, Boca Raton, FL; 2EndoRheum Consulting LLC, Makvern, PA

Objective: To compare plasma, uterine, and salivary gland levels of progesterone, allopregnanolone (ALLO), and ALLO-sulfate in the rat following either transdermal or subcutaneous delivery of progesterone. Design: Thirty-two 8-week-old, female, Crl:CDB rats underwent oophorectomy 2 weeks prior to study start. Rats were randomly assigned to 4 groups of 8 rats each. Three of the groups received 3 mg/kg/day 17 beta-estradiol, subcutaneously (SC), for 8 days as well as one of the following: (a) placebo cream, (b) 10 μg/kg/day (2.5 μg/rat/day) progesterone, SC, or (c) 3.13 mg/day progesterone transdermally beginning on Day 4. A fourth group received the E2 vehicle (corn oil), SC for 8 days and placebo cream beginning on Day 4. Two hours post the final dose (Day 8), the rats were euthanized and plasma, and salivary glands were collected. Tissues and plasma were extracted and progestins were analyzed for progesterone, ALLO, and ALLO-sulfate using LC-MS/MS. ALLO-sulfate was analyzed for progesterone, ALLO, and ALLO-sulfate using LC-MS/MS. ALLO-sulfate was analyzed for progesterone, ALLO, and ALLO-sulfate using LC-MS/MS. Progesterone, ALLO, and ALLO-sulfate were analyzed for progesterone, ALLO, and ALLO-sulfate using LC-MS/MS. Mean (±SD) progesterone levels in the salivary glands and log-transformed means (lower, upper) of ALLO-sulfate in plasma were ~12-times higher with SC administration compared to topical (7.8 ± 6.8 and 0.60 ± 0.25 ng/mL/mg dose, respectively). In all instances, the mean tissue levels of both ALLO and ALLO-sulfate were higher with SC administration compared to topical. Furthermore, the sum of the levels of these metabolites in the plasma was ~2-times the levels of progesterone after SC dosing as compared to equivalent levels after topical dosing. Conclusion: Transdermal delivery of progesterone cream resulted in similar progesterone levels in the uterus compared with SC delivery; however, lower plasma levels of progesterone and ALLO were reported. These data suggest that this formulation of topical progesterone may provide protective endometrial effects from estradiol while limiting systemic exposure.

P-9

HbG Serum Enzyme Catalase Level in Menopausal Paramedics As A Marker Of Oxidative Stress; A Study Based In Indonesia

Muhammad Fidel G. Siregar, Ph.D, D.Ked (OG ), Panta S. Sibarian, Yostoto B. Kaban, Henry S. Siregar, Iman H. Effendi, Riza Rivany. Obstetric and Gynaecology, Universitas Sumatera Utara, Medan, Indonesia

Objective: A recent estimation stated that 25 million women will reach menopause age each year. Based on survey conducted by Indonesian Menopause Society (PERMI/Perkumpulan Menopause Indonesia) on 2005, the average age of menopause among Indonesian women is 49 ± 0.20 years old. Data from Indonesian Statistical Bureau (BPS/Biro Pasat Statistik) stated that the number of menopausal women in Indonesia is 5,320,000 on 2008. In Province of Sumatera Utara Indonesia, especially in its capital city, Medan, the average life expectancy for women increase each year, with data from 2008 shows the average age of 72.7 years old. These facts are important because that means one third of women’s life will be spent in menopausal age. Menopause is a predisposing factor for the development of oxidative stress, marked by estrogen deficiency, which also has a role as an antioxidant. Oxidative stress is defined as an imbalance of oxidants and antioxidants which have an important role in the aging process. Increased oxidant metabolism and decreased antioxidant capacity as aging acceleration and degenerative process including heart disease, and pathological imbalance of oxidants and antioxidants which have an important role in the aging process. Paramedic needs professionalism in patient management, clinical skill, and drug administration. Deteriorating health in patient that is a subject of high oxidative stress is paramedic. That means one third of women’s life will be spent in menopausal age. Menopause is a predisposing factor for the development of oxidative stress, marked by estrogen deficiency, which also has a role as an antioxidant. Oxidative stress is defined as an imbalance of oxidants and antioxidants which have an important role in the aging process. Increased oxidant metabolism and decreased antioxidant capacity as aging acceleration and degenerative process including heart disease, and pathological imbalance of oxidants and antioxidants which have an important role in the aging process. The inclusion criteria were : never had a hysterectomy or bilateral oophorectomy, being at least 40 years old, not consuming alcohol, not smoking, no history of mental disorder and cancer. Design: In all instances, the mean tissue levels of both ALLO and ALLO-sulfate were higher with SC administration compared to topical. Furthermore, the sum of the levels of these metabolites in the plasma was ~2-times the levels of progesterone after SC dosing as compared to equivalent levels after topical dosing. Conclusion: Transdermal delivery of progesterone cream resulted in similar progesterone levels in the uterus compared with SC delivery; however, lower plasma levels of progesterone and ALLO were reported. These data suggest that this formulation of topical progesterone may provide protective endometrial effects from estradiol while limiting systemic exposure.
Specific Quality Of Life) questionnaire to be filled. This study use MENQOL as an instrument to confirm that the patients is in menopause period. To confirm the validity of MENQOL, L-MMPI scale was used because the examination instrument in this study are subjective and influenced by the respondents honesty. Blood sample then withdrawn from subjects in both group to analyze their catalase enzyme serum level. Data then analyzed descriptively to determine the frequency distribution of subjects to characteristic, mean, standard deviation and numeric data. To analyze the differences between variables, t-independent test was performed with confidence interval of 95% (p < 0.05). Results: Majority of subjects from menopause group were from age group of 50-54 years old (56,0%), from menopause group were from age group of 31-40 years old (50%). Mean level of serum catalase enzyme in control and menopause group were 105,94 ± 22,37 mU/ml and 155,53 ± 12,24 mU/ml respectively (CI: 95%; p < 0.05). From 29 MENQOL questions, the highest score came from sexual complaint with 5,89 ± 2,06, vasomotor complaint 2,74 ± 1,34, and psychosocial complaint 2,36 ± 1,12. Conclusion: There is a significant difference of serum catalase enzyme level between menopause and reproductive aged women. Serum catalase enzyme level in menopausal women is higher than its level in reproductive aged women. This finding means that women in menopause is subjected to higher level of oxidative stress, especially in paramedic.

P.10. Imunoexpression of BCL-2 and BAX in ovarian follicles of pilaeneclatomized or melatonin-treated pilaeneclatomized rats
Luiza M. de Almeida, post doctoral1, Gustavo F. S. Simões, Dr2, Eduardo C. Baracat3, José Maria Soares-Jr. 3Obstetrics and Gynecology, University of Sao Paulo, Sao Paulo, Brazil; 2Obstetrics and Gynecology, Federal University of Sao Paulo, Sao Paulo, Brazil

Objective: To evaluate the expression of Bcl-2 and Bax in ovarian follicles of pilaeneclatomized or melatonin-treated pilaeneclatomized rats. Design: Thirty adult rats were randomly divided into three groups of 10 animals; Group I – Control; Group II - pilaeneclatomized (Px), and Group III - Px treated with melatonin (10μg/night, per animal). After two months' treatment, on the night of proestrus, the animals were placed in metabolic cages for night urine collection and subsequent measurement of 6-sulfatoxymelatonin (6-SMT). The rats were anesthetized, blood samples were taken for estrogen and progesterone determinations, and they were then euthanized. The ovaries were collected, fixed in 10% buffered formaldehyde and processed for paraffin embedding. From the paraffin blocks, 5 μm thick sections were collected to silanized slides and submitted immunohistochemical methods for the detection of Bcl2 (Spring Bioscience Corp. US) and Bax (Spring Bioscience Corp. US). Images were obtained using a light microscope (Axioskop Standard 2.0 - Carl Zeiss) attached to a high definition camera (AxioCam MRC - Carl Zeiss) and by the image analyzing image (AxioVision Rel. 4.8.2 - Carl Zeiss). Reaction expression was analyzed and quantified according with the color intensity with the aid of the Image 2 Pro Plus, having photographed 5 fields each slide, with the 40x objective. Obtained data was submitted to statistical analysis using ANOVA test complemented by the Tukey-Kramer test (p<0.05). Results: The urinary levels of 6-SMT and serum progesterone were lower in the Px group (GII). Exogenous melatonin treatment restored both blood melatonin and 6-SMT urinary levels in Px group (GII) - that was highly immunohomogeneous in the GII - Px treated with melatonin (GII - 60,93±3,95) when compared with the Control (GII - 40,39±3,05). Objective: To evaluate the expression of Bcl-2 and BAX in ovarian follicles of pilaeneclatomized or melatonin-treated pilaeneclatomized rats. Design: Thirty adult rats were randomly divided into three groups of 10 animals: Group I – Control; Group II - pilaeneclatomized (Px), and Group III - Px treated with melatonin (10μg/night, per animal). After two months' treatment, on the night of proestrus, the animals were placed in metabolic cages for night urine collection and subsequent measurement of 6-sulfatoxymelatonin (6-SMT). The rats were anesthetized, blood samples were taken for estrogen and progesterone determinations, and they were then euthanized. The ovaries were collected, fixed in 10% buffered formaldehyde and processed for paraffin embedding. From the paraffin blocks, 5 μm thick sections were collected to silanized slides and submitted immunohistochemical methods for the detection of Bcl2 (Spring Bioscience Corp. US) and Bax (Spring Bioscience Corp. US). Images were obtained using a light microscope (Axioskop Standard 2.0 - Carl Zeiss) attached to a high definition camera (AxioCam MRC - Carl Zeiss) and by the image analyzing image (AxioVision Rel. 4.8.2 - Carl Zeiss). Reaction expression was analyzed and quantified according with the color intensity with the aid of the Image 2 Pro Plus, having photographed 5 fields each slide, with the 40x objective. Obtained data was submitted to statistical analysis using ANOVA test complemented by the Tukey-Kramer test (p<0.05). Results: The urinary levels of 6-SMT and serum progesterone were lower in the Px group (GII). Exogenous melatonin treatment restored both blood melatonin and 6-SMT urinary levels in Px group (GII) - that was highly immunohomogeneous in the GII - Px treated with melatonin (GII - 60,93±3,95) when compared with the Control (GII - 40,39±3,05). GII - Pinealectomized (Px) (GII = 51.09 ± 3.05) and GIII - Pinealectomized + melatonin (Px + melatonin) (GIII = 52.58 ± 2.85) (p<0.05)

P.11. Gene expression and immunolocalization of the small leucine-rich proteoglycans (SLRPs) in the ovary of pinealectomized or melatonin-treated pinealectomized rats
Luisa M. de Almeida, post doctoral1, Gustavo F. S. Simões, Dr2, Edmund C. Baracat3, José Maria Soares-Jr. 3Obstetrics and Gynecology, University of Sao Paulo, Sao Paulo, Brazil; 2Obstetrics and Gynecology, Federal University of Sao Paulo, Sao Paulo, Brazil

Objective: To evaluate the expression of small leucine-rich proteoglycans (SLRPs) in the ovary of pinealectomized or melatonin-treated pinealectomized rats. Design: Four groups, each containing 10 animals, namely: CG - received saline solution, EG - received estradiol benzoate (37.6 μg per animal/day) for 7 consecutive days, PG - received medroxyprogesterone acetate (11.28 mg per animal/day) for 23 consecutive days, EPG - received estradiol benzoate (37.6 μg for 7 consecutive days followed by medroxyprogesterone acetate (11.28 mg, for 23 consecutive days). Results: Dermatan sulfate in breast tissue of hormonal-treated animals showed a lower concentration in all groups compared to CG, p<0.05. Heparan sulfate and Hyaluronic acid in breast of P-treated animals showed a lower concentration compared to others groups (EG and EPG), p<0.05. The results of 6-SMT urinary levels and serum progesterone were lower in the Px group (GII). The results showed that the treatment with estrogen in their composition were able to stimulate the production the sulphated glycosaminoglycans (heparan and dermatan) and non-sulphated glycosaminoglycans (hyaluronic acid) in breast tissue compared to progesterone treatment. Although the concentration of GAGs analyzed was higher in the breast of the control group animals.

P.13. The Accuracy of Self-Reported Glaucoma in the Women's Health Initiative
Thasarat S. Vajaranant, MD, Pauline Maki, Ph.D.2, Louis R. Pasquale1, Farzan Khan, Julie Mares3, Kristin J. Meyer 4, Mary N. Haan 5. 1Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, IL; 2Psychiatry, University of Illinois, Chicago, IL; 3Ophthalmology, Harvard Medical School, Boston, MA; 4Ophthalmology and Visual Sciences, University of Wisconsin, Madison, WI; 5 Department of Epidemiology and Biostatistics, University of California at San Francisco, San Francisco, CA

Objective: Women comprise the majority of individuals affected by glaucoma, a leading cause of irreversible blindness worldwide. Previous studies suggest that early menopause increases the risk for glaucoma. Epidemiologic studies of large national health cohorts sometimes rely on self-reported eye disease without validation of self-reports against medical records. We determined the accuracy of self-reported vs. medically diagnosed glaucoma in a subset of the Women’s Health Initiative (WHI), a large NIH-funded cohort study involving 161,808 post-menopausal women. Design: We recruited women who reported glaucoma at WHI enrollment (1994-1998) or in annual health update questionnaires through 2005. Eligible women were selected from two ancillary eye studies: the WHI Sight Exam (WHISE) study and the Carotoids in Age-Related Eye Disease Study (CAREDS). In a follow-up phone interview for this pilot study, the selected women were asked if eye care providers told them that they had glaucoma. Additionally, they were asked to release their medical records to verify the diagnoses. We used a method described in the Nurses’ Health Study (NHS) to confirm the diagnosis of primary open-angle glaucoma (POAG). POAG was defined as glaucoma without secondary causes and open-angle was confirmed by gonioscopy or absence of adverse effects after dilated exams. Reliable characteristic glaucomatous visual field defects were used as a main diagnostic criterion (perimetric POAG). Results: A total of 276 women were contacted and 200 (72.5%) consented to a phone interview (15.9% declined, 2.5% were deceased, and 9.1% were non-responders). Medical records were obtained on 186 of the 200 consented (93.0%). Of the 186, 52.7% (98/186) had no available or insufficient visual field data. POAG was verified in 29.3% (55/186). Limiting to the 88 women with sufficient visual field data, POAG was verified in 62.5% (55/88). Although all women reported glaucoma in sometime between 1994 and 2005, only 46.5% (86/185) confirmed during phone interviews during 2013. Of those who reported glaucoma twice, POAG was verified in 50.0% (43/86). Of these 86 women, 63 had sufficient visual fields and POAG was verified in 68.3% (43/63). Conclusion: We were able to observe the effects of perimetric POAG in the WHI, which is similar to that of the NHS (53%). The accuracy of self-reported glaucoma increased from 29% to 50% if glaucoma was reported twice. This information is essential as it helps assess the validity of epidemiologic analyses of self-reported POAG and/or plan future nested case-control study of POAG in the WHI.
P-14. 
Knowledge Deficits Related to Menopause: A Focused Review and Thematic Analysis of the Literature
Patricia Camillo, PhD. Nursing Professor LLC, Bloomington, MN; Carmeta Health Innovations PLC, Minneapolis, MN
Objective: Objective: Menopause is a lived experience that is difficult to quantify due to various socio-cultural and environmental factors. This can be problematic when designing education programs to meet the needs of this population. A focused literature review and thematic analysis was conducted to gain a better understanding of current knowledge deficits, both among midlife women as well as their healthcare providers, related to this transition. Design: Design: A search of PubMed was conducted using the key word “menopause” in combination with each of the following three words: education, knowledge, and information. Publications were limited to the time period from January 2010 through June 2015. A total of 182 articles were retrieved. These articles were all peer reviewed and written in English. Of these, 127 were eliminated, primarily to avoid the word “education” used as a demographic variable within studies that did not address knowledge of menopause. Thematic analysis was conducted for the remaining 55 studies focusing on knowledge deficits related to menopause identified by the researchers. This was a mixed method approach incorporating the findings from both qualitative as well as quantitative studies. Thematic analysis was conducted with the goal of being descriptive rather than critical. Results: Results: The top three knowledge deficit themes identified were: (1) menopause management during and after cancer treatments, (2) options for hormone therapies, and (3) maintenance of sexual health. Further analysis resulted in specific content items for each of these three major areas. In addition to women’s knowledge deficits, competency in menopause management was identified as a growing concern for a variety of health professionals. Menopause encompasses multiple body systems that are not the focus of ob-gyn curriculums and although internists have that expertise, they lack the knowledge specifically related to menopause management. Similar knowledge deficits were also identified among nursing specialties with midwives focused primarily on the reproductive years. Finally, the provision of culturally sensitive educational content was a pervasive theme across all content areas in this review. Conclusion: Conclusion: This focused review of the literature provided insight into the current knowledge deficits related to menopause found among midlife women as well as those providing their care. Although not prescriptive in design, this review provides the basis for further investigation into these educational needs. The most dominant concern for women, identified in this review, was the knowledge deficit experienced during and after treatments for various cancers. There are few educational resources for this population and there are indications from this review that many health professionals would not be prepared to address these specific learning needs. Educators designing programs for either midlife women and/or their healthcare providers need to be vigilant in identifying current knowledge deficits as the population changes and the state of the science continues to evolve.

P-15. 
MsFLASH Participants’ Priorities for Alleviating Menopausal Symptoms
Janet Carpenter1, Nancy F. Woods, PhD, RN, FAAN2, Julie Otte, PhD, RN3, Katherine Guthrie, PhD2, Chancellor Hohensee1, Katherine M. Newton, PhD4, Hadine Joffe, MD5, MSc6, Investigator. 1, 2, 3 Barbara Sturmfels, PhD5, Jane Lau5, Susan DD7, MPH9, Andrea Z. LaCroix, PhD9. 1Science of Nursing Care, School of Nursing, Indiana University, Indianapolis, IN; 2Biobehavioral Nursing, University of Washington, Seattle, WA; 3Fred Hutchinson Cancer Research Center, Seattle, WA; 4Group Health Research Institute, Seattle, WA; 5Psychiatry, Harvard Medical School, Boston, MA; 6Center for Women’s Health Research and Perinatal & Reproductive Psychiatry Research Program, Massachusetts General Hospital, Boston, MA; 7Division of Research, Kaiser Permanente Medical Program of Northern California, Oakland, CA; 8Department of Obstetrics and Gynecology, School of Medicine, Indiana University; Indianapolis, IN; 9Departments of Obstetrics-Gynecology and Epidemiology, University of Washington School of Medicine, Seattle, WA; 10Department of Preventive Medicine, University of California San Diego, San Diego, CA
Objective: To describe self-reported menopausal symptom priorities and their association with demographics and other symptom measures among women randomized to an intervention trial for vasomotor symptoms (VMS). Design: Design: Cross-sectional study embedded in the MsFLASH 02 trial, a three by factorial design of yoga vs. exercise vs. usual activity and omega-3-fatty acid vs. placebo. At baseline, women (n=355) completed hot flashes diaries, a card sort task to prioritize symptoms they would most like to eliminate, and standardized symptom questionnaires. Results: Results: The 4 most common symptom priorities were: VMS (n=322), sleep (n=191), memory (n=140), and energy (n=116). In multivariate models, (1) women who chose VMS as their top priority symptom (n=210) reported significantly greater VMS severity (p<0.004) and never smoking (p<0.03) and (2) women who chose sleep as their top priority symptom (n=100), were more educated (p=0.002) and had worse sleep quality (p<0.001). ROC curve analysis of subscale scores that were highly predictive of top menopause symptom priority. Conclusion: Among women entering an intervention trial for VMS and with relatively low prevalence of depression and anxiety, VMS was the priority symptom for treatment. A card sort may be a valid tool for quickly assessing symptom priorities in clinical practice and research.

P-16. 
Diagnostic frequency of the vasomotor syndrome (Greene’s scale vs. Garrie Gast’s scale)
Perla Aldama, Imelda Hernandez. Hospital Juárez de México, Mexico D. F., Mexico
Objective: The vasomotor syndrome is the main reason of consultation in menopause. Additionally, it has been associated with cardiovascular risk increase. Thus, the importance of its diagnosis. However the assessment scale used in our country (Greene’s scale) is inadequate to assess this syndrome. The scale proposed by Garrie Gast et al in 2008 assesses vasomotor syndromes specifically. The objective of this study is to determine the diagnostic frequency of the vasomotor syndrome using the Greene’s scale vs. the Garrie Gast’s scale in patients in transition stage to menopause and post-menopause, seeking to apply it in our population and improve the diagnosis and treatment of the vasomotor syndrome. Design: Comparative, observational, descriptive, cross-sectional and prospective trial of a group using different measurement scales, with a qualitative approach. Inclusion criteria: patients who went to the Climacteric Clinic of the Juárez Hospital of Mexico, in stage STRAW: +1, +2, -1, +1, +2 (transition to early and late menopause; early and late post-menopause); patients who are assessed with the Greene’s scale and the Garrie Gast’s scale. Exclusion criteria: patients under treatment (hormonal treatment, non-hormonal treatment, natural treatment, phytoestrogens). A statistical analysis was made of the differences using the t student test. Results: Two hundred and one patients were assessed with the Greene’s and Garrie Gast’s scales from June 30, 2014 to January 15, 2015. The average age was 52 years. The most frequent stage is +2 (late post-menopause) with a total of 73 patients (36 %). The patients assessed with the Greene’s scale presented vasomotor symptoms (mild, moderate, and severe) in 74 %; this percentage increased to 86 % when the Garrie Gast scale was applied (mild, moderate, and severe) p<0.001. Of the 52 patients without symptoms with the Greene’s scale, 38 patients (73 %) had vasomotor symptoms (mild, moderate and severe) with the Garrie Gast’s scale. And of the 28 patients without symptoms with the Garrie Gast’s scale, 14 patients presented mild symptoms with the Greene’s scale (due to a higher score in somatic, psychological, and sexual scale). Conclusion: The scale proposed by Garrie Gast presents greater diagnostic frequency of the vasomotor syndrome, because it has more specific items for assessment of hot flashes and nocturnal sweating. Therefore, using is in our population is suggested to obtain greater diagnostic accuracy and deliver better menopause care to vasomotor syndrome treatment.

Symptom frequency comparing the Greene’s scale vs. the Garrie Gast’s scale as assessment method

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Greene’s scale</th>
<th>Garrie Gast’s scale</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absent</td>
<td>52</td>
<td>25</td>
<td>0.025</td>
</tr>
<tr>
<td>Present</td>
<td>149</td>
<td>75</td>
<td>0.031</td>
</tr>
</tbody>
</table>

Scale proposed by Garrie-Gast et al.

Mark the number of a day a week you had hot flashes, the average number of hot flashes, and the maximum number of hot flashes in one day. Mark the number of nights a week you wake up for nocturnal sweating, and the number of times when they disrupt your sleep in one night.

P-17. 
Effects of Recent Abuse on Menopausal Symptom Bother: Results from the Data Registry on Experiences of Aging, Menopause and Sexuality (DREAMS)
Sannecla Veguina, MD1, Carol Kuhle, DO2, Juliana M. Kling, MD, MPH1, Julia Files, MD1, Erika Kapor, MBBS1, Sara S. David, MD1, Jordan Ruliss, PhD, LP1, Richa Sood, MD2, Jacqueline Thielen, MN2, Lynne T. Shuster, MD2, Aminah Jatoi, MD3, Darrell R. Schroeder, M.Sc4, Stephanie Fanibbon, MD1. 1Division of Women’s Health Internal Medicine, Mayo Clinic, Scottsdale, AZ; 2Women’s Health Clinic, Division of General Internal Medicine, Mayo Clinic, Rochester, MN; 3Division of Medical Oncology, Department of Oncology, Mayo Clinic, Rochester, MN
Objective: Abuse of women in the US is prevalent and associated with adverse health outcomes. While a history of adverse childhood experiences has been associated with the reporting of vasomotor symptoms, the relationship between recent abuse and menopausal symptoms has not been fully explored. Our objective was to determine whether there is an association between menopausal symptom bother (MSB) and MSB and a history of abuse (physical, sexual or emotional/verbal) in the last year. Design: We will be presenting for menopause consultation in the women’s Health Clinic (Rochester, MN) complete the Menopause Health Questionnaire (MHQ). MHQ data were collected between January 1, 2006 and October 7, 2014. Menopausal symptom presence and severity were assessed in the MHQ with 33 questions, rated with a score of 0-5.
1 to 4 for degree of bother (1 = not at all; 2 = a little bit; 3 = quite a bit; 4 = extremely). In addition to total score, menopausal symptoms were grouped into 6 domains based on content: vasomotor, sleep, neurocognitive, bowel/bladder function, sexual function, and general. Abuse in the last year was assessed as present/absent (yes/no); menopausal status was self-reported as premenopausal, perimenopausal or postmenopausal, current tobacco use was assessed as present/absent (yes/no). Demographic data (BMI, education, employment status, and race/ethnicity) were obtained from the electronic medical record. Data were summarized using mean (SD) for continuous variables and frequency percentages for nominal variables. The MHQ total and subscale scores were calculated as the mean response of the items included in the given domain. Scores were analyzed as continuous variables; total scores were the primary endpoint and subscale scores the secondary endpoint. MHQ scores were compared between women self-reporting abuse versus not using the two-sample test. Analysis of covariance was used to assess whether abuse was associated with MSB after adjusting for baseline patient characteristics. Two-tailed p-values ≤ 0.05 were considered statistically significant. Results: Of 4,956 women who completed one or more MHQs during the study period, 3,740 were included after exclusion of women who did not provide authorization for use of their records, those under 40 years of age and those who did not complete any of the MHQ items assessing MSB or abuse in the last year. Of these 3,740 women, 253 (6.8%) reported experiencing one or more forms of abuse in the last year; 245 of 253 (96.8%) reported verbal/emotional abuse, 34 (13.4%) reported physical abuse and 10 (3.9%) reported sexual abuse. Demographic characteristics (age, race/ethnicity, BMI, menstrual status, education, employment, cigarette smoking, alcohol use, and self-reported history of alcoholism) were similar between groups based on prior abuse, with the exception of employment status (p<0.001). A higher percentage of those reporting abuse in the last year were classified as work disabled. The prevalence of cigarette smoking was higher in those who reported abuse in the last year (p<0.001). The prevalence of current alcohol use was lower in women who reported abuse in the last year (p=0.017), but the prevalence of self-reported lifetime alcoholism was higher in those who reported abuse (p<0.001). Those reporting abuse in the last year had higher (p<0.001) mean total MSB scores and higher (p<0.001) scores for each of the individual subscales than those who did not report abuse with the exception of vasomotion (p=0.387). Consistent findings were obtained from multivariable analyses adjusting for all demographic and substance use characteristics. Conclusion: In the present study from the Data Registry on Experiences of Aging, Menopause and Sexuality (DREAMS), MSB scores were significantly associated with recent abuse, particularly verbal or emotional abuse. On subanalysis of menopausal symptoms, individual subscales of symptoms were associated with recent abuse, whereas the subscale of vasomotor symptoms was not.

P-19.
Q-1001: A Phase 1 Study of the Safety and Effect of Q-122 on Vasomotor Symptoms in Females with Breast Cancer

Elizabeth O. Oriol, MD, MPH, FACC,*, April L. Speed, MD,1 Alice T. Robertson, PhD,1 Earl E. Sands, MD, FACOG,1 Wendy P. Painter, MD, MPH.1 Clinical Development, QUE Oncology, Atlanta, GA; 2Clinical Research Center, Morehouse School of Medicine, Atlanta, GA; 3Consultant, QUE Oncology, Atlanta, GA

Objective: QUE Oncology is developing Q-122, a novel, orally available small molecule with the chemical formula N-(4-(pyrimidin-2-ylamino)methyl)benzyl)-pyrimidin-2-amine, as a treatment for vasomotor symptoms (VMS) commonly associated with menopause. The initial target population for the development program is females with a history of breast cancer who are taking tamoxifen or an aromatase inhibitor (AI). The first proof of concept study in this population was Q-1001, a Phase 1b, open-label, two dose, dose-escalation study evaluating the safety, tolerability and preliminary effectiveness of Q-122 therapy. Design: Study Overview: Q-1001 was a single-site study that enrolled females who were menopausal, age 30 – 70 years, with a history of breast cancer and taking tamoxifen or an AI. To be eligible for the study, subjects had to be experiencing at least 7 moderate to severe hot flashes (HF) per day or 50 per week. Key exclusion criteria included significant renal or hepatic disease, untreated hyperthyroidism and clinically significant abnormal laboratory findings. All paroxetine is approved for treatment of moderate to severe VMS, concurrent therapy with SSRIs or SNRIs was not an exclusion criterion. The study period consisted of a 2-week drug free screening period to establish baseline values of VMS, a 4-week treatment period, and a final 2-week drug-free follow-up period before the final study termination visit. Subjects were initially enrolled into Group 1 (100 mg Q-122). After Group 1 was fully enrolled, safety parameters were reviewed prior to enrolling subjects into Group 2 (200 mg Q-122). Methods: Safety was monitored by reporting of adverse events (AEs) and serious adverse events (SAEs), and evaluation of treatment emergent adverse changes in physical findings and laboratory values. Efficacy was assessed by calculating the mean changes in frequency and severity of moderate to severe HF from baseline to Week 4. For comparison across treatment weeks, a daily average frequency of HF was calculated for each subject. Severity was assessed by calculation of HF severity score (HSSS) that was normalized to frequency for each treatment week. Results: Twenty-one subjects received Q-122 of which 22 were included in the efficacy analysis; 8 subjects in each group completed the study. Safety: A total of 29 AEs with one SAE were reported during the study (10 in 7 of 10 subjects in Grp. 1; 19 (including 1 SAE) in 7 of 11 subjects in Grp. 2). All the reported AEs were mild (79%) or moderate (21%) in severity. Three AEs reported by one subject (headaches (2 events), and insomnia) were the only events considered possibly related to study drug by the Investigator. There were no remarkable or dose-related changes in adverse events, physical findings or laboratory values. Efficacy: After 4 weeks of treatment with Q-122, both frequency and normalized severity of moderate to severe HF were significantly reduced from baseline values. The reduction was seen in each dose group, in all subjects combined, and in subgroups who were taking an SSRI or SNRI. Baseline (BLSN) and Change from Baseline (CBF) in moderate and severe HF frequency and severity is displayed in Table 1. Conclusion: No safety issues associated with the use of Q-122 were identified in this study. Further, Q-122 therapy resulted in reduction in both frequency and severity of VMS over the 4-week treatment period. These results compare favorably with published results from studies assessing the ability of other non-hormonal drugs to treat VMS in various populations.

Table 1: Change in Frequency and Severity of Moderate to Severe Hot Flashes Following Treatment with Q-122

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Gp 1 (N=9)</th>
<th>Gp 2 (N=11)</th>
<th>All (N=20)</th>
<th>S-SRN-R (N=4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency (daily average)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BLSN</td>
<td>9.86</td>
<td>8.58</td>
<td>9.16</td>
<td>8.11</td>
</tr>
<tr>
<td>CBF</td>
<td>-5.81</td>
<td>-5.69</td>
<td>-6.07</td>
<td>2.07</td>
</tr>
<tr>
<td>BLSN</td>
<td>2.48</td>
<td>2.41</td>
<td>2.44</td>
<td>2.54</td>
</tr>
<tr>
<td>HFFS (normalized to freq.)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CBF</td>
<td>-0.47</td>
<td>-0.38</td>
<td>-0.42</td>
<td>-1.21</td>
</tr>
</tbody>
</table>

** Ultrasound structure > 16 mm seen in one of the ovaries and interpreted as a functional cyst. **

POSTER PRESENTATIONS

Cycle And Hormonal Differences In 20 Year Olds And 40 Year Olds

James S. Martin, BSc MD FRCS(C). Southern Ontario Fertility Technologies, London, ON, Canada

Objective: This study examines 100 consecutive, monitored, spontaneous cycles per group, initially performed for intrauterine insemination (IUI), in women aged 20 to 44 compared to women aged 40 to 44. The purpose of the comparison is to gain insight into hormone and cycle differences in potentially perimenopausal women (40-44) compared to younger women (20-24). Design: An arbitrary start point for collection of cycles was January 2008. The first consecutive 100 monitored cycles for spontaneous IUI for women aged 20 to 24 were compared and excluded for women aged 40 to 44. The day-3 estradiol is quite different (99 vs. 298 pmol/L). More residual follicles remain in these two age groups. Although day-3 FSH is not very different (4.7 vs. 6.5 IU), the prevalence of one or more developing follicle (4 vs. 12) which is perhaps related to the observed higher spontaneous twinning rate in older women. The follicular phase (12.8 vs. 10.6 days), the luteal phase (14.9 vs. 12.1 days) and the cycle length (27.7 vs. 24.7 days) are shortened. The pregnancy rate (especially the ongoing pregnancy rate) is decreased. Some of these observations may help to explain commonly observed perimenopausal symptoms.
P-20. Characteristics and Symptom Severity of Women Referred to an Interdisciplinary Menopause Clinic
Tami Shandro, MD1, Nese Yuksel, BScPharm, PharmD1, Lori Battochio, RN1, Beate Sydora, MSc, PhD2, Sue Ross, BScPharm, PhD, MBA1. 1Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta, Edmonton, AB, Canada; 2Lois Hole Hospital For Women, Edmonton, AB, Canada
Objective: To describe the characteristics of women, who are referred by their physicians, to an interdisciplinary menopause clinic and to assess FSH and estradiol levels and symptom severity of the types and severity of symptoms reported. Design: A retrospective chart review was conducted of women attending the Lois Hole Hospital for Women (LHHW) Menopause Clinic in Edmonton, Alberta, Canada from 2008 - 2013. Women who did not have a completed health profile were excluded. Data from the patient charts included demographics, medical conditions, menopause symptoms and treatment recommendations. Menopause symptom severity scores were captured on a scale of 1 – 4 (none, mild, moderate, severe). Symptom scores were compared from initial to follow-up visits. A convenience sample of 200 patients was chosen. Summary statistics were used to describe the extracted data. Results: Physicians referred women most commonly for severe vasomotor symptoms (53%), sleep disturbance/tachycardia (45%) and mood changes (42%). The women had a mean age of 52 years (SD 6.28), presented with a mean BMI of 29 (SD 7). Thirty five percent were perimenopausal, 52% had experienced a natural menopause and 15% were menopausal secondary to bilateral salpingo-oophorectomy (BSO). Almost 55% of the women had 4 or more medical conditions – the most prevalent being mood disorder (depression 37%, anxiety 31%), followed by migraines (26%), high blood pressure (20%), high cholesterol (19%), diabetes (16%), osteoporosis (10%), and IBS (8%). Mean symptom severity scores at the first visit were 2.85, 2.63, 2.61 and 2.27 for sleep disturbance, vasomotor, muscle/joint pain and mood symptoms respectively. Women at higher cardiovascular (CV) risk had higher symptom severity scores for each of these symptoms at 3.10, 2.76, 2.88 and 2.38 respectively. Recommendations included calcium and vitamin D supplementation (59%), dietary changes (39%), and exercise (15%), as well as hormone therapy (79%). The majority of women were followed for three visits, approximately 3.5 months apart, and 75% of the women experienced symptom improvement by their last visit. Women referred to the interdisciplinary Menopause Clinic were more likely to have moderate to severe menopausal symptoms, and the highest rated severity score was sleep disorder. Those with multiple medical conditions, at higher cardiovascular risk, self-reported more severe symptoms. Three quarters of the women experienced symptom improvement after attending the clinic.

P-21. Vaginal pH As An Alternative Diagnostic Tool For Menopause In Remote Area; A Study Based In Indonesia
Muhammad Fidel G. Sirerag, Ph.D, M.Ked (OG ), Hotbin Purba, Syamsul A. Naution, Sarma N. Lumbaranja, Asoor Aboet, Riza Rivany. Obstetrics & Gynaecology, Faculty of Medicine, University of Sumatera Utara, Medan, Indonesia
Objective: A recent estimation stated that 25 million women will reach menopausal age each year. This number will increase along with development in healthcare, which in turn will increase the overall life expectancy. Based on survey conducted by Indonesian Ministry of Health (PERMENKES No.132 / Menopause Indonesia 2002) the average age of menopause amongst Indonesian women is 49 ± 0.20 years old. Data from Indonesian Statistical Bureau (BPS/Biro Pusat Statistik) stated that the number of menopausal women in Indonesia is 5,320,000 on 2008. In Province of Sumatera Utara Indonesia with the largest capital city, Medan, the average life expectancy for women increases each year, with data from 2008 shows the average age of 72.7 years old. These data are important because that means one third of women’s life will be spent in menopause age. Indonesia is an archipelago country with many remote and rural areas which is not covered by medical facilities. Moreover, the average level of education and economy in Indonesia is still low, affecting the availability and affordability of medical examination. Many Indonesian women are still uninformed about menopause and often assumed that they had already experienced menopause even without adequate medical examination. Compared with serum hormonal examination, vaginal pH examination is relatively easy to perform, and inexpensive as an alternative method to diagnose menopause definitively. Design: This diagnostic study was performed in the gynecology outpatient clinic of Haji Adam Malik General Hospital Medan and the affiliated hospitals of Universitas Sumatera Utara Medical Faculty on September 2014. This study included menopausal woman as sample and non menopausal women as control. The inclusion criteria for both groups are: not having sexual intercourse for 3 days before the sampling, not suffering from vaginitis or diabetes mellitus, not receiving hormone replacement therapy for 3 months before the sampling, not smoking or consuming alcohol, not currently in treatment with intravaginal medication or douche, and willing to sign the informed consent of the study. Vaginal pH was measured using pH test strips. Blood were withdrawn from samples and analyzed for FSH and estradiol levels. Statistical analysis was performed using Mann-Whitney test and multivariate analysis for sensitivity, specificity, ROC, and vaginal pH cut off point. Results: Majority of menopausal group subjects was from the age group of 50-59 years old (80.4%), with parity of 3-4 (38.6%), and normal BMI (43.2%). Mean vaginal pH levels in menopausal and non menopausal women were 5.11 ± 0.71 and 3.79 ± 0.55 respectively. Mean FSH level in menopausal and non menopausal women were 71.98 ±36.07 and 24.29 ±32.79 respectively. Vaginal pH levels has an optimal diagnostic value as the curve approaches 100% with an AUC value of 98.5%. Vaginal pH level cut off point is ≥ 5.5 with sensitivity and specificity of 80.4% and 93.2% respectively. Conclusion: With cut off point of ≥ 5.5, vaginal pH is a feasible, accurate and inexpensive alternative for definitive diagnosis of menopause. The result of this study could be applied to another region with similar geographical and economical background as Indonesia.

P-22. Vaginal symptoms are associated with circulating adipocyte-derived hormones in postmenopausal women
Hung-Ming Wu, MD, PhD1, Wan-Yu Huang2,1. 1Department of neurology, Changhua Christian Hospital, Taichung city, Taiwan; 2Institute of Basic Medical Sciences, National Cheng Kung University, Tainan, Taiwan
Objective: Vaginal symptoms are the main symptoms of menopause. These symptoms have been postulated to play a role in the development of metabolic disorders. The research aimed to evaluate the impact of vagasomatos symptoms on metabolic risk-related profiles in postmenopausal women. Design: A cross-sectional study conducted at a hospital. Healthy postmenopausal women with or without vagasomatos symptoms were enrolled. Clinical data, sleep, hot flashes, and fasting blood samples were analyzed. Serum glucose, lipid profile, hs-C-reactive protein, plasma insulin, adipocyte-derived hormones, and IL8 were analyzed Results: There were significant differences between both groups in plasma levels of HDL, adiponectin, and resistin. Vagasomatos symptoms were inversely correlated to adiponectin concentrations, and positively to leptin levels Conclusion: The present study found that vagasomatos symptoms significantly affected circulating concentrations of adiponectin, and leptin. Those factors are involved in insulin signal pathways, playing important regulatory roles in insulin sensitivity. The results suggest that vagasomatos symptoms are potential risk factors for development of insulin resistance.

ESTROGEN THERAPY POSTER PRESENTATIONS

P-23. Compounded Bioidentical Hormone Replacement Therapy (BHRT) Improves Bone Density In Menopausal Women With Low Bone Density
James S. Martin, BSc MD FRCS(C). Southern Ontario Fertility Technologies, London, ON, Canada
Objective: To demonstrate improved bone density in a group of women with low bone density taking BHRT for at least 1 year. Design: A consecutive case series of women presenting for consultation to consider use of BHRT for menopausal symptoms who had a previous bone density performed (Dual-energy X-ray Absorptiometry = DEXA), which demonstrated low bone density were asked to consider our study. Inclusion criteria were: willingness to repeat their bone density after being on BHRT for at least 12 months without other treatments, an initial-visit FSH over 40 pmol/L confirming menopause, our ability to obtain a copy of their previous bone density study, (completed within a year of the consultation) confirming low bone density at both the femoral neck and the lumbar spine, and not taking pharmacological medications effecting bone density except Calcium and Vitamin D supplements. BHRT included Biest (80% Estradiol / 20% Estradiol) and 3% Progesterone cream in all women and 3% Testosterone cream in some women (33/94 =35%) prescribed in levels appropriate to relieve their menopausal symptoms. All women were encouraged to take Calcium and Vitamin D supplements and to perform strength bearing exercise. Results: 94 women evaluated from Jan. 2003 to Jan. 2012 the met the inclusion criteria and all agreed to take part in the study. Ages ranged from 42 to 69 years with an average of 53.1 years. Initial average bone densities were 0.69 ± 0.11 grams per cm. squared at the femoral neck and 0.91 ± 0.10 grams per cm. squared at the lumbar spine. After at least 12 months (average 15.2 months) of treatment with BHRT, bone densities were redone using the original lab facilities and found to be 0.72 ± 0.09 grams per cm. squared at the femoral neck and 0.93 ± 0.07 grams per cm. squared at the lumbar spine. Both density measurements demonstrated a strong improved trend but did not reach statistical significance. However, 87/94 measurements at the femoral neck improved and 91/94 of the measurements at the lumbar spine improved. Conclusion: BHRT appears to be effective, with calcium, vitamin D and exercise, at improving bone densities in menopausal women with low bone density. Although the improvements were modest, this in group of women probably would be more expected. Larger studies over longer periods of time are certainly indicated.

P-24. Application of Testosterone Cream to the Clitoral Area vs. To General Skin May Be Beneficial in Bioidentical Hormone Replacement Therapy (BHRT)
James S. Martin, BSc MD FRCS(C). Southern Ontario Fertility Technologies, London, ON, Canada
Objective: Bioidentical hormone replacement therapy (BHRT) usually includes replacement of estrogen, progesterone and sometimes testosterone in trans-dermal cream form. The most difficult aspect of testosterone replacement is obtaining patient/approach that best act benefit and side effects. Recently we have found that direct application of the testosterone to the clitoral area improves benefit. This randomized study investigates the blood values, and benefit / risk profiles when testosterone cream was applied to the clitoral area as opposed to general body surface. Design: 200 consecutive women seen in consultation, diagnosed as menopausal, interested in Bioidentical Hormone Replacement Therapy, and listing one of their concerning symptoms as decreased libido were selected for study. All were originally treated with Biest (80% Estradiol / 20% Estradiol) and Progesterone cream and were seen in a review visit 6 months later.
P-25. Average Serum Estradiol Levels In Women Switching From Pharmaceutical Hormone Replacement Therapy (HRT) to Bioidentical HRT (BHRT)

James S. Martin, BSc MD FRCC(S). Southern Ontario Fertility Technologies, London, ON, Canada

Objective: Our observation has been that many women obtain excellent relief of their vasomotor symptoms using either on HRT and BHRT but usually can do so while reaching significantly lower serum estradiol levels on BHRT. The purpose of this investigation was to compare the serum estradiol levels in women switching from pharmaceutical hormone replacement therapy (HRT) to bioidentical hormone replacement therapy (BHRT). Results: Hormonal blood work was obtained and recorded in both an Immulite 1,000 and recorded in pmol/l.*

Results: The patients ranged from 48 to 71 years old with an average age of 55.2 years old. 129 of the 137 (94%) were continuing testosterone at the third visit. Two women did not start it, 6 women discontinued it because they saw no benefit or had side effects. Of the 64 women who took testosterone, their blood levels averaged 146 ± 109 nmol/l. Of the 70 women taking testosterone on the general or in the clitoral area, we could maintain or improve benefit, and decrease side effects and blood level. A study comparing 1% testosterone on the general area compared to 3% testosterone on the general skin was underway. *1 ng/dl = 0.034 pmol/l and 1 nmol/l = 28.2181 ng/dl

P-26. Hormone therapy or soy isoflavones for a better quality of life after menopause: is there a best option?

Adriana O. Pedro, Lucio O. Carmignani, MD, Lucia S. Costa-Paiva, MD, PhD, Aarao M. Pinto-Neto, MD, PhD. Department of Obstetrics and Gynecology, State University of Campinas

Objective: To identify factors associated with the quality of life (QOL) in symptomatic postmenopausal women according to the type of treatment used for the climacteric syndrome. Design: In this double-blind, randomized, placebo-controlled trial, sixty healthy symptomatic postmenopausal women were divided into three groups: a soy dietary supplement group (isoflavone 90mg), a low-dose hormone therapy (HRT) group (estradiol 1mg plus noretisterone 0.5mg) and a placebo group. Menopausal symptoms were evaluated through Menopause Rating Scale (MRS). QOL was assessed by the abbreviated version of the World Health Organization’s Quality of Life instrument (WHOQOL-BREF) at baseline and at 16 weeks of treatment. Statistical analysis was performed using the chi-square test, Fisher’s exact test, Kruskal-Wallis nonparametric test and analysis of variance (ANOVA). Multiple linear regression performed used to identify QOL related factors. Results: The mean age of the patients was 52.4 years (SD ±3.9) and mean age at menopause was 48 ±3.7 years. Comparison between groups revealed a statistically significant improvement in somatic (p=0.02) and urogenital (p=0.04) symptoms in the users of HT and dietary soy supplementation. A significant improvement in QOL was observed in women with a better improvement in those with urogenital symptoms. A significant improvement in QOL was observed in women with a better improvement in those with urogenital symptoms.

NON-ESTROGEN THERAPY POSTER PRESENTATIONS

P-27. Novel regimen of Hormone Replacement Therapy: Efficacy and Safety of Transdermal Estrogen plus Intermittent Progesterone

Aila H. Gomaia, MD, MSc1, Debra Evanki1, Shanya Klachkow2, Wendy L. Wolfman, MD, FRCS1. ‘Obstetrics and Gynecology, University of Toronto, Toronto, ON, Canada; 2Faculty of Medicine, University of Toronto, Toronto, ON, Canada

Objective: Hormone replacement therapy (HRT) is widely used for the successful relief of moderate to severe menopausal symptoms. Traditional oral regimens of HRT are associated with decreased rates of osteoporosis, yet increased rates of vascular thrombosis. However, transdermal therapies are associated with lower risk of VTE and stroke in observational studies. The WHI in the P<1 (CEF= medroxy progesterone acetate) arm risk of breast cancer increased by 8/10000/y, however it showed estrogen alone for patients with hysterectomy that estrogen alone taken for a median of 9.3 years significantly lowered the risk of breast cancer in this subgroup (hazard ratio [HR], 0.77, p= 0.81). Therefore, we postulate that using intermittent progesterone may be the preferred preparation of HRT with fewer side effects and maintain endometrial safety. The purpose of the study is to determine the efficacy and safety of reducing the progesterone dosage of continuous combined hormone therapy to 3-5 days/week with continuous transdermal estrogen 37.5 mg or 25 mg in postmenopausal women. The theoretical goal is to optimize breast safety of HRT while maintaining endometrial safety by minimizing the progesterone dosage. Design: This is a retrospective observational study. Following institutional Research Ethics Board approval, we reviewed health records of 155 menopausal women in a specialized menopause clinic within our tertiary health care centre. All women were using transdermal 17α estradiol 37.5 [117 patients] or 25 microgram [38 patients] either transdermal patches twice a week and transdermal estradiol 1 mg per week. Results: We have reviewed available mammogram results, and transvaginal ultrasounds. Results: We have identified and reviewed medical records of 155 patients, each using HRT consisting of 17β estradiol 25 or 37.5 micrograms patches and progesterone 100mg capsules 3-5 times orally per week. All patients had relief of post menopausal vasomotor symptoms. Follow up transvaginal ultrasound was done for 54.4% of patients (86/155) at least 1 year after using our low dose therapy. The average endometrial thickness was 5.9a ± 2.1mm. 69.76% (60/86) of patients had endometrium measuring less than 5mm in thickness. Only 5.16% (8/155) of patients had vaginal bleeding or breakthrough bleeding; no abnormal endometrial biopsies. Seventy four percent (48.38%) of patients reported that any bleeding was not a problem. All reports were normal. Conclusion: A combined transdermal 17β estradiol 25 or 37.5 microgram and intermittent administration of micronized progesterone either vaginal or oral is a novel approach to providing relief of menopausal symptoms while maintaining endometrial safety and a favorable tolerability profile.


Caroline Brandon, MD1,2, Christine Derzko, MD1, Amy Straus, MS2, Mark Messina, Ph.D., M.Sc.1, Dorothy Faulkner, Ph.D., M.Sc.1,2, Christopher Ireland, B. Sc., David Jenkins, MD, Ph.D.1. 1Obstetrics and Gynecology, New York University, New York, NY; 2Obstetrics and Gynecology, University of Toronto, Toronto, ON, Canada

Objective: Retrospective chart review aimed to evaluate 23 postmenopausal women who complained with the deepening of the endometrial lining for varying time of time to determine whether there was a correlation between cumulative soy exposure and thickness of the endometrial lining. Design: We assessed the endometrial thickness of 23 postmenopausal women with varying cumulative soy protein exposures using ultrasonography. We also reviewed medical records of the patient that served as the control group for the visual endometrial index (VMI). Results: There was a statistically significant association between increasing log cumulative soy consumption and thinner endometrium (r= 0.3655, p=0.0460). There was also a non-significant trend toward an increase in the superficial layer of the VMI. Conclusion: The implication of our finding is that soy protein consumption, as part of a balanced diet, is a safe and effective method for lowering serum cholesterol levels without adverse effects on the endometrial lining of postmenopausal women.
P.29
A SERM (Selective Estrogen Receptor Modulator) Treatment Based Approach to Menopause.
Heather D. Foreman, Holly Thacker. Women’s Health, Cleveland Clinic, Cleveland, OH
Objective: A SERM (selective estrogen receptor modulator) is compound that acts directly on the estrogen receptor. Their action is different in various tissues, allowing SERMs to have specific positive effects on certain tissues. In the treatment of menopause, an ideal SERM would stimulate bone but inhibit actions in breast and uterine tissue, and most recently has been used in conjugation with estrogen for the treatment of vasomotor symptoms (VSM) in menopause. This narrative review research data highlights the convenient utilization of selective SERMs, including raloxifene, tamoxifen, ospemifene, and bazedoxifene for the treatment of menopausal vasomotor symptoms (VSM), genitourinary syndrome of menopause (GSM), osteoporosis and other uniquely midlife concerns. Design: This is a narrative review that uses current literature to summarize clinical findings in the use of SERMs in the treatment of menopausal symptoms. This study is a narrative review that uses current literature to summarize clinical findings in the use of SERMs in the treatment of menopausal symptoms. It also provides the women’s health physician or the primary care physician with quick notes in order to determine which patients are ideal candidates for the different SERMs features in this review. Results: SERMs should be considered as a viable treatment options for pre- and postmenopausal women depending on their clinical condition. Raloxifene has been shown to reduce the risk of new vertebral fractures and has also shown to decrease the incidence of invasive breast cancer in postmenopausal women with osteoporosis. Raloxifene has a slightly lower risk of endometrical cancer compared to tamoxifen. Its major adverse reaction is hot flashes and has not been shown to improve GSM over placebo. Tamoxifen has been shown to be an antagonist in the breast, and is used for ER+ breast cancer treatment and prevention. Recent research shows that tamoxifen for ten years or more have positive breast cancer outcomes compared to treatment with for 5 years. Tamoxifen has shown positive effects on the bone, though not FDA approved for this indication, and is limited by its increased risk of endometrial hyperplasia and adverse effects on vaginal tissue. Three randomized double blind placebo-controlled studies demonstrated suppression of use of osphemenine 60 μg vs. placebo in the treatment of GSM. In terms of its agonistic effects on the bone, the use of osphemenine does show a decrease in bone turnover markers in postmenopausal women, yet it does not carry and FDA approval for treating osteoporosis. Bazedoxifene in combination with estrogen has shown great promise in the reduction of VMS and GSM. In several randomized placebo controlled trials (the SMART trials) bazedoxifene has overall demonstrated a significant reduction in the number and severity of hot flashes compared to placebo and proved to have a good safety profile. It also shows antagonist effects on the breast and acts as an agonist in the bone. It also shows lower rates of amenorrhea and decreases breast cancer. Conclusion: The pharmacological aim of SERMs as treatment for menopause is to have specific positive effects on certain target tissue such as breast, heart, and brain with neutral or antagonist effects on other tissue such as the endometrium. Serotonin selective SERMs are used and ideal candidates should be noted by physicians. An ideal candidate for treatment with Raloxifene is in a postmenopausal woman with osteoporosis, with an increased risk of breast cancer. An ideal candidate for tamoxifen is the prevention or treatment of ER positive breast cancer patient who does not have bothersome VSM or GSM, as it may worsen these conditions. An ideal candidate for osphemenine would be a postmenopausal woman suffering from GSM or severe dyspareunia who does not want to take hormone therapy and prefers an oral treatment. An ideal candidate bazedoxifene conjugated with estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment. An ideal candidate for conjugated estrogen is in a postmenopausal woman with an intact uterus suffering with severe vasomotor symptoms and prefers an oral treatment.
Although obesity was associated with decreased systemic exposures to BZA and CE, the relative systemic exposures for each component were not altered in a manner that would be expected to compromise the endometrial protection provided by the BZA component.

**PK Parameters in Postmenopausal Women Following Single-Dose Administration of CE 0.45 mg/BZA 20 mg**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Baseline</th>
<th>Equol Group</th>
<th>HRT Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC&lt;sub&gt;0-72&lt;/sub&gt;, μg·h·mL&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>0.36</td>
<td>0.36</td>
<td>0.36</td>
</tr>
<tr>
<td>AUC&lt;sub&gt;0-12&lt;/sub&gt;, μg·h·mL&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>0.40</td>
<td>0.40</td>
<td>0.40</td>
</tr>
<tr>
<td>C&lt;sub&gt;max&lt;/sub&gt;, μg·mL&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>0.17</td>
<td>0.17</td>
<td>0.17</td>
</tr>
</tbody>
</table>

**Secondary Vascular Actions in Women with Climacteric Symptoms**

**P-34. Relationship between Equol Producer Status and Metabolic Parameters in 743 Healthy Women**

Remi Yoshikata, MD, PhD<sup>1,2</sup>, Hiroaki Ohta, MD, PhD<sup>3</sup>, Khin Z. Myint, MBBS, MHS<sup>2</sup>, Hamastic Clinic, Minato-ku, Japan; <sup>2</sup>Tokyo Midtown Medical Center, Minato-ku, Japan; <sup>3</sup>Samno Medical Center, Minato-ku, Japan

**Objective:** Equol is an active metabolite produced by the action of intestinal flora on soy isoflavones and possesses the estrogen-like actions. It could be produced naturally from the consumption of soybean isoflavones in about 50% of Japanese female population. There is increasing evidence on its efficacy in the relief of menopausal symptoms, suppression of decreased bone mineral density, improving lipid profiles, and decreasing the risk for breast and prostate cancer. This study aimed to examine the relationship between equol producer status and the parameters related to lifestyle disease related diseases in women in their twenties to eighties. **Design:** This was an open, non-randomized, single-center clinical trial comparing equol-progestin therapy.

**Results:** The investigation included 46 women (45–63 years, average age: 51.3 ± 2.7 years), who were enrolled into two groups in a nonrandom fashion. The first group of 24 women received equol containing supplement 10 mg once daily and the second group of 22 women received combined therapy for estradiol 0.62 mg and norestroide 2.7 mg patch every two weeks. Before intervention and at monthly follow-ups, vasomotor symptoms (hot flushes and sweating) in both groups were assessed with the use of four point likert scale (No=0, mild=1, moderate=2, severe=3). Also, equol production status is evaluated before intervention. Blood pressure and branchial ankle pulse wave velocity (baPWV) measurements were taken before intervention and after three months of follow-up. **Results:** Fifteen out of 46 women were equol producers (7 in equol group and 8 in HRT group). At one month after intervention, more significant improvements in scale of vasomotor symptoms were observed in HRT group than in equol group (HRT (hot flush): -1.2 ± 0.38, p<0.05; HRT (sweating): -1.0 ± 0.43, p=0.001; Equol (hot flush): -0.38 ± 0.36, p<0.05; Equol (sweating): -0.1 ± 0.35, p=0.583). After three months both group showed significant improvement in vasomotor symptoms. Only equol group showed significant reduction in both systolic and diastolic blood pressures (SBP, DBP) and pulse pressure (ppPWV) after three months (See Table). **Conclusion:** Although inferior to HRT in improving vasomotor symptoms such as hot flashes, significant improvements were observed with equol dietary supplements. Equol showed more significant improvements in vascular health than HRT in this study. These results suggest that equol could be a potential alternative agent for the wellbeing of postmenopausal women.
P.35. Hot Flush (HF) Frequency and Severity at Baseline (BL) as Predictors of Time to Transient and Stable Treatment Success: Pooled Analysis of 2 CE/BZA Trials

JoAnn V. Pinkerton, MD,1,2 Andrew Bushmakin, MS,1 Joel Bobula, MA,1,3 Joanne Lavenberg, BS,1 Barry Kommm, PhD,1 Lucy Abraham, MS,2 CPychiol3 1PRO Center for Excellence, Pfizer Ltd, Tadworth, United Kingdom; 2University of Virginia Health System, Charlottesville, VA; 1Pfizer Inc, Groton, CT; 2Pfizer Inc, Collegeville, PA

Objective: Conjugated estrogens/bazedoxifene (CE/BZA) reduces HF frequency/severity in postmenopausal women. This post hoc analysis was conducted to determine the impact of BL HF frequency/severity on the time to achieve transient and stable treatment effects with the approved CE 0.45 mg/BZA 20 mg dose, to provide clinicians an estimated time for patients to expect improvement. Design: In the randomized, placebo-controlled, phase 3, 2-y SMART-1 and 12-wk SMART-2 trials of CE/BZA, non-hormonally treated postmenopausal women recorded the frequency of moderate/severe HFs in daily diaries. SMART-2 restricted enrollment to women with ≥2 moderate/severe HFs/d or ≥50/ wk at screening; SMART-1 did not, but only women with HFs at screening were included here. This analysis used nonparametric models to estimate median times to transient treatment success (first day that ≥50% improvement in HF frequency/severity was attained) and stable success (day that was achieved and sustained for remainder of the study) based on daily frequency/severity of HFs at BL. Daily severity was calculated as (number of mild HFs) + 1 x (not moderate HFs) + 2 x ( severe HFs) + 3 x total HFs that day. Pool data from women treated with CE 0.45 mg/BZA 20 mg or CE 0.625 mg/BZA 20 mg through wk 12 were analyzed using the SAS Proc Lifetest. Women not achieving a ≥50% improvement within 12 wk were censored. Results: Results for CE 0.45 mg/BZA 20 mg are shown in the figure. Women with fewer BL HFs achieved a transient ≥50% reduction in HF frequency/severity sooner than women with more BL HFs. Similarly, women with less severe vs more severe BL HFs achieved a transient ≥50% reduction in severity sooner. The same pattern was seen for stable success, which was typically achieved within a few days after the first ≥50% reduction, but these results were not statistically significantly different across BL frequency/severity subgroups. Findings with CE 0.625 mg/BZA 20 mg were comparable. Conclusion: Women with more frequent or severe HFs take longer to achieve treatment success with CE/BZA, but stable improvement is less influenced by BL status. These findings allow for an estimate of how long it will take an individual patient to achieve ≥50% improvement in HF frequency/severity based on pretreatment HF frequency/severity. For example, a woman who has an average of 5 HFs/d that are, on average, moderate in severity can expect to see transient improvement in HF frequency/severity after about a week of CE 0.45 mg/BZA 20 mg therapy. Stable improvements of ≥50% are expected quickly thereafter, regardless of HF frequency/severity. Women with frequent/severe HFs should be encouraged to stay with treatment, as it may take a few weeks to achieve a significant improvement.

P.36. Lasofoxifene, an estrogen agonist/antagonist improves symptoms of genitourinary syndrome of menopause (GSM) and physiologic markers associated with vulvovaginal atrophy (VVA) in two large Phase 3 studies

David J. Portman, MD,1,2 James Symons, MS, PhD1 1Sermonix Pharmaceuticals, Columbus, OH; 2Columbus Center for Women’s Health Research, Columbus, OH

Objective: Many women suffer from genitourinary symptoms in menopause as a consequence of falling sex steroid levels. A significant number remain untreated due to associated with vulvovaginal atrophy (VVA) in two large Phase 3 studies

Design: Two identical 12 week randomized placebo-controlled Phase 3 treatment studies evaluated lasofoxifene 0.25mg and 0.5mg daily, in each of the individual and pooled studies, demonstrated a statistically and clinically meaningful improvement in the 4 co-primary endpoints, with several demonstrating beneficial effect as early as 2 weeks. Lasofoxifene is an effective and well-tolerated treatment of moderate to severe symptoms of VVA and offers women an alternative to vaginal and oral estrogens that provide a meaningful benefit for the relief of bothersome symptoms of GSM/VVA while conferring extra-genital benefits to bone and breast health.

P.37. Pharmacokinetics of S-equol after administration of a fermented soy germ in equal producing and non-producing postmenopausal women

Shigeto Uchyanuma1, Soh Iwashita2, Tomonori Ueno1, Belinda H. Jenks1, James Brooks1 1Otsuka Pharmaceutical Co.Ltd., 2Saga Nutrceuticals Research Institute, Saga, Japan; 3Otsuka Pharmaceutical Co.Ltd., Nutraceuticals Division, Tokyo, Japan; 3Pharmavite LLC, Scientific Affairs, Northridge, CA

Objective: S-equol, a metabolite of soy isoflavone daidzein, is suggested to have multiple non-hormonal effects including menopausal symptom relief. We found an equal producing lactic acid bacterium Lactococcus 20-92 and first developed a fermented soy germ ingredient with S-equol, SES-5OH. Pharmacokinetics of S-equol after administration of SES-5OH was investigated in human including climacteric women. S-equol in plasma exists as both conjugated and unconjugated forms. S-equol conjugates are recognized as bioactive S-equol form. However, pharmacokinetics of S-equol conjugate/unconjugated form are not well elucidated. Thus, the objective in this study was to investigate the pharmacokinetics of free S-equol and sulfate conjugates in healthy postmenopausal women. Healthy postmenopausal Japanese women aged 43-62 years participated in this study. Oral S-equol administration was accomplished using a fermented soy germ SES-5OH. In a single-center, randomized, open-label study, the subjects ingested a single-bolus of SES-5OH tablet including 10 mg SES-5OH. Plasma samples were collected before and after 0.5, 1, 2, 3, 6, 12, 24, and 48 hours of the administration and urine was collected over the 48 hours period. In Plasma and urine samples were analyzed then hydrolyzed overnight using a mixed beta-glucuronidase and sulfatase enzyme. Results: In the 11 subjects, equal producers and non-producers were 6 and 5, respectively. To reach maximum plasma concentrations (Tmax) in free, sulfate conjugates and total S-equol were all ~1 hour. The maximum plasma concentrations (Cmax) of S-equol in sum of free and sulfate conjugated forms was 0.89μmol/L and that in total was 2.38μmol/L. The plasma elimination half-life (T1/2) was ~6-9 hours in both the area under the curve (AUC) for the first 24 hours (AUC24h) of plasma S-equol concentrations in sum of free and sulfate conjugated forms was 0.30μmol/L and that in total was 10.12μmol/L. Percentage of sum of plasma free and sulfate conjugated forms versus the total S-equol in AUC24h was 43.4%. The majority of sulfate conjugated forms was equol 7-sulfate, then equol 4'-sulfate. Only little equol 4',7-disulfate was detected. The fraction of dose excreted during the 48 hours into urine was 76 %. All pharmacokinetics parameters of S-equol after single-bolus oral administration of SES-5OH were not different in equal producing status. Conclusion: This study addressed pharmacokinetics of S-equol after administration of SES-5OH in equal producing and non-producing postmenopausal women. The data demonstrated the 40% of total plasma S-equol was bioactive form, which may involve in potential benefits of S-equol.
VAGINAL HEALTH POSTER PRESENTATIONS

P-38. The Impact of a Women’s Sexual Health Product on Genital Engorgement as Measured by Thermography: A Proof of Concept Study
Irwin Goldstein, MD; Sue Goldstein, BA,CCRC; Leah Millheiser, MD; 1Nuelle, Inc, Mountain View, CA; 2San Diego Sexual Medicine, San Diego, CA
Objective: Sexual function is a vital component of quality of life for many midlife women. Despite noting that it is moderately important and extremely important, decline in circulating estrogen levels that occurs during perimenopause/ menopause has been shown to negatively affect clitoral arterial blood flow and engorgement as well as vibratory perception. This, in turn, can increase latency to achieving genital arousal during sexual activity. The primary aim of this study was to determine the degree of engorgement, as measured by temperature change in the external genitalia, produced by a sexual health product utilizing suction and vibration technology to enhance genital blood flow. The secondary aims were to determine the time of onset of self-reported sexual arousal during use of the product as well as development of sexual desire. Design: A single-site, prospective, non-blinded study of a women’s sexual health product was conducted in 12 sexually active, postmenopausal women (mean age: 59.2 ± 5.4 years; time since last menstrual period: 9.5 ± 8.3 years) from March 2015 to July 2015. Cohort eligible women must not have experienced a menses for at least 12 months, have a Female Sexual Function Index (FSFI) total score ≥ 26.5, and have been sexually active in the 30 days prior to enrollment. Use of postmenopausal hormone therapy was not an exclusion criteria, however, only 2 of the participants were using systemic therapy while none reported the use of local estrogen therapy. Each subject underwent a single visit procedure lasting up to 55 minutes that included the establishment of baseline temperature, use of the sexual health product placed over the clitoris, and post-product skin temperature assessment. Temperature was measured using Forward Looking Infrared InfraRed Thermography. Participants were alerted telegraphic notes of the temperature change and audio recording was used throughout the use of the product. At the end of the procedure development of sexual desire was assessed using a Likert scale. Results: A two-sided paired t-test was used to assess the statistical significance of the temperature increase from baseline to post- product use. The temperature increases for the clitoris and vestibule were statistically significant at all time points (0,2,4,6,8,10 minutes) following removal of the product. Temperature increase for the labia was only significant at 0 and 2 minutes. The most significant temperature increase was observed at 0 minutes for all sites: clitoris (mean 2.47°C ± 0.9, p = 0.002), labia (mean 1.63°C ± 0.58, p < 0.0001), and labia (mean 0.82°C ± 0.48, p = 0.0001). Ten out of the 12 participants developed sexual arousal during use of the product with the average time to onset being 4.5 ± 2.4 minutes. An analysis of variance showed statistically significant differences in scores across domains of the FSFI with orgasm (mean 5.6 ± 0.6), satisfaction (mean 5.7 ± 0.5), and arousal (mean 5.6 ± 0.4) scoring the highest. Fifty-eight percent of participants (n=7) strongly agreed that they “felt in the mood for sex” after use of the product, 25% (n=3) agreed, and 17% (n=2) somewhat agreed. None of the participants disagreed with the statement. No adverse events were reported during the study period. One additional subject is scheduled for enrollment to be included in the final analysis, but no significant variances are expected. Conclusion: To date, there has been limited information quantifying the degree of genital arousal produced by products that incorporate clitoral suction or suction. The women’s sexual health product used in this study, which employs both, produced statistically significant increases in vulvar temperatures, which is a marker of genital blood flow and engorgement. A notable finding that warrants further investigation is the congruence of genital arousal and development of sexual desire as a result of product use in this cohort of postmenopausal women.

Min Kyong Kim, M.D., YaeKyoo Koh, M.D, ByangSeok Lee, Seok Kyo Seo. Obstetrics and Gynecology, Yonsei University College of Medicine, Seoul, Korea (the Republic of
Objective: The common causes of postmenopausal bleeding (PMB) according to the data from the western world are vaginal or endometrial atrophy, hormone therapy, endometrial cancer, endometrial or cervical polyps, endometrial hyperplasia, and other miscellaneous diseases. However, there is no existing data from Asia concerning the PMB’s causes. Therefore, we conducted a retrospective study to compare whether the causes of PMB in Korean menopausal women are similar to the already known data. Design: A retrospective study using 10-year medical records (March, 2005 to December, 2014) of PMB women in Yonsei University Health System, Seoul, South Korea. Total of 980 women who stopped menstruating for more than 12 months were enrolled in the study. The medical records were thoroughly reviewed and arranged into a few categories: past history, diagnosis, the method in which the diagnosis was confirmed, and sonographic data. All data were input into Excel database (Microsoft, USA) for analysis. The mean The most common cause of PMB in Korean women was ‘atrophy’ (39.4%). ‘Endometrial and cervical polyps’ were the second common cause (8.0%), ‘cervix cancer’ was the third (7.3%), ‘hormone therapy’ (5.7%), ‘cervicitis’ (5.3%), ‘endometrial cancer’ (4.8%), and ‘endometrial hyperplasia’ (4.1%). The other causes were ranked next. Conclusion: Only the most common cause of PMB was the same as the conventional data and other causes were all ranked differently in Korean postmenopausal women. Due to high prevalence of cervix cancer and human papilloma virus infection in Korea, ‘cervix cancer’ was noted as the third common cause. It seems possible that the etiology of PMB is largely affected by the ethnicity and different cultural backgrounds.

Michael Krychman1, Stephanie Pendergast, MPT2, Mark Juravic3. 1Southern California Center for Sexual Health, Newport Beach, CA; 2Pelvic Floor and Rehab, Los Angeles, CA; 3Aeterna Medical, San Francisco, CA
Objective: Vaginismus are recommended and used for many clinical indications including but not limited to dyspareunia, pelvic floor hypertonus and vulvar vestibulitis. Although they are commonly used in sexual medicine, there is limited data about its clinical utility with respect to treatment paradigms. Online clinician and patient surveys are necessary to ascertain further data concerning dilation use and practical implications in clinical practice Design: Two online clinical surveys were created in order to ascertain detailed information concerning practical and clinical information with respect to dilator use. Random health care professionals were emailed a page 32 questions survey and were asked to complete it online. Participants received a small financial remuneration for their time. We present the first 77 respondents who completed the survey from July 2 to and including July 7, 2015. Further comprehensive clinician and patient data are scheduled to be gathered and presented. Results: The preliminary report consisted of 77 respondents (72 female; 5 male) who were in clinical practice for an average of 15.9 years. The majority were physical therapists (86%) 60%; and (13) were medical doctors. The most common indication for prescribing dilators was for painful intercourse and vaginismus. Approximately 14% of those surveyed prescribed over 100 dilators per year whereas 16% prescribed approximately fifty. Health care professionals estimated their success rate as measure by painless penetration at 71% and that patients achieved success on average 4.7 months after starting their dilator program. Clinicians prescribed an average of 80% of their patients with vaginismus and suffered from the condition for 2 or greater seeking treatment with 20% suffering for 5 years or longer. Most HCP instruct patients to use dilators every other day and follow up is commonly 2-4 weeks with only 8.3% following up every 3 months. Half are instructed to use dilators at night and the other half are instructed to use them whenever they feel comfortable in their scheduling. In 80% of the time patients are taught mindfulness, 57% of the time meditation and more than half are instructed to listen to calming music during dilator exercises. The most common reasons for non-compliance is perceived to be – fatigue, pain during use, fatigue and dilators being cumbersome. HCP report patient commonly expressed emotions are anxiety, hopeful, empowered, embarrassed and frustration. The most commonly recommended dilators are Soul Source (30%), Vaginisms.com (27%) and Syracuse (19.7). Only 38.5% of clinicians sell dilators in their offices and 65% report the remainder is found at online purchasing. However, 77% of HCP would consider selling dilators through their office. Conclusion: Vaginal dilators are widely used in sexual medicine practice for a variety of health care conditions however largely remain an understudied and under appreciated sexual accessory. HCP perception of use and impression of emotional barriers to compliance are important facets to understand. Patient educational programs and support are necessary to ensure compliance. Further data is being collected as well as a comparative analysis of information from dilator patients will be gathered and presented.

P-41. Use of Some Biest Cream Vaginally (As Part of Biodentifical Hormone Replacement Therapy (BHRT)) is Effective At Relieving Vaginal Dryness In Menopause
James S. Martin, BSc MD FRCs(C). Southern Ontario Fertility Technologies, London, ON, Canada
Objective: BHRT is often prescribed as creams containing hormones, which are rubbed into skin surfaces of the body. Previously, we had found instructing patients to rub some of their Biest cream into the vagina, very effective treatment for vaginal dryness. The purpose of this study was to further investigate the effectiveness of Biest (80% Estrol) to 20% Estradiol at concentrations of 0.625, 1.25 or 2.5mg/ml in Vagibase ® Cream) used partially vaginally at relieving vaginal dryness for menopausal women. Design: 565 consecutive untreated menopausal women who gave one of their complaints as “vaginal dryness” and were seen in consultation for consideration of biodentifical hormone replacement between Jan. 2005 and Dec. 2011 were considered for inclusion in the study. Inclusion criteria also were menopausal status, defined as an FSH level greater than 40 IU/l* and at least one year of no menstruation, sexual activity despite vaginal dryness or a desire to return to sexual activity and an opportunity to do so. Exclusion criteria were the use of any prescribed pharmaceutical products for either vaginal dryness or hormone replacement therapy. 397 of the 565 (70%) of the women met these criteria. These women were instructed to use 0.2-0.4-ml of their Biest cream vaginally by placing the cream on their finger, inserting their finger to between the 1st and 2nd knuckle into the vagina and rubbing the Biest cream vigorously into the vaginal mucosa. First follow-up visit was 6 months and they were asked to estimate their compliance and the % improvement in their vaginal dryness. Results: 375 of 397 (94%) women accepted and filled a prescription for BHRT and returned for their first recheck visit. 293 of the dilators, 38% of the women claimed at least slight improvement in their vaginal dryness. Improvement of the 82 women who returned but did not claim 80% improvement, 28 (34%) had not started or had stopped the vaginal component of the prescription and 42 of the 82 (51%) had not resumed sexual intercourse. Many of the remaining 82 had had long duration vaginal dryness in the many had been found to have very severe vaginal atrophy (consistent loss of labia minora and/or decreased diameter or length of the vagina) on their initial physical examination. Conclusion: Use of some part of Biest cream vaginally to treat menopausal patients complaining of vaginal dryness is very effective.
P-42. The Pre-menopausal vs. Postmenopausal Vagina: A Comprehensive Comparison
Objective: Changes to the vagina from the reproductive years through to menopause have been long recognized. It also has been noted that vaginal symptoms reported by reproductive aged women are usually different from those of the aging woman due to differences in estrogen reliance and aging. The purpose of this study was to provide a comprehensive comparison of the pre-menopausal to the postmenopausal vagina from the macro to micro level. Design: A systematic literature review of vaginal changes from the reproductive years through menopause was conducted using PubMed/ MEDLINE, Embase, Academic Search Complete, and CINAHL databases. Results: The reproductive aged woman is rich with estrogen and androgen receptors which decline in density with menopause. Decreasing estrogen levels in the postmenopausal vagina lead to epithelial atrophy and reduced secretions as compared to the pre-menopausal vagina that exhibits a thicker epithelium, higher glycogen content and parakeratosis. The pH of the postmenopausal vagina also is significantly higher than that of the pre-menopausal vagina. The pathologic processes that dominate the pre-menopausal vagina include bacterial vaginosis and yeast infections whereas the postmenopausal vagina has increased diversity of microbial species with less fluctuation in microbiota over time. Blood vessel quantity, blood flow, and transvaginal potential difference are lower in postmenopausal vagina as compared to the pre-menopausal one. The vinas of both pre- and post-menopausal women are immunocompetent with no noticeable differences in immune cell populations. Transvaginal ultrasound was associated with the decrease in number and density of epithelial function are down regulated whereas genes associated with inflammation are upregulated in the postmenopausal vagina. Conclusion: The postmenopausal vagina significantly differs from the reproductive-aged vagina in many ways. As more microorganisms vaginally advances occur, future assessments of vaginal health across the life cycle should consider the use of these measures in addition to the standard ones currently in use.

P-43. Ovulatory bladder syndrome in climacteric women: a population-based study
Adriana O. Pedro1, Cassia T. Juliato, MD, PhD, Luiz F. Baccaro, pHD, Jeffrey L. Fui, MSc2, Lucia S. Costa-Paiva, MD, PhD, Arao M. Pinto-Neto, MD, PhD, Gynecology, CLINICA LANE, Campinas, Brazil; Obstetrics and Gynecology, UNICAMP, Campinas, Brazil
Objective: Ovulatory bladder syndrome (OAB) is characterized by the presence of urinary urgency with or without urinary incontinence. Increased urinary frequency is the most frequently reported symptom of OAB (85%), followed by urinary urgency (54%) and urgency incontinence (36%). Diagnosis of OAB is essentially clinical and can be performed through a structured questionnaire. There are few population-based studies evaluating the epidemiology of OAB in women, especially in the climacteric stage where there is a decrease in estrogen production, with an effect on the prevalence of OAB. The objective was to assess the prevalence of OAB and associated factors in climacteric Brazilian women. Design: An exploratory, descriptive, cross-sectional, population-based study was conducted with 749 climacteric women aged 45-60 years. Inclusion criteria were native Brazilian women, aged 45-60 years, and residing in the metropolitan region of Campinas. Women who were unable to complete an interview for any reason, such as language or comprehension problems, were excluded. The interviews were performed in a structured interview. For the variable was OAB, which was considered as present when the participant answered that she had urinary urgency ("urge to urinate and have to run to the bathroom"), with or without urinary incontinence, and when there was no stress urinary incontinence. Trained research assistants held home interviews or a phone interview was scheduled. The questionnaire included four sections: sociodemographic information, health habits, health problems, and self-reported health status. Statistical analysis was performed using the chi-square test and multiple Poisson regression model was created to assess which variables were independently associated with a higher prevalence of OAB. Prevalence ratios (PRs) and 95% confidence intervals (95% CI) were calculated by backward selection of significant variables. Results: The mean age was 52.5 ± 4.4 years. With regard to menopausal status, 16% were premenopausal, 16% were perimenopausal, and 68% were postmenopausal. The mean age of menopause was 46.5 ± 5.8 years. Of the 749 women, 59 (7.8%) answered that they had urinary urgency without stress incontinence as compared to the pre-menopausal vagina that exhibits a thicker epithelium, higher glycogen content and parakeratosis. The pH of the postmenopausal vagina also is significantly higher than that of the pre-menopausal vagina. The pathologic processes that dominate the pre-menopausal vagina include bacterial vaginosis and yeast infections whereas the postmenopausal vagina has increased diversity of microbial species with less fluctuation in microbiota over time. Blood vessel quantity, blood flow, and transvaginal potential difference are lower in postmenopausal vagina as compared to the pre-menopausal one. The vinas of both pre- and post-menopausal women are immunocompetent with no noticeable differences in immune cell populations. Transvaginal ultrasound was associated with the decrease in number and density of epithelial function are down regulated whereas genes associated with inflammation are upregulated in the postmenopausal vagina. Conclusion: The postmenopausal vagina significantly differs from the reproductive-aged vagina in many ways. As more microorganisms vaginally advances occur, future assessments of vaginal health across the life cycle should consider the use of these measures in addition to the standard ones currently in use.

P-44. Menopausal vulvovaginal atrophy: comparative effectiveness of vaginal therapies
Guilherme Fernandez, MD, Adriana O. Pedro, Luiz F. Baccaro, pHD, Lucia S. Costa-Paiva, MD, PhD, Arao M. Pinto-Neto, MD, PhD. Obstetrics and Gynecology, State University of Campinas, Campinas, Brazil
Objective: Vaginal atrophy is a common chronic condition among postmenopausal women that affect their quality of life. According to the North American Menopause Society, symptoms related to vulvovaginal atrophy affect approximately 45% of postmenopausal women, but only 25% of women receive medical treatment. Recent studies have evaluated new treatment alternatives for vaginal atrophy; however, few therapeutic options have been thoroughly evaluated. This study aimed to compare the effectiveness and adverse effects of estrogen, testosterone, polyacrylic acid, and placebo lubricant for the treatment of postmenopausal women with vulvovaginal atrophy. Design: We conducted a randomized clinical trial with 80 postmenopausal women aged between 40 and 70 years who were being followed up at the Menopause Clinic of CAISM, State University of Campinas, between November 2011 and January 2013. Inclusion criteria were as follows: women aged 40–70 years with physiological menopause, history of amenorrhea for more than 3 years, and a follicle stimulating hormone (FSH) level of <30 mIU/mL. Exclusion criteria for menopausal symptoms or other diseases, normal Papanicolaou smears and mammograms for the past 12 months, and complaints compatible with the symptoms of vulvovaginal atrophy. Women were randomly assigned to topical vaginal treatment with estrogen, testosterone, polyacrylic acid and placebo lubricant, three times a week for 12 weeks. It was used the vaginal maturation index, vaginal pH, vaginal health score, vaginal flora, laboratory hormonal tests and transvaginal ultrasound to evaluate changes of vaginal trophism and endometrium at baseline and after 6 and 12 weeks of treatment. Data were analyzed on an intention-to-treat basis, excluding all participants who were lost to follow-up in each outcome. Comparative characteristics data were analyzed using chi-squared test, nonparametric Kruskal–Wallis test and analysis of variance (ANOVA). Analysis of percentages in each group compared with the control group for vaginal maturation index, pH, vaginal health and presence of lactobacilli were performed with the chi-squared and Fisher tests.

Results: No significant differences in vaginal pH when comparing placebo with polyacrylic acid. The use of polyacrylic acid as compared with placebo showed no clinical improvement of vaginal atrophy. Treatment with topical estrogen improved the vaginal maturation index and showed increased levels of estradiol after 12 weeks of treatment with topical estrogen and testosterone compared with the lubricant, resulting in a percentage of patients with vaginal pH<5, increased in the number of lactobacilli. There were no significant differences in vaginal pH when comparing placebo with polyacrylic acid. The use of polyacrylic acid as compared with placebo showed no clinical improvement of vaginal atrophy. Treatment with topical estrogen improved the vaginal maturation index and showed increased levels of estradiol in three women, but remained within the normal postmenopausal range. No changes were observed in the endometrial evaluation of all treatment groups. Conclusion: The postmenopausal women who underwent 12 weeks of treatment for vulvovaginal atrophy with testosterone proinate and estrogen showed significant clinical improvement of vaginal trophism compared with the placebo lubricant and polyacrylic acid. Funding source: FAPESP 2011/14775-9

P-45. Treatment of pain using a non-implanted intra-vaginal electrical stimulation device compared to sham device in chronic pelvic pain patients
Eli Shih, MD, Mary J. Uy-Koh, MD. Center for Specialized Women’s Health Women’s Health Institute, Cleveland Clinic Foundation, Kent, OH
Objective: Chronic pelvic pain (CPP) is a complex and devastating diagnosis, encompassing many different conditions and involving many organ systems. This can result in challenging cases characterized by pain that is refractory to standard treatment. In a study conducted by Mathias et al., one in seven women experience CPP. The economic burden can be substantial, with previous estimates of 2.8 billion dollars per year. (1) Dyspareunia is defined as recurrent or persistent pain associated with sexual intercourse and affects approximately 8-21% of women in the United States (19, 20). Dyspareunia may lead to sexual dysfunction and may affect a woman’s reproductive health and overall quality of life. Previous estimates indicate that 35% of women with dyspareunia report pain during or after intercourse (1).Treatment of chronic pelvic pain is challenging due to a poor understanding of pain processing and physiology. A comprehensive approach is ideal and may include physical therapy, medications, or cognitive behavioral therapy. Pelvic floor physical therapy (PFPT) is an effective treatment for pelvic floor dysfunction. One modality used in PFPT is electrical stimulation (ES). ES is delivered in multiple ways including peripheral nerve stimulation, a transcutaneous electrical nerve stimulation (TENS) unit, or sacral neuromodulation using an implantable device. The goal of action for ES is unclear. One theory, termed the gate theory, suggests that electrical stimulation of nerves via a specific dermatome results in a blocking or gating effect at the dorsal horn of the spinal cord. This inhibits the transmission of pain impulses to the upper nervous system. Also, low frequency stimulation of the dermatome surface to the level of endorphins is observed, providing pain relief. The hypothesis, benefits, ES through PFPT is time intensive and dependent upon a health care provider’s schedule. It often causes the patient social embarrassment resulting in its inaccessibility. Although ES provides pain relief, even highly motivated patients report that anxiety prohibits them from participation in physiotherapy (6). InControl Medical created a
line of products FDA approved for urinary incontinence and fecal incontinence (10). These devices are non-implanted, customizable, intra-vaginal probes made of medical grade silicone and provide electrical stimulation to the pelvic floor. One of the devices, ApexM™ provides electrical stimulation at frequencies alternating between 13 Hz and 50 Hz and allows the clinician to adjust the intensity as well as the duration. We propose a novel randomized controlled trial comparing the investigated device to a sham device. Subjects will perform 12 minute sessions, six times each week for a total of 12 weeks. The primary outcome is pain control using the visual analog scale and brief pain inventory (18). Secondary goals include the effect of ES on quality of life using SF-36, sexual function measured by FSFI, and overall use of the investigated device to a sham device. Subjects will perform 12 minute sessions, six times each week for 12 weeks.

P-46. What is the most prevalent metabolic syndrome component that cause sexual dysfunction in postmenopausal women?
Gustavo M. Silva, MD, Sônia Maria Rolim Rosa Lima, Benedito Fabiano dos Reis. Departamento de Obstetricia e Ginecologia, Faculdade de Ciências Médicas da Santa Casa de São Paulo, São Paulo, Brazil
Objective: To evaluate the influence of the long-time treatment of sex steroids combined with the metoclopramide on the production of the HA in the cervix of the animals. Design: 10 mice were distributed into 5 groups: EG (saline solution); PG (progesterone + met); PGF (progesterone + met + estradiol); PGF met (progesterone + met + estradiol + metoclopramide); and S (saline solution). The animals were sacrificed after 100 days of treatment and the cervical tissues were collected. Results: The production of the HA was assessed by immunohistochemistry. The highest production of HA was observed in the group treated with saline solution. The production of HA was significantly lower in the groups treated with metoclopramide. Conclusion: The long-time treatment of sex steroids combined with the metoclopramide reduces the production of the HA in the cervix of the animals.

P-47. Use of a novel fractional CO2 laser for the treatment of genitourinary syndrome of menopause
Eric R. Sokol, MD, Mickey Karram, MD. 1OB/GYN, Stanford University, Stanford, CA; 2OB/GYN, The Christ Hospital, Cincinnati, OH
Objective: The primary objective was to assess the safety and efficacy of a novel fractional CO2 laser for the treatment of Genitourinary Syndrome of Menopause (GSM). Secondary objectives were to: 1. Assess the effect of treatment on female urogenital health using the “Vaginal Health Index” (VHI) score 2. Assess the effect of treatment on vaginal wall pliability by tracking the maximum dilator size tolerable for the patient 3. Assess the change in vaginal pH before and after each treatment session 4. Assess the effect of treatment on female sexual function using the “Female Sexual Function Index” (FSFI) specific questionnaire 5. Assess the effect of treatment on general quality of life using the “Short Form 12” (SF-12) questionnaire 6. Assess the degree of physician ease of treatment using the Patient Global Impression of Improvement (PGI).

P-48. Evaluation of the Hyaluronic Acid in murine cervix after treatment with steroid hormones combined with the metoclopramide
Rafaela C. Vaz, Fernanda Verna, Dr, Alice Alvarez, Leal, Ms1, José M. Soares Júnior, MD, Ph.D., Ricardo S. Simões, Dr, Manuel J. Simões, Ph.D. 1Department of Morphology, Federal University of São Paulo, São Paulo, Brazil; 2Gynecology, Federal University of São Paulo, São Paulo, Brazil; 3Ophthalmology, Federal University of São Paulo, São Paulo, Brazil; 4Obstetrics and Gynecology, Faculty of Medicine University of São Paulo, São Paulo, Brazil
Objective: To evaluate the influence of the long-time treatment of sex steroids combined with the metoclopramide on the production of the HA in the cervix of the mice. Design: 100 female mice (from > ovarioctomized, ovx) were divided into ten groups with 10 animals each: Control groups of the experiments: CG (control, non-ovx group) and OG (ovx group); treated with saline solution; and metG (met group/ovx) and metOG (met group/ovx); treated with metoclopramide (met). Experiment with hormonal treatment: EG (progesterone plus met); PG (progesterone plus estradiol); PGF (progesterone plus estradiol plus met); PGF met (progesterone plus estradiol plus metoclopramide). Experiment with hormonal treatment combined with metoclopramide: metEG (met/EG group/ovx); 17β-estradiol plus met; metPG (ovx/PG group); progesterone plus met and, metPGF (ovx/met/PG group); 17β-estradiol conjugated to progesterone plus met. The treatments started after 30 days of the bilateral ovariectomy and, all animals were treated for 50 consecutive days subcutaneous with injections (saline solution or metoclopramide) and the hormone dissolved in sunflower oil for gavages. After 50 days the animals were euthanized and the cervix were removed and evaluated the hyaluronic Acid concentration by Elisa-Like fluorometric assay method. Data were statistically analyzed by ANOVA (p<0.05). Results: The concentration of HA: (OG=metG) and (PG=metO) > compared to CG and compared to groups treated with sex steroid hormones with or without metoclopramide (p<0.05), and finally (OG=metG) > compared to (PG=metO), (p<0.05). In comparing the other groups there was no significant difference. Conclusion: Our results allow us to some conclusions: 1. The ovariectomy increases the concentration of the HA and the treatment with metoclopramide reduces the concentration of the HA of the 2. The combined action of the hormone and metoclopramide modulates the action on synthesis of the HA in the cervix of the ovarioctomized animals. 3. The metoclopramide interferes on synthesis of the HA in the cervix of the animals with ovaries, and 4. The metoclopramide no interferes in action of the exogenous steroid hormones on synthesis of the HA in the cervix of the ovarioctomized animals.
diseases, depression, anxiety and cancer. Results: From the 736 women, 53% reported multimorbidity and from these 49.6% reported having sexual dysfunction. The average age of the entire group was 52.5 (± 4.4) years. With respect to menopausal status, 16% were premenopausal, 16% perimenopausal, and 68% postmenopausal. The average age of menopause was 46.5 (± 5.8) years. Multiple regression analysis showed no association between sexual dysfunction and multimorbidity. Multiple regression analysis showed no association between sexual dysfunction and multimorbidity. Sexual dysfunction in whole sample (with and without multimorbidity) was associated with sexual activity in the last month (PR=0.27, CI95% 0.22-0.33, p<0.001), having physical activity ≥2 times a week (PR=0.70, CI95% 0.58-0.84, p<0.001), menopause rating scales (MRS)>8 (PR=1.25, CI95% 1.09-1.43, p=0.002), perimenopausal or postmenopausal status (PR=1.57, CI95% 1.13-1.7, p=0.007), alcohol use ≥1 drink per week (PR=0.81, CI95% 0.67-0.97, p=0.025) and anxiety (PR=1.15, CI95% 1.01-1.31, p=0.05). In the group with multimorbidity, the main factors associated with sexual dysfunction were sexual activity in the last week (PR=0.31, CI95% 0.25-0.39, p<0.001), anxiety (PR=1.33, CI95% 1.15-1.53, p<0.001) and physical activity (PR=0.70, CI95% 0.56-0.87, p=0.002). Conclusion: There was no association of multimorbidity and sexual dysfunction in this sample of women aged 45 to 60 years. The main factors associated with sexual dysfunction in women in multimorbidity sample were lack of sexual activity in the last month, physical inactivity, and anxiety. This highlights the importance of sexual counseling as a proactive physical activity for a satisfactory sexual life in the case of women with multimorbidity. Factors associated to sexual dysfunction – Multiple Poisson regression *

<table>
<thead>
<tr>
<th>Factor</th>
<th>PR</th>
<th>CI95%</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1: All group (n=736)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sexual activity in the last month (yes)</td>
<td>0.27</td>
<td>0.22-0.33</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Physical activity ≥2 times/week</td>
<td>0.70</td>
<td>0.58-0.84</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MRS &gt;8</td>
<td>1.25</td>
<td>1.09-1.43</td>
<td>0.002</td>
</tr>
<tr>
<td>Perimenopausal or postmenopausal status</td>
<td>1.57</td>
<td>1.13-1.7</td>
<td></td>
</tr>
<tr>
<td>Alcohol use ≥1 drink per week</td>
<td>0.81</td>
<td>0.67-0.97</td>
<td>0.025</td>
</tr>
<tr>
<td>Anxiety (yes)</td>
<td>1.15</td>
<td>1.01-1.31</td>
<td>0.039</td>
</tr>
<tr>
<td>Model 2: Women with multimorbidity (n=389)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sexual activity in the last month (yes)</td>
<td>0.31</td>
<td>0.25-0.39</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anxiety (yes)</td>
<td>1.33</td>
<td>1.15-1.53</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* Analysis considering the cluster (census tracts)

P-50. Examining Differences in Cortical Thickness in Perimenopausal Middle Aged Females with Major Depressive Disorder and Healthy Controls

Gésime L. Alders, MSc (PhD Candidate)1, Luciano Minuzzi, MD, PhD2, Geoffrey B. Hall, PhD2, Lauren Cudney, MSc2, Meir Steinier, MD, MSc, PhD, FRCPCC,1, Claudio Sorace, MD, PhD, FRCPCC, MBA1, Benicio Frey1,3. Women’s Health Concerns Clinic, St. Joseph’s Healthcare Hamilton, Hamilton, ON, Canada; 2Department of Psychology, Neuroscience & Behaviour, McMaster University, Hamilton, ON, Canada; 3Mood Disorders Program, St. Joseph’s Healthcare Hamilton, Hamilton, ON, Canada.

Objective: To examine differences in cortical thickness in middle aged females with MDD and healthy control participants. Design: Twenty-four healthy control participants (mean age = 51±1.51 years), and 19 unmedicated participants with MDD (mean age = 51±4.5 years) were included in the analysis. Depression symptoms were assessed with the Montgomery-Asberg Depression Rating Scale (MADRS), with healthy control participants reporting mean MADRS scores of 3.2±2.5, and MDD participants reporting mean scores of 19.6±6.0. Whole brain T1-weighted anatomical images were collected in a 3T MRI. Brains were examined for cortical thickness differences, using FreeSurfer models, and Spearman correlation coefficient (rho). A statistically significant value was considered with a p < 0.05. Results: Forty-four women (55%) presented stress; 42 women (52.5 %) anxiety; and 41 women (51.4 %) depression. A positive association of stress was observed with high triglyceride levels (r=0.29, p=0.008), total cholesterol (r=0.26, p=0.018), and total alkaline phosphatase (r=0.27, p=0.014). Anxiety was associated with high triglyceride levels (r=0.31, p=0.007), and insulin resistance (rho: 0.26, p=0.019). As far as depression is concerned, a statistically significant positive association was observed with high total cholesterol levels in serum (rho: 0.326, p=0.003). High blood pressure had a positive association with the presence of anxiety (rho: 0.460, p=0.000) and depression (rho: 0.641, p=0.000). Conclusion: Conclusions: this study shows that there is a high prevalence of stress, anxiety, and depression in these life stages of women and shows that there is a statistically significant association between the presence of stress, anxiety, and depression with insulin resistance, high total cholesterol and triglyceride serum levels, metabolic syndrome, and high blood pressure. We obtained similar results to those reported in the pilot study. Accordingly, it is essential to perform a comprehensive research on stress, anxiety, and depression to avoid the appearance of metabolic and cardiovascular complications. Gratitude: to my professor Dr. Imelda Hernández Marin for her support and dedication in this project.

P-51. Association of stress, anxiety and depression conditions with the presence of co-morbidities in patients in middle age and post-menopause transition stage.

Imelda Hernández, MARISELA ADRIANA NÚÑEZ RODRIGUEZ. Residente. Biología de la Reproducción Humana, Hospital Juárez de México, México. Objetivo: Este estudio tiene como objetivo determinar la asociación entre el estrés, la ansiedad, la depresión, y eventos vitales estresantes con condiciones de enfermedad crónica en mujeres de la transición a menopausia y en mujeres en el estadio post-menopausia. Metodología: Para el análisis se seleccionaron 20 mujeres con estrés, 20 con ansiedad, 20 con depresión y 20 controles sanos, con una edad promedio de 50 años. Los datos se recogieron a través de preguntas de cuestionario estructurado y se obtuvo un valor de p<0.05. Conclusion: En este estudio se observó una asociación significativa entre el estrés, la ansiedad, la depresión y eventos vitales estresantes con condiciones de enfermedad crónica en mujeres de la transición a menopausia y en mujeres en el estadio post-menopausia.
P-53. Hippocampal volumetric analysis in unmedicated midlife women with major depressive disorder

Herman Bami1,2, Sabrina Syan1,2, Geoffrey Hall, MSc, Ph.D1, Lauren Cudney1, Meir Steiner, MD, MSc, PhD, FRCP(C)1,2, Claudio N. Soares, MD, PhD, FRCP(C)1,2, Benicio Frey, MD, MSc, Ph.D1,2, Luciano Minuzzi, MD, Ph.D1,2, St. Joseph’s Healthcare Hamilton, Hamilton, ON, Canada; McMaster University, Mississauga, ON, Canada; Psychology, Neuroscience & Behaviour, McMaster University, Hamilton, ON, Canada

Objective: The menopausal transition in women is a period of intense hormonal fluctuation and has been associated with an increased risk for the development of major depressive disorder (MDD). The hippocampal complex (HC) is a brain region primarily associated with learning and memory but has been shown to be a critical region in the pathophysiology of depression. Imaging studies have shown reduced hippocampal volumes in patients with depression. The present study examined the volumes of HC in midlife women presenting with MDD compared to healthy controls.

Design: Unmedicated peri/postmenopausal women (N=19) and age-matched healthy controls (N=19) underwent a high-resolution MRI scan. Volumes of interest corresponding to the HC were manually drawn onto the MRI images, according to Pruessner et al (2000). An automatic segmentation was also completed using FreeSurfer imaging software. Depressive symptoms and cognitive functioning were assessed with the Montgomery-Asberg Depression Rating Scale (MADRS) and the Cognitive Failures Questionnaire (CFQ), respectively. Normalized hippocampal volumes were compared between groups using age, MADRS and CFQ scores as covariates. A linear regression model was applied with group, age, MADRS and CFQ scores as predictors. Results: Significant differences in MADRS and CFQ scores were observed between the two groups (p<0.001). Paired t-tests showed significant differences between automatic and manual tracings for both right and left hippocampal volumes (p<0.001), with automatic tracings overestimating manually traced volumes. The Pearson correlation between the two types of tracing was strong in both the right (r=0.692 p<0.001) and left (r=0.679 p<0.001) HC. The data obtained from the manual tracings for the right and left hippocampal volumes showed no significant differences in hippocampal volumes between groups, upon adjusting for age and CFQ. A significant difference was however found in the automatic tracings of the left hippocampus between control and MDD patients (p=0.047), with a smaller hippocampal volume being displayed in patients with MDD. Stepwise linear regression analysis showed that group and MADRS score could predict right hippocampal volume changes in the manual tracing (adjusted r squared=0.316, p=0.003; group beta=−0.925, p=0.003; MADRS beta=0.373, p=0.025) and automatic tracings (adjusted r squared=0.154, p=0.10; MADRS beta=−0.422, p=0.10). Conclusion: Automatic segmentation showed to overestimate HC volume in this population. This preliminary study found no significant differences in peri/postmenopausal women compared to age-matched control subjects in the manual hippocampal tracing. However, a significant decrease in left hippocampal volume was found in patients with MDD compared to the control group in the automated tracings. Additionally, severity of depressive symptoms was found to be a predictor of changes in HC volumes in both manual and automatic tracings.

P-54. SEVERE DETERIORATION OF THE QUALITY OF LIFE, PERCEIVED STRESS AND SLEEP DISORDERS ACCORDING TO CLINICAL HISTORY OF ABDOMINAL HYSTERECTOMY

Alvaro Monterrosa-Castro, Professor1, Marlon Salguedo-Madrid, Estudiante1, katherin Portela-Buelvas, Estudiante1, Jouen Mo-Carrascal, Estudiante1,2, Universidad de Cartagena, Cartagena, Colombia; Grupo de Investigación Salud de la Mujer, Cartagena, Colombia

Objective: To compare the prevalence of severe deterioration of the quality of life, sleep disorders and presence of perceived stress according to clinical history of abdominal hysterectomy. Design: Methods: A cross-sectional study that included 204 women. The MRC (Madrid Scale for Menopausal and Other Chronic Conditions) was used to determine the presence of SLE (Scales of Perceived Stress) and the CES-D (Cuadro de Vida en la Menopausia y Etnias Colombianas) research project, which was carried out in women with mestizo ethnic group with ages between 40 and 59 years, who were residents in the Colombian Caribbean. They were polled in their own communities and their data were analyzed by scales of Perceived Stress Scale (PSS-10), CES-D Score, Hospital Anxiety and Depression Scale (HADS), and the Menopause Sleep Scale. Results: 471 women participated, 237 were hysterectomized and 234 non-hysterectomized women who were polled in 2015. Those women with hysterectomy had significantly major age: 50.7±10 vs 45.7±5. Those with hysterectomy had significantly major age: 50.7±10 vs 45.7±5. There were no observed differences in BMI, waist-hip ratio, diabetes, arterial hypertension, to smoke and hormonal therapy. The average score of the perceived stress scale was similar in both groups, hysterectomized 19.5±3.3 and non-hysterectomized women 17.6±4.7 (p=0.05). The average Jenkins sleep Scale were hysterectomized 5.2±3.9 and non-hysterectomized women 4.5±3.9 (p=0.97). A hysterectomy women reported presence mayor of “awakenings during the night” and “morning wake up tired despite having slept as usual”. Neither, differences in the prevalence of severe menopausal symptoms nor severe deterioration of mood, psychological, and the quality of life were observed (p<0.05). 46% of the hysterectomized were uninvolved severe deterioration compared with 36% of non-hysterectomized (p=0.009). Conclusion: Differences were not observed in the severe deterioration of the quality of life, stress and sleep disorders according to clinical history of hysterectomy.

P-55. Feeling of Unattractiveness in Peri- and Postmenopausal Women is Associated with Depressed Mood, Poor Memory, and Unsatisfactory Sexual Relationship

Masakazu Terauchi, MD, PhD1, Asuka Hirose2, Mihoko Akiyoshi3, Yoko Owa4, Kiyoko Kato5, Toshiko Kubota6. 1Department of Women’s Health, Tokyo Medical and Dental University, Tokyo, Japan; 2Department of Obstetrics and Gynecology, Tokyo Medical and Dental University, Tokyo, Japan

Objective: This study was undertaken to investigate the prevalence and the determinants of the feeling of unattractiveness in peri- and postmenopausal women. Design: Cross-sectional study of 351 women who enrolled in the Systematic Health and Nutrition Education Program at the Menopause Clinic of the Tokyo Medical and Dental University Hospital from November 2007 to December 2012 were subjected to a cross-sectional analysis. Their feeling of unattractiveness was estimated on the basis of their responses to the item #21 “Feeling unattractive” on the Menopausal Health-Related Quality of Life [MHR-QOL] Questionnaire. The effects of their background characteristics, including age, menopausal status, body composition, cardiovascular parameters, physical fitness, vaginal dryness, and physical and psychological symptoms of menopause (MHR-QOL and the Hospital Anxiety and Depression Scale [HADS]), on the feeling of unattractiveness were assessed using multivariate logistic regression analysis. Results: The average age of the participants was 52.4±6.7 years (mean ± standard deviation). The average age of women who felt they were less attractive than before 3-4 times a week was 58.1±7.3 years (p=0.001) compared to 50.7±6.9 years (p=0.001) for those who did not feel that way. Increasing number of SLE experienced was associated with a 33% adjusted increased risk of having CES-D score ≥16 at T2. The mean number of reported episodes of SLE over the past 2 years was 1.4 ± 0.2 (p=0.002). The percentages of women who experienced severe deterioration of the quality of life, stress and sleep disorders according to clinical history of hysterectomy.

P-56. Menopausal Experience of Physical Activity

Lily Stojanovska, PhD1, Vasso Apostolopoulos, PhD2, Erika Borkoles, PhD. 1College of Health and Biomedicine, Victoria University, Melbourne, VIC, Australia; 2Institute of Sport, Exercise and Active Living, Victoria University, Melbourne, VIC, Australia

Objective: Menopausal symptoms can be severe and disruptive to overall quality of life. HRT can ameliorate symptoms; however, associated side effects have resulted in the onset of most conditions associated with ageing and with menopause. We identified the meanings of exercise to menopausal women, and the influence of menopausal symptom severity. Design: Interpretative phenomenological analysis was employed as the theoretical and methodological framework in this qualitative study. We conducted semi-structured interviews with eleven women with different levels of exercise participation and symptom severity. Women associate various meanings with the experience of exercise during menopause. Results: Regardless of exercise behavior and symptom severity,
participants associated exercise with both physical and psychological benefits. The women with high-severity symptoms valued the role of exercise in fighting ageing, whereas women with low-severity symptoms associated exercise with feeling better able to cope with difficult situations. All of the participants recalled the presence of barriers to exercise. Conclusion: Exercisers enjoyed exercise more than non-exercisers, and exercisers with high-severity symptoms have more influence in the perception of symptom severity as a barrier to exercise than symptom severity itself.

P-57. Menopause and Avoidance of Physical Activity
Lily Stojanovska, PhD,1 Erika Borkoles, PhD,1 Remco Polman, PhD.1 College of Health and Biomedicine, Victoria University, Melbourne, VIC, Australia; 2Institute of Sport, Exercise and Active Living, Victoria University, Melbourne, VIC, Australia

Objective: Physical activity improves overall health in menopausal women. Lack of consistent findings of physical activity effects on symptom relief or menopausal management relates to not understanding why women avoid exercise whilst experiencing menopausal symptoms. We examined the association between menopausal symptom severity and self-reported physical activity behaviours and active living habits.

Design: 506 women aged 52.5 years accessed online survey. 77% of respondents were Caucasian, 60% perimenopausal and 40% postmenopausal. Greene Climacteric Scale; Perceived Stress Scale and Kaiser Physical Activity Scale were used to measure severity of symptoms; stress; household duties, active living activities and exercise behaviour respectively. Data was assessed for normality while descriptive statistics were analysed according to menopausal status. Stepwise linear regression models were used assessing differences in activity based on symptom severity controlling for menopausal status, age and stress.

Results: Menopausal symptom severities for each group strongly correlated with each other and with perceived stress (r = 0.35; p < 0.001). Regression analyses showed association of menopausal symptoms with reduced participation in moderate intensity exercise (R² change = 0.04; F change = 2.98; p = 0.032) and reduced household activities (R² change = 0.06; F change = 5.26; p < 0.002). Effects were observed after controlling reductions in activity associated with age, menopausal status and stress. 20% avoided activity due to symptoms including tiredness, heavy sweating, weight gain, irregular and heavy bleeding and general lack of motivation. Conclusion: Severity of menopausal symptoms can have significant influence on self-reported activity across in and associated with avoidance of physical activities ranging from household duties to moderate and vigorous exercise pursuits.

P-58. Objectively measured physical activity (PA) and sedentary behavior (SB) are differentially associated with measures of body composition in pre- versus postmenopausal women
Lisa M. Troy, PhD, Marquis Hawkins, PhD, Sarah Witkowski, PhD. UMMS Amherst, Amherst, MA

Objective: Menopause is related to changes in body composition. PA is associated with lower body fat % and higher lean mass in women. Less is known about differences between pre- and postmenopausal women in terms of PA intensity and SB in relation to body fat and muscle mass. The objective was to examine the association between objectively-measured PA (LPA, MVPA) and SB and common measures of body composition (i.e., body mass index (BMI), waist circumference (WC), body fat (%BF), and lean mass (%LM)) in pre- and postmenopausal women.

Design: NHANES (2003-04 and 2005-06) data were used to examine PA and SB on body composition in 630 pre- (mean age 42.8y) and 274 postmenopausal (mean age 54.6y) women. Menopausal status was defined using self-reported data in women aged 35-60y. Women were classified as premenopausal if menstruating in past 2 months; postmenopausal if age>40y and no menses in past 12 months. Women reporting hysterectomy or oophorectomy were excluded. ActiGraph accelerometers were used to estimate time spent in light intensity PA (LPA), moderate/vigorous intensity PA (MVPA) and SB using validated methods. SB was defined as a proportion of monitor wear time spent sedentary. %BF and %LM measured by DXA. Age-adjusted linear regression models were used to examine associations between each measure of PA, SB and body composition in pre- and postmenopausal women separately. Two-way interactions were used to determine differences in the main effect by menopausal status. Statistical significance was alpha=0.05.

Results: Postmenopausal women had significantly higher mean BMI (29.7 vs 28.4 kg/m² p<0.02), WC (97.7 vs 92.8 cm, p<0.01), and %BF (42 vs 39%, p<0.01) and lower %LM (55 vs 58%, p<0.01); and less total movement (254 vs 292 counts/minute, p<0.01), time in MVPA (17.3 vs 22.7 minutes, p<0.01), and more sedentary time (61.6 vs 59.3 %, p<0.02) than premenopausal women. Time spent in LPA was similar between the groups (339.7 vs 350.8 minutes, p<0.015). Higher total movement, LPA, MVPA and lower SB were associated with lower BMI, WC, and %BF and higher %LM in both groups, with the exception of LPA and BMI in premenopausal women (see Table). LPA was more strongly associated with each measure of body composition in post- compared to premenopausal women (p for interaction <0.05). SB was more strongly associated with WC in post- compared to premenopausal women (p for interaction=0.01). Conclusion: It appears LPA and SB may be more important determinants of body composition in post- than premenopausal women.

P-59. Common Iliac Artery Vitamin D Receptor Expression Patterns During the Development of Atherosclerosis in Postmenopausal Nonhuman Primates
Xuezi Jiang, MD,1 Matthew S. Nudy, B.S.1,2, Susan E. Appt, DVM3; David M. O’Sullivan, PhD3, Jay R. Kaplan, PhD2; Peter F. Schnatz, D.O.1,2; O’Bryn, The Reading Hospital, West Reading, PA; 2Pathology/Comparative Medicine, Wake Forest University, Winston-Salem, NC; 3O’Bryn, Sidney Kimmel Medical College of Thomas Jefferson University, Philadelphia, PA

Objective: The results of recent studies suggest that vitamin D receptor (VDR) expression in the coronary arteries of female cynomolagus monkeys is negatively associated with atherosclerosis severity and duration. The objective of this study is to assess the changes in VDR expression in the common iliac arteries of postmenopausal monkeys during the development of atherosclerosis. Design: After 32 months of consuming an atherogenic diet, 37 premenopausal monkeys underwent ovariectomy. The same diet was then consumed for an additional 32 months until necropsy. Atherosclerosis extent and VDR expression were measured in the left iliac artery (LCI) at the time of ovariectomy, and in the right common iliac artery (RCI) at necropsy. Atherosclerosis severity (American Heart Association grading system) and VDR expression (VDR H-score) were quantified.

Results: Despite increasing atherosclerosis over the course of the study, the total mean (SD) VDR H-score was significantly higher in the RCI in postmenopausal monkeys after consuming the athrogenic diet for a total of 64 months compared to the LCI of premenopausal monkeys who consumed the diet for 32 months (152.62[18.55] vs. 126.15[22.13], p<0.001). There was a significant positive correlation between the absolute (and percentage) change in total H-score and absolute change of AHA severity from pre- to post-menopause (Absolute: r=0.43, p=0.08; Percentage: r=0.44, p=0.007). Conclusion: Overall, contrary to our expectation, VDR expression was significantly increased in direct correlation with atherosclerosis increase in postmenopausal monkeys. A higher increase in VDR expression, from pre- to post-menopause, correlated with more severe atherosclerotic changes in the common iliac arteries.

P-60. The Association between Common Iliac Artery Vitamin D Receptor Expression and Atherosclerosis in Postmenopausal Nonhuman Primates
Matthew S. Nudy, B.S.1,2, Xuezi Jiang, MD,2 Susan E. Appt, DVM3; David M. O’Sullivan, PhD3, Jay R. Kaplan, PhD2; Peter F. Schnatz, D.O.1,2; O’Bryn, The Reading Hospital, West Reading, PA; 2Pathology/Comparative Medicine, Wake Forest University, Winston-Salem, NC

Objective: The vitamin D receptor (VDR) has been localized to many tissues in the cardiovascular system including the coronary arteries of female nonhuman primates. The objective of the current study is to determine whether VDR expression in a peripheral artery (common iliac) is associated with atherosclerosis extent and severity in a cohort of postmenopausal cynomolgous monkeys. Design: For 32 months, premenopausal cynomolgous monkeys (n=37) consumed an atherogenic diet containing a women’s equivalent of 1,200 mg/day of elemental calcium and 1,000 IU/day of vitamin D. After 32 months, the monkeys were ovariectomized and consumed the diet for an additional 32 months until artery specimens were collected at necropsy. Cross sections of the iliac artery were immunohistochemically stained for the VDR. Atherosclerosis extent was assessed by measuring iliac artery intimal (plaque) areas (IA) and maximal intimal plaque thickness (MXT). Plaque severity was determined using American Heart Association (AHA) atherosclerosis severity grades. Results: In the common iliac artery, a significant
positive correlation was observed between the proportion of VDR negative cells and plaque size (both cross-sectional area = 0.578, p = 0.001) and plaque thickness [r = 0.523, p = 0.001]. Also, a significant positive correlation was observed between the proportion of VDR negative cells and the AHA atherosclerotic lesion severity score [r = 0.530, p = 0.001]. Lower VDR expression was seen in common iliac arteries with more severe atherosclerosis in female monospermic monkeys. Further research is needed to elucidate the extraskeletal benefits of vitamin D and the pattern of change in VDR expression over the natural course of atherosclerosis.

P-64

Diagnostic Accuracy of FRAX in Predicting the 10-year risk of Osteoporotic Fractures: A Systematic Review and Meta-analysis
Xuezhi Jiang, MD1,2, Morgan Gruner, BS1, Florence Trémollieres, MD, PhD3, Wojciech Pluskiewicz, MD4, Elisabeth Sornay-renaud, MD5, Piotr Adamczyk, MD6, Peter F. Schnetz, DO7,8, O’Gyn, The Reading Hospital, West Reading, PA; O’Gyn, Sidney Kimmel Medical college, Thomas Jefferson University, Philadelphia, PA; 5Centre de Ménopause, Hôpital Paule de Viguier, Toulouse, France; 3Centre de Ménopause, Hôpital Paule de Viguier, Toulouse, France; 4Département and Clinic of Obstetrics, Medical University of Silesia, Katowice, Poland; 5INSERM Unit 831, Hospital E Herriot, Lyon, France; 3Département and Clinic of Pediatrics, Medical University of Silesia, Zabrze, Poland

Objective: The aim of this study is to conduct a systematic review and meta-analysis on the performance of the WHO’s Fracture Risk Assessment (FRAX) instrument for predicting 10-year risk of Major Osteoporotic Fractures (MOF) and Hip Fractures (HF) in postmenopausal women. This study aimed to compare FRAX in their derivation cohorts. Design: PubMed, Google Scholar, Embase, Cochrane Library, and MEDLINE were searched for the English-language literature from 2008 to 2015. Limiting our search to articles that analyzed both MOF and HF as an outcome, 7 longitudinal cohorts from 5 countries (USA, Poland, France, Canada, New Zealand) were identified and included in this meta-analysis. SAS (v. 9.3) and R (v. 3.4) was applied to fit the Hierarchical Receiver Operating Characteristics (HSROC) model for meta-analysis. Forest plot and HSROC plot were generated by Review Manager (RevMan v 5.3). Results: Seven studies (n = 57,027) were analyzed and assessed clinical accuracy of FRAX in predicting MOF. Using 25% as the 10-year fracture risk threshold, the mean sensitivity, specificity, and diagnostic odds ratio (DOR) along with their 95% confidence intervals (CI) were 10.25% (3.76% - 25.06%), 97.02% (91.17% - 99.03%) and 3.71 (2.73 - 5.05), respectively. For HF prediction, using 3% as the 10-year fracture risk threshold, six studies (n = 50,944) were analyzed. The mean sensitivity, specificity, and DOR along with their 95% confidence intervals (CI) were 45.70% (24.88% - 68.13%), 84.70% (76.41% - 90.44%) and 4.66 (2.39 - 9.08), respectively. Conclusion: Overall, FRAX performs better in identifying patients who will have a MOF or HF within 10 years. However, a substantial number of patients who developed fractures, especially MOF within 10 years of follow up, were missed by the baseline FRAX assessment using the 10 year intervention thresholds of 20% for MOF and 3% for HF.

P-65

Effect of vitamin D deficiency and daily calcium intake on BMD and osteoporosis in postmenopausal Korean women
Yaekyu Koh, MD, PhD1, Jinju Lee2, Mi Kyung Song3, Min Kyoung Kim, MD, D1,2, Byon Yun4, BYungseok Lee5, Seok Kyo Seo1,3. 1Department of Obstetrics and Gynecology, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea (the Republic of); 2Department of Biostatistics Collaboration, Yonsei University College of Medicine, Seoul, Korea (the Republic of); 3Institute of Women’s Life Medical Science, Seoul, Korea (the Republic of)

Objective: This study aimed to determine the combined effect of vitamin D deficiency and daily calcium intake on BMD and osteoporosis in postmenopausal Korean women. Design: This study is a cross-sectional study of 3268 participants (more than 45 years and younger than 70 years Korean postmenopausal women without any thyroid dysfunction) recruited from the 2008-2011 Korean National Health and Nutrition Examination Survey. Participants were divided into groups according to the 25(OH)D level (<20 and ≥20 nmol/L) and the daily calcium intake(<400, 400-800, and ≥800 mg/day). BMD was measured using dual-energy X-ray absorptiometry at the femur and the lumbar spine (L1-L4). The serum vitamin D concentrations were measured by radioimmunoassay. Results: BMD in the femoral neck has a trend to be higher according to the daily calcium intake (P=0.047 and 0.001, respectively). The participants with MS had significantly higher odds for vitamin D insufficiency (less than 20 nmol/L) (odds ratio: 1.48, 95% confidence interval: 1.07-2.06) (P=0.02). However, the number of MS components was not associated with vitamin D concentration. After adjusting confounding factors, the global component of MS demonstrated an association with the value of vitamin D in postmenopausal women (P=0.01). Conclusion: In conclusion, vitamin D level is associated with MS in Korean postmenopausal women, and the participants with MS demonstrated significantly higher odds for vitamin D insufficiency.

P-66

Changes in Bone Density after Cancer Treatment in Patients with Cervical and Endometrial Cancer
Heungyeol Kim1, Ari Kim2. 1Kosin University, Busan, Korea (the Republic of); 2Kosin University, Busan, Korea (the Republic of)

Objective: This study aimed to evaluate the impact of cancer treatment on bone mineral density (BMD) in the lumbar spine (LS) and femur in the postmenopausal women with cervical or endometrial cancer without bone metastasis compared to normal control women. Design: Laboratory data of bone turnover markers at baseline and after one year in 130 patients with cervical cancer and 68 with endometrial cancer, and 140 age-matched control subjects. We also compared serum calcium, phosphorus, intact PTH, osteocalcin, and urinary deoxypyridinoline levels. Results: T-scores were significantly lower in patients with cervical cancer (P = 0.002) than in women with cervical cancer, but no other biochemical variable differed among groups. Conclusion: Cervical cancer was associated with lower BMD and may be a risk factor for secondary osteoporosis. However, endometrial cancer generally seemed to have no damaging effect on bone. A larger follow-up study is required to clarify these findings.
related to the daily calcium intake and 25(OH)D level. ANCOVA analyses demonstrated subjects who are taking calcium less than 800mg per day and vitamin D deficiency had increased risk of osteoporosis at femur neck. **Conclusion:** The low daily calcium intake and vitamin D deficiency were significantly associated with low BMD and increasing prevalence of osteoporosis in postmenopausal Korean women older than 45 years. It is important to take sufficient calcium and vitamin D in order to decrease the risk of osteoporosis.

**P-66. A randomized study on the effect of vitamin D3 supplementation on skeletal muscle function in fallers postmenopausal women**

Luciana V. Cangussu, MSC, Jorge Nahas-Neto, PhD, MD, Claudio L. Orsatti, Flavia B. Dias, Eneida B. Schmitt, MD, Eliana A. Nahas, MD. Gynecology and Obstetrics, Botucatu Medical School-Sao Paulo State University, Botucatu, Brazil  

**Objective:** Hypovitaminosis D is common in postmenopausal women in worldwide. This condition may cause muscle weakness and fall, in addition to an important loss of muscle mass. We aimed to evaluate the effect of supplementation of vitamin D alone (VITD) on muscle function in fallers postmenopausal women.  

**Design:** In this double-blind, placebo-controlled trial, 160 Brazilian postmenopausal women were randomized into two groups: VITD group, vitamin D3 supplementation 1,000IU/day orally (n=80) or placebo group (n=80). Women with amenorrhea a 12 months and age 50-65 years, with a history of falls (previous 12 months) were included. Those with neurological or musculoskeletal disorders, vestibulopathies, drug use that could affect balance and osteoporosis were excluded. The intervention time was nine months. Muscle mass was estimated by Total-body DXA (dual energy X-ray absorptiometry) and muscle strength by handgrip strength and chair-rising test. The plasma concentrations of 25-hydroxyvitaminD [25(OH)D] were measured by HPLC (high-performance liquid chromatography). This study was registered at and approved by the Brazilian Clinical Trials Registry under the registration number RBR-222wrk. Statistical analysis was by intention-to-treat (ITT), using ANOVA, Student’s t-test, Tukey test and logistic regression.  

**Results:** The mean age of the patients included was 58.8 ± 6.6 years in the VITD group and 59.3 ± 6.7 years in the placebo group, with time since menopause of 12.0 ± 8.8 years and 12.3 ± 8.4 years, respectively (p<0.05). After nine months, the average value of 25(OH)D increased from 15.0 ± 7.5 ng/mL to 27.5 ± 10.4 ng/mL (+45.4%) in VITD group, and decreased 16.9 ± 6.7 ng/mL to 13.8 ± 6.0 ng/mL (-18.5%) in placebo group; in the VITD group, there was significant increase (+25.3%) in muscle strength of the lower limbs by chair-rising test (p<0.05). In women in the placebo group, there was considerable loss (-6.8%) in the muscle mass (p=0.030). The rate of fall was higher in the placebo (+46.3%, p<0.001), that presented an adjusted risk of 1.9 (CI 95% 1.23-3.08) times higher of falls and 2.80 (CI 95% 1.43-5.50) times higher of recurrent falls than the VITD group. **Conclusion:** Supplementation of vitamin D alone in fallers postmenopausal women provided significant protective factor against the occurrence of sarcopenia, with significant increases in muscle strength and control of progressive loss of body muscle mass. * Financial support from FAPESP, process number 2011/11447-1.

**P-67. Evaluation of risk factors for low bone mineral density in postmenopausal breast cancer survivors**

Priscila Poloni, MD, PhD, Jorge Nahas-Neto, PhD, MD, Heloisa D. Vespoli, MD, Gilberto Uemura, MD, Benedito Almeida-Filho, MD, Eliana A. Nahas, MD. Gynecology and Obstetrics, Botucatu Medical School-Sao Paulo State University, Botucatu, Brazil  

**Objective:** We aimed to evaluate the risk factors for low bone mineral density (BMD) in postmenopausal breast cancer survivors compared to postmenopausal women without breast cancer (control).  

**Design:** In this case-control study, 112 breast cancer survivors were compared with 224 postmenopausal women. Women with amenorrhea ≥12 months and age 45-75 years, histological diagnosis of breast cancer, have completed surgical treatment, radiotherapy, hormone therapy, and chemotherapy (whenever recommended) and metastasis-free for at least five years were included. The control group consisted of postmenopausal women without breast cancer, matched by age and menopause status, in a proportion of 1 case to 2 controls. The risk factors for low BMD (osteopenia and osteoporosis) were assessed by interviews. Clinical and anthropometric data were collected. BMD was measured by DEXA (dual energy X-ray absorptiometry) (HologicÒ, QDR-2000) at the lumbar spine (L1-1.4) and femoral neck. Logistic regression model (odds ratio, OR) was used to identify factors associated with low BMD. This study was based on data obtained from the 2008-2011 Korean National Health and Nutrition Examination Survey and (KHNANES). A whole body dual energy X-ray absorptiometry (DXA) scan were performed on individuals of ≥10 years old from July 2008 to May 2011. 11633 women were included in the analysis. ASM was calculated and SMI was obtained as ASM/height². Cut-off value was defined two standard deviations below mean values for young reference group. **Results:** Of 11,633 women aged 10-97 years, mean and SD of year was 46.73 ± 18.54 years. The highest level of height was noted in 20% and the highest total sum of skeletal mass was seen 14.87kg in 40’s. The highest value of SMI was noted in 60’s in women. Cut-off value as mean value of young women was decided with SMI of 30’s and 40’s that have peak ASM. Mean and standard deviation of SMI in those ages was 5.9 ± 0.7kg/m². A SMI of two standard deviations below the mean SMI of reference groups was 4.4kg/m² as cutoff value. **Conclusion:** This study shows that 4.4kg/m² in SMI in Korean women was cutoff value of sarcopenia. Further study is clearly required to decide cutoff value of SMI for sarcopenia, especially for Korean woman.

**P-68. The reference value of skeletal muscle mass index for defining the sarcopenia of women in Korea**

Hyoun Moo Park, PhD, Tak Kim, MD, PhD. Obstetrics and Gynecology, Korea Univ, Seoul, Korea (the Republic of); ObStetrics and Gynecology, Chung-ang Univ, Seoul, Korea (the Republic of)  

**Objective:** Sarcopenia is considering important disease entity in elderly. Several study groups define the sum of the muscle masses of the four limbs as appendicular skeletal mass (ASM) to calculate appendicular skeletal mass index (SMI). The purpose of this study was to determine cut point of SMI for sarcopenia in Korean women.  

**Design:** This study was based on data obtained from the 2008-2011 Korean National Health and Nutrition Examination Survey and (KHNANES). A whole body dual energy X-ray absorptiometry (DXA) scan were performed on individuals of ≥10 years old from July 2008 to May 2011. 11633 women were included in the analysis. ASM was calculated and SMI was obtained as ASM/height². Cut-off value was defined two standard deviations below mean values for young reference group. **Results:** Of 11,633 women aged 10-97 years, mean and SD of year was 46.73 ± 18.54 years. The highest level of height was noted in 20% and the highest total sum of skeletal mass was seen 14.87kg in 40’s. The highest value of SMI was noted in 60’s in women. Cut-off value as mean value of young women was decided with SMI of 30’s and 40’s that have peak ASM. Mean and standard deviation of SMI in those ages was 5.9 ± 0.7kg/m². A SMI of two standard deviations below the mean SMI of reference groups was 4.4kg/m² as cutoff value. **Conclusion:** This study shows that 4.4kg/m² in SMI in Korean women was cutoff value of sarcopenia. Further study is clearly required to decide cutoff value of SMI for sarcopenia, especially for Korean woman.

**P-69. CORRELATION BETWEEN OSTEOPOROTIC FRACTURE RISK IN 10 YEARS CALCULATED BY FRAX WITH AND WITHOUT BONE DENSITOMETRY IN POSTMENOPAUSAL BRAZILIAN WOMEN**

Lucia S. Costa-Paiva, MD, PhD, Yasmin Bastos, Luiza Borges, Luiz F. Baccaro, PhD, Adriana O. Pedro, Aarao M. Pinto-Neto, MD, PhD. Obstetrics and Gynaecology, Universidade Estadual de Campinas, Campinas, Brazil  

**Objective:** The risk of osteoporotic fracture can be clinically evaluated based on clinical risk factors and by bone mineral density (BMD), but these parameters are not good predictors of fracture risk. Recently, Brazil was included in the fracture risk assessment tool - FRAX-BRAZIL, but its use has been limited in clinical practice.  

**Objective:** To compare Fracture Risk Assessment Tool (FRAX) calculations with and without bone mineral density (BMD) in predicting the 10-year probability of major and hip osteoporotic fractures in Brazilian postmenopausal women.  

**Design:** A cross-sectional study was conducted with 402 women followed at the Menopause Ambulatory at the Women’s Hospital Prof. Dr. José Aristodemo Pinotti in Campinas-SP. Inclusion criteria was: postmenopausal women over 40 years of age and with amenorrhea at least 12 months and who were never treated with any approved agents for osteoporosis. Height, weight, FRAX questionnaire, femoral neck BMD (g/cm²) and T-score data were obtained. FRAX scores with BMD and without BMD were calculated in order to obtain the probability of major and hip fractures. Statistical analysis: To analyze the correlation between the probability of fractures with and without bone densitometry, it was used the associated with lower variation in the FRAX score only in major fracture. **Conclusion:** The prevalence of 1.9 (CI 95% 1.23-3.08) times higher of falls and 2.80 (CI 95% 1.43-5.50) times higher of recurrent falls than the VITD group. **Conclusion:** The supplementation of vitamin D alone in fallers postmenopausal women provided significant protective factor against the occurrence of sarcopenia, with significant increases in muscle strength and control of progressive loss of body muscle mass. * Financial support from FAPESP, process number 2011/11447-1.
P.70. **Women’s Health Initiative Clinical Trials: The Effects of Calcium and Vitamin D Supplementation and Hormone Therapy on LDL-Cholesterol and Other Cardiovascular Disease Risk Factors**

Peter F. Schatz, D.O.1,2, Xueyi Jiang, MD1,4, Matthew S. Nudy, B.S.1,4, David M. O’Sullivan, PhD2, Karen A. Aragaki, M.S.3, Mark Williams, MD1, Ern LeBlanc4, Lisa W. Martin1,2, JoAnn E. Manson, MD, DrPh1,2, James M. Shikany, Dr.P.H.1,2, Karen C. Johnson, MD2, Marisa L. Stefancik, Ph.D.1,2, Martha E. Payne, RD, PhD, MPH1,2, Jane A. Cauley, DrPH1,2, Barbara V. Howard1,2, John Robbins, MD1,2, ObGyn & Internal Medicine, The Reading Hospital and Medical Center, Reading, PA; 3Departments of ObGyn and Int Medicine, Thomas Jefferson University, Philadelphia, PA; 4ObGyn, Reading Hospital, Reading, PA; ObGyn, Thomas Jefferson University, Philadelphia, PA; 5Division of Public Health Sciences, Fred Hutchinson Cancer Research Center, Seattle, WA; 6Center for Health Research NW, Kaiser Permanente, Portland, OR; 7Department of Int Medicine, George Washington University, University of Medicine and Health Sciences, Washington, DC; 8Preventive Medicine, University of Alabama at Birmingham, Birmingham, AL; 9Preventive Medicine, University of Tennessee Health Science Center, Memphis, TN; 10Prevention Research Center, Stanford University, Stanford, CA; 11Psychiatry, Duke University, Durham, NC; 12Graduate School of Public Health, University of Pittsburgh, Pittsburgh, PA; 13MedStar HlthHealth Research Institute, Hyattsville, MD; 14UC Davis Medical Center, Sacramento, CA; 15Preventive Medicine, Harvard Medical School, Boston, MA

**Objective:** To analyze the treatment effect of calcium and vitamin D (CaD) supplementation, hormone therapy (HT), both CaD and HT, and neither on cardiovascular disease (CVD) risk factors. **Design:** A prospective, randomized, double-blind, placebo controlled trial among Women’s Health Initiative postmenopausal participants. In the HT trial 27,347 women were randomized to HT (0.625 mg of conjugated equine estrogens [CEE] alone or 0.625 mg of CEE plus 2.5 mg of medroxyprogesterone [MPA]); In the CaD trial 27,347 women were randomized to HT-alone, CaD-alone, and HT-CaD alone. The primary outcome was changes in biomarkers of CVD risk factors (cholesterol, triglycerides, glucose, blood pressure, weight, and waist circumference) as randomized and were followed with repeated blood sample collections at baseline and years 1, 3, and 6. The predefined primary outcome of this analysis was low density lipoprotein cholesterol (LDL-C) and other CVD risk factors (such as high density lipoprotein cholesterol, triglycerides, glucose, blood pressure, weight, and waist circumference). **Results:** The average reductions in LDL-C during follow-up were greater in the HT-alone (−9.8) mg/dL for HT-alone, and −5.5, 2.2) mg/dL for CaD-alone, −5.0, −5.1) mg/dL for HT-alone, and −3.8 (−17.8, −9.8) mg/dL for CaD plus HT. The p-value for interaction was 0.26, indicating no evidence of a synergistic effect of CaD x HT on LDL-C. However, there was evidence that CaD x HT had a synergistic effect on decreasing LDL at low total intakes (dietary and supplements) of vitamin D (p = 0.03) and calcium (p = 0.06). The effect of HT plus CaD, on all of the remaining CVD risk factors, tended to be larger in magnitude than the effects of either HT-alone or CaD-alone, but none of the HT x CaD interactions were statistically significant. **Conclusion:** The average reductions in LDL-C during follow-up were greater among women randomized to both CaD and HT than for those randomized to either intervention alone or to placebo. However, statistical tests for interaction between CaD and HT were not significant.

**Average Group Means (95% CI) during follow-up of Treatment Group Effects**

<table>
<thead>
<tr>
<th>Group</th>
<th>LDL-C</th>
<th>HDL-C</th>
<th>Systolic BP</th>
<th>Triglycerides</th>
<th>Glucose</th>
<th>Waist-Hip Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>HT-alone</td>
<td>130.1</td>
<td>128.5</td>
<td>126.4</td>
<td>132.5</td>
<td>108.1</td>
<td>0.830</td>
</tr>
<tr>
<td>CaD-alone</td>
<td>137.6</td>
<td>125.3</td>
<td>126.9</td>
<td>132.5</td>
<td>102.2</td>
<td>0.830</td>
</tr>
<tr>
<td>HT-CaD</td>
<td>131.1</td>
<td>125.3</td>
<td>126.9</td>
<td>132.5</td>
<td>102.1</td>
<td>0.830</td>
</tr>
</tbody>
</table>

**p-value:** Overall comparison by row, not a two group comparison; **p-interaction:** HT x CaD interaction effect

**P.71. Low muscle mass and decreased muscle strength in perimenopausal women: Implications with oxidative stress**

Martha Sánchez-Rodríguez, PhD1, Mariano Zacarias-Flores, MD ObGyn, Elsa Correa Muñoz1,2, Víctor Manuel Mendoza-Núñez1,2, 1Facultad de Estudios Superiores Zaragoza, Unidad de Investigación en Gerontología, UNAM, México, DF, Mexico; 2Hospital General de Buena Prada, Instituto de Salud del Estado de México, Nezahualcóyotl, Mex, Mexico

**Objective:** To determine the lipoperoxides levels as oxidative stress (OS) biomarker in perimenopausal women and their relationship with loss of skeletal muscle mass and muscle strength. We carry out a cross-sectional study with 65 perimenopausal women of Mexico City, 44-60 year (51±3.6 year). We measured lipoperoxides levels (LPO) by TBARS assay, muscle mass by bioimpedance analysis and muscle strength (MS) with a dynanometer. We also measured weight and height and we calculated the body mass index (BMI). Skeletal muscle mass (MM) was calculated using the biocircumferential impedance equation of Janssen et al. Absolute muscle mass was normalized for height (muscle mass [kg]/height [m²]) and termed as skeletal muscle index (SMI), and free fatty acid (FFA) was estimated using the Su’s equation. An alternative cut-off value of LPO ≥ 0.320 μmol/L was defined on the basis of the 90th percentile of young healthy subjects, and handgrip strength <20 kg according the Sarcopenia European Consensus.

**Results:** We found that 33 (51%) of the women had low handgrip strength. A negative correlation between follows LPO and SMI was observed in women with low MS (r = −0.327, p<0.05), other muscle mass markers were also related, but were not significant. In women with normal/high MS we did not find correlation (Figure). All the muscle mass markers were low in women with high LPO and low MS, compared with women with low LPO and normal/high MS: SMI 7.2±0.7 vs. 7.9±0.2 kg/m², p<0.05; MM 16.6±1.8 vs.19.3±1.7 kg, p=0.0001; FFM 40.3±3.2 vs. 45.5±3.7 kg, p<0.0001. **Conclusion:** Our findings suggest that the oxidative stress is related with muscle mass and low muscle strength during perimenopausal period. This work was supported by grant DAGAPA-UNAM IN224115.

**Figure. Correlation between lipoperoxides levels and SMI separated by muscle strength.**

**CANCER POSTER PRESENTATIONS**

**P.72. METABOLIC SYNDROME AS RISK FACTOR FOR BREAST CANCER**

Dayna P. Aztun, Imelda Hernández-Bevez, BH, Hospital Juarez de Mexico, Mexico, Mexico

**Objective:** Metabolic syndrome is present in 46.6% of menopausal women. Some studies (Colonna, ORDET, Me-Can) suggest that the existing association between metabolic syndrome and breast cancer promotes carcinogenesis. Associated with this, obesity favors a chronic inflammatory condition, creating a favorable environment for epithelial cell proliferation. In Mexico, the prevalence of obesity in women from 50 to 59 years of age is 47.6%. Breast cancer is currently the first cancer death cause. Objectives: learn the association between metabolic syndrome and breast cancer; define the risk of breast cancer with each metabolic syndrome component. **Design:** An observational, comparative, cross-sectional and prospective trial was performed with women who went for the first time to the Breast Cancer and Climacteric Clinic. The metabolic syndrome was diagnosed based on the ATP III criteria. One hundred and two patients (inclusion criteria) and they were divided into 2 groups: 1) breast cancer and 2) no breast cancer, with 51 patients in each. Measures were made in each patient of weight, height, abdominal girth, blood pressure, HDL cholesterol, triglycerides, breast cancer histopathological diagnosis. They were examined using descriptive statistical methods. Additionally the groups were compared through odds ratios. **Results:** 45% (n=23) of patients with cancer and 47% (n=24) without cancer had metabolic syndrome. The metabolic syndrome is not a breast cancer risk factor (OR 0.92); however, with the discrimination of the metabolic syndrome components based on the ATP III criteria, hypertriglyceridemia was determined to be the main risk factor, with OR 2.64 (86%, n=20); followed by hyperglycemia (OR 1.56), and hypertriglyceridemia (OR 1.91), ruling out abdominal girth (OR 0.77) and blood pressure (OR 0.34) as risk factors. Additionally, when the BMI was assessed, the findings show that obesity (BMI > 30) associated with metabolic syndrome (p=0.04 in group cases and 45.8% in control group) represents a risk factor for breast cancer development (OR 1.24) **Conclusion:** As the metabolic syndrome components and obesity represent public health problems and evidence was found of the existing association with breast cancer, it is essential to engage in timely interventions, educating the women about changes in their diet and lifestyle to have a positive impact on the prevention of chronic diseases.
P-73. Histopathological analysis of ovarian tumors in pre- and post-menopausal women in Korea

Eun-Joong Kang, Department of Obstetrics and Gynecology, Busan Paik Hospital, Inje University, Busan, Korea (the Republic of)

Objective: The purpose of this study was to evaluate the histopathologic conditions of ovarian tumors in pre- and post-menopausal women in Korea.

Design: Women who had undergone surgery for ovarian tumors and histopathologically confirmed at Busan Paik Hospital in Korea from 1997 to 2013 were enrolled in this study. The histopathological distribution of ovarian tumors according to menopausal status were analyzed. Ovarian tumors were classified as non-neoplastic and neoplastic and subdivided into several categories based on the World Health Organization's classification system.

Results: A total of 4013 cases with ovarian tumors were reviewed and 3090 (3090/4013, 77.0%) cases were premenopausal women and 923 (923/4013, 23%) cases were postmenopausal women. The histopathological characteristics of 4013 cases with ovarian tumors by menopausal status are summarized in Table 1. There were 1600 cases (39.9%) of non-neoplastic masses and 2413 cases (60.1%) of neoplastic masses. In the neoplastic masses, there were 1713 cases (71.0%) of benign tumors, 190 cases (7.9%) of borderline tumors and 510 cases (21.1%) of malignant tumors.

Conclusion: There were significant differences in the histopathological distribution of ovarian tumor between pre- and post-menopausal women. Non-neoplastic masses were significantly associated with premenopausal women (P < 0.0001). Of ovarian masses, endometrioma is the most common type of all tumors (888/4013, 22.1%) and commonly occurred in premenopausal women (883/3090, 27.7%). Benign tumor were significantly higher in premenopausal women (P < 0.0001), especially in epithelial origins and germ cell origins. Borderline tumors were predominantly occurred in premenopausal women (P = 0.0001). Of malignancy tumors, epithelial origins were significantly associated in postmenopausal women (P = 0.0479), whereas germ cell origins were significantly associated in premenopausal women. Conclusion: We found that there were significant differences in the histopathological distribution of ovarian tumor between pre- and post-menopausal women. Non-neoplastic masses, benign, and borderline ovarian tumors were significantly associated with premenopausal women, whereas malignant tumors of epithelial origins were significantly associated with postmenopausal women. And we observed the increased prevalence of endometrioma in Korean women during the last 16 years compared with previous report in 1980s.

Table 1. The histopathological characteristics of ovarian tumors by menopausal status

<table>
<thead>
<tr>
<th></th>
<th>Premenopausal</th>
<th>Postmenopausal</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-neoplastic mass</td>
<td>1430 (90.9%)</td>
<td>161 (10.1%)</td>
<td>1591</td>
<td></td>
</tr>
<tr>
<td>Endometrioma</td>
<td>855</td>
<td>33</td>
<td>888</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Simple or follicular cyst</td>
<td>259</td>
<td>75</td>
<td>334</td>
<td></td>
</tr>
<tr>
<td>Corpus luteal cyst</td>
<td>164</td>
<td>5</td>
<td>169</td>
<td></td>
</tr>
<tr>
<td>Tubo-ovarian abscess</td>
<td>161</td>
<td>48</td>
<td>209</td>
<td></td>
</tr>
<tr>
<td>Benign neoplasm</td>
<td>1275 (74.3%)</td>
<td>438 (25.2%)</td>
<td>1713</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Epithelial ovarian tumor</td>
<td>50 (36.7%)</td>
<td>244 (32.7%)</td>
<td>747</td>
<td>P = 0.0001</td>
</tr>
<tr>
<td>Germ cell tumor</td>
<td>726 (60.1%)</td>
<td>117 (13.9%)</td>
<td>843</td>
<td>P = 0.0603</td>
</tr>
<tr>
<td>Sex cord-stromal tumor</td>
<td>46</td>
<td>77</td>
<td>123</td>
<td>P = 0.0068</td>
</tr>
<tr>
<td>- Benign neoplasm</td>
<td>12 (26.4%)</td>
<td>6 (35.8%)</td>
<td>18</td>
<td>P = 0.0001</td>
</tr>
<tr>
<td>- Malignant neoplasm</td>
<td>34 (73.6%)</td>
<td>11 (64.2%)</td>
<td>45</td>
<td>P = 0.0049</td>
</tr>
<tr>
<td>Ovarian cancer</td>
<td>306 (64.7%)</td>
<td>104 (55.3%)</td>
<td>410</td>
<td>P = 0.0479</td>
</tr>
<tr>
<td>Germ cell tumor</td>
<td>280 (64.6%)</td>
<td>1 (3.4%)</td>
<td>281</td>
<td>P = 0.0001</td>
</tr>
<tr>
<td>Sex-cord stromal tumor</td>
<td>16 (25.4%)</td>
<td>16 (51.6%)</td>
<td>32</td>
<td>P = 1.0000</td>
</tr>
<tr>
<td>Metastatic ca</td>
<td>36 (60.0%)</td>
<td>24 (40.0%)</td>
<td>60</td>
<td>P = 0.1556</td>
</tr>
<tr>
<td>Uncommon ovarian ca</td>
<td>10 (47.6%)</td>
<td>21 (52.4%)</td>
<td>31</td>
<td>P = 1.0000</td>
</tr>
</tbody>
</table>

P-74. Effects of Korean red ginseng extract on breast cells and breast cancer cells

Min Kyong Kim, M.D.1, Yaekyu Koh, M.D.2, Eun Bee Noh, M.D.1, Bo Hyon Yun1, Ji Young Lee2, Seok Kyo Seo2, Byungseok Lee2. Obstetrics and Gynecology, Yonsei University College of Medicine, Seoul, Korea (the Republic of); 2Obstetrics and Gynecology, Konkuk University, Seoul, Korea (the Republic of)

Objective: This study was to investigate the effects of Korean red ginseng (KRG) extracts on breast (MCF-10A) cells and breast cancer (MCF-7) cells. Design: MCF-10A cells and MCF-7 cells were cultured with different concentrations of KRG extracts. Cell viability was assessed by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assays, and apoptosis was assessed by flow cytometry. Results: KRG extracts inhibited cell proliferation and induced apoptosis in MCF-10A cells and MCF-7 cells in a concentration-dependent manner. KRG extracts inhibited protein expression of Bcl-2, Bcl-xL, and Survivin, and induced expression of BAD, leading to activation of caspase 3 and cleavage of PARP. KRG extracts induced caspase dependent cell proliferation and induce apoptosis in breast cells and breast cancer cells. KRG could be an alternative herbal supplementation having anti-proliferative effects on breast which might be used safely in postmenopausal women.

P-75. A preliminary study of the effectiveness as a screening of nipple aspiration fluid (NAF) for breast cancer risk assessment in Korean peri- and post-menopausal women by comparing with mammography and breast ultrasound

Tak Kim, M.D.,Ph.D.1, Hang Yang Jung, M.D.1, Hoon Choi1. 1Department of Obstetrics and Gynecology, Konkuk University College of Medicine, Anam Hospital, Seoul, Korea (the Republic of); 2Department of Obstetrics and Gynecology, College of Medicine, Inje University, Sanggye Paik Hospital, Seoul, Korea (the Republic of)

Objective: The HALO breast Pap test is an automated nipple aspiration fluid (NAF) system that was recently introduced into the market in Korea. Since NAF screening has never been compared to either mammography or breast ultrasound, no evidence of efficacy its use as a screening still remains investigational. We evaluated the effectiveness as an aid of breast cancer screening with the NAF system by comparing with either routine mammography or breast ultrasound examination. Design: We sampled NAF from 237 Korean women with a median age of 54.3±6 years. Of 237 separate assessments, 183 mammograms and 83 ultrasound examinations were evaluated with NAF cytology. NAF with cells was obtainable from 51.4% (122 of 237 participants) women sampled, and the sampling rate of breasts was 60.7% (288 of 478 participants). There was no statistical correlation between NAF collection age, BMI, menopausal status, breast feeding, breast cancer history, and the breast imaging reporting of mammogram and ultrasound. However, participants with increased parity were more likely to yield NAF (p=0.05). Conclusion: The rate of sampling NAF in Korean women (51.4%) appears to be higher than in other Asian women, but lower than in non-Asian women (American and European women). There was no statistical correlation between NAF collections of both NAF producers and non-producers and the breast imaging reporting of mammogram and ultrasound. NAF producers were not more likelihoods of higher risk of developing breast cancer than non-NAF producers by comparing with the breast imaging reporting. Although NAF with cytological evaluation can be used as a complement to other breast screenings, like routine mammograms and breast exams, but a nipple aspirate test should not take the place of the standard breast cancer screening technique.

P-76. Clinical Characteristics of Breast Cancer Detected on Hormone Therapy in Korean Women

Kyu-Sup Lee, MD PhD1, Sung-Tack Oh, MD PhD1, Jung-Bin Son, MD, Jong-Kil Joo, MD1, Dept of Obstetrics and Gynecology, Konkuk University Medical School, Gwangju, Korea (the Republic of); 2Department of Obstetrics & Gynecology, Pusan national university, Busan, Korea (the Republic of)

Objective: This study was performed to assess the risk factors, histologic and clinical features of breast cancers occurred from postmenopausal women who receiving hormone therapy (HT).

Design: We evaluated 40 breast cancer patients who receiving HT due to postmenopausal symptoms by reviewing their medical charts in university hospitals. Research variables including history of the patients, kinds and duration of received HT, term of the cancer outbreaking after starting HT, the radiological characteristics of breast, cancer stage, histologic type, tumor size, grade, lymph node metastasis, the estrogen receptor and the progesterone receptor status, and 5-year survival were investigated.

Results: In risk factors of breast cancer patients, only one patient had familial history of breast cancer. No one had smoking history. Average body mass index (BMI) was 23.24 kg/m². Twelve patients (30%) had estrogen only therapy, 13 patients (32.5%) had combined estrogen and progesterone therapy, 10 patients (25%) had tamibole therapy and the others consecutively received combination therapy of above regimens. Duration of treatment was 31 ± 27.9 (6.4 - 115) months. In distribution of the cancer outbreaking after starting HT, 4 cases (10%) was within 1 year, 5 cases (12.5%) within 1-2 years, 10 cases (25%) within 2-3 years, 4 cases (10%) within 3-4 years, 1 case (2.5%) within 4-5 years, and 16 cases (40%) within more than 5 years. Average diameter of tumor size was 1.7±0.6 cm. Clear type of histology consisted of 92.5%, Her2+ type of histology was consisted of 7.5%. 18 cases (45%) were stage II, 2 cases (5%) were stage III, 1 case (2.5%) was stage IV. Recurrences of disease were uncommon and came out favorable 5-year survival rates (92%) and good prognosis.
The anti-proliferative effects of Maca on breast cancer cell lines

Lily Stojanovska, PhD1, Kristina Nelson, BSc, Stephanie Day, PhD, Vasso Apostolopoulos, PhD. 1College of Health and Biomedicine, Victoria University, Melbourne, VIC, Australia; 2Brent Institute, Melbourne, VIC, Australia

Objective: Cancer is a disorder of uncontrolled cell proliferation, caused by changes to genes impairing normal mechanisms that regulate cell growth and division. The World Cancer Research Fund has a body of convincing or at least probably evidence that dietary intake and particular foods and nutrients can be both causative and preventative in cancer and it is estimated that 3 in 4 cancers are linked to diet. Obesity, red/processed meat, alcohol and salt/salty food intake are considered increased risk factors, whereas plant food intake of pulses and non-starchy vegetables, and foods containing folate, Vitamin C, Selenium and β-Carotene are associated with decreased risk. Popular health food supplements are attributed with cancer prevention benefits, many of which include chemoprevention. Lepidium meyenii (Maca) is a popular supplement widely available in retail outlets, yet its therapeutic mechanism is not well understood and rigorous studies in cancer are lacking. This study examined the anti-proliferative effects of Maca on a human breast cancer cell line, MCF-7 as to the chemoprotective potential of this plant.

Design: We previously demonstrated that Maca reduced symptoms of depression and improved diastolic blood pressure in premenopausal women. Given that breast cancer is a high risk factor in postmenopausal women, we determined the effects of Maca on breast cancer cell lines in vitro. Maca a dried powders of raw product is largely insoluble in water, and required soluble portion extraction prior to use in the cell-based assays. Breast cancer cell line MCF-7 was seeded in triplicate in 96-well plates and incubated with either crude or artificially digested extracts ranging from 0.01 mg/ml - 100 mg/ml for 24 hours. Kupferia alone was used as a background control. The difference in the amount of cells/well of the MCF-7 cell line, was attributed to the different growth rates of each cell line in vitro. Results: The addition of Maca (0.1 mg/ml - 100 mg/ml) to MCF-7 cells over 8 days, showed some anti-proliferative effects at 100 mg/ml within the first 4 days, but lower concentrations of Maca were not sustained. There was no difference in cell proliferation, even though enhanced proliferation was noted at day 8 at 1.0 mg/l and 10 mg/ml. Compared to control cells, Maca reduced MCF-7 breast cancer cell proliferation. Conclusion: Very little is known about the effects of Maca in cancer, and this study determined its anti-proliferative effects in vitro on the MCF-7 breast cancer cell line, MCF-7. Maca may have anti-proliferative effects in cancer. Further research is required to determine in Mac has anti proliferative effects in vivo.

P-78. Effects of Müllerian Inhibiting Substance on myoma

Sue-Yen Song1, Do Young Kim1, Youn-Jae Chung1, Moo-Ree Kim1, JangHeub Kim1. 1OBGYN, Catholic University of Korea, Seoul, Republic of Korea

Objective: Müllerian inhibiting Substance (MIS), also known as anti-Müllerian hormone (AMH), is known to not only act as a regulator of female reproductive function but also inhibits the growth of Müllerian duct-derived tumors in vivo and in vitro. But the role of MIS in myometrium and myoma is unclear. Therefore, this study is aimed to confirm the expression of MISRII and effects of MIS on myometrium and myoma.

Design: We gathered the tissues from the 26 patients who had hysterectomy for myoma and histologically confirmed myoma and normal myometrium. These tissues were divided into two groups, MIS and MTT assay. Induction of cell cycle and apoptosis was observed in the cells treated with MIS as measured by using DNA PI staining and annexin V binding. The cells were analyzed on a flowcytometer. We evaluated the expression of proteins which is related apoptosis and cell cycle arrest in myometrium and myoma. Results: MISRII was strongly stained in myoma tissues, whereas myometrial tissues showed weak immunoreactivities. Myoma cells treated with MIS significantly exhibited 26.4% growth inhibition in myometrium and myoma (P<0.05). Changes in cell cycle distribution after exposure to MIS demonstrated that the S phase was decreased, G0/G1 and subG0/G1 phases were increased 8.9% and 24.3% in myoma and 3.2% and 8.3% in myometrium respectively. In the cultured myometrium and myoma cells treated with MIS increased 5.2% and 20.2% binding annexin V. Treatment with MIS up-regulated p107 and p130, the cell cycle related protein and down-regulated Cdk2 and caspase-3, the apoptosis related protein. Conclusion: We found that the expression of MISRII in myoma and normal myometrium. MIS induced cell cycle arrest and apoptosis of myoma. These findings suggest that MIS has a greater role on myoma than myometrium in cell cycle inhibition and apoptosis. Therefore, MIS could be used as a biological modifier or therapeutic agent for the treatment of myoma.
correlation coefficient due to the non-normality of data. Two sided p-values < 0.05 were considered to be statistically significant. The statistical analyses were performed using R (www.R-project.org). Results: Correlation between VAT in pounds and volume was r = 0.85; standard error 0.16; the correlation between BMI and VAT (either pounds or volume) was r = 0.80. Conclusion: This underscores the notion that BMI, while commonly employed in standard medical practice, does not correlate well with VAT, a recognized risk factor for developing carcinoid tumors. Furthermore, the correlation between standard A/G ratio or even just percent fat in the android region on DXA, compared with VAT produced with newer proprietary software, is sufficiently strong to continue to use standard A/G ratio as a surrogate for visceral adiposity, although, further prospective study is necessary to see its actual correlation with cardio metabolic parameters.

P-81. Reproductive aging and associated hormonal changes are related to metabolic syndrome and cardiovascular disease risk factors in menopausal African women
Nicole G. Jaff, PhD Research Fellow1,2, Shane A. Norris, PhD1, Tracy L. Syman2, Marketa Tomáň1, Frederik Raal3, Nigel J. Crowther, PhD3, MRC/Developmental Pathways Design: The relationship between serum cystatin-C level and metabolic syndrome components in healthy Korean women.
Objective: To assess the relationship between serum cystatin-C level and metabolic syndrome occurrence in healthy Korean women.
The aim of this study is to investigate the association between serum uric acid level and metabolic syndrome according to menopausal status in Korean women.

P-83. The Association between Serum Uric Acid Level and Incidence of Metabolic Syndrome according to Menopausal Status in Korean Women
Sun Suk Kim, Kyu Sup Lee, Kyung Yoon, Si Eun Han, Youn Hwa Kim. Department of Obstetrics and Gynecology, Pusan National University, Busan, Korea (the Republic of)
Objective: To assess the relationship between serum cystatin-C level and metabolic syndrome components in healthy Korean women.
Method: A total of 2,241 women who visited the health promotion center at Pusan National University Hospital from 2010 to 2014 were included in this cross-sectional study. Self-report questionnaires and interviews with healthcare providers were used to assess disease history, medication history, menstrual history, and hormone replacement therapy. Anthropometric measurements and laboratory results were compared as presence of metabolic syndrome and menopausal status by student-t test. Logistic regression analysis was performed between presence of metabolic syndrome and serum cystatin-C levels.

P-84. Metabolic Syndrome: predictive factor for endometrial polyps in postmenopausal women
Flavia B. Dias, Daniel Spadoto-Dias, MD, Priscila F. Poloni, MD, Lucia Delamanto, MD, Jorge Nahas-Neto, PhD, MD, Elaina A. Nahas, MD. Gynecology and Obstetrics, Botucatu Medical School-Sao Paulo State University, Botucatu, Brazil
Objective: To assess the relationship between serum cystatin-C level and metabolic syndrome occurrence in healthy Korean women.

Objective: The prevalence of metabolic syndrome (MetS) and cardiovascular disease risk factors (CVD) risk factors increase in women as they transition into menopause. Whether this is due to reproductive or chronological aging, or both is not fully known. There is little evidence in midlife sub-Saharan African women, although diabetes and hypertension are all prevalent in this group. Therefore, the aim of this study was to determine whether reproductive aging and associated hormonal changes were related to MetS risk and CVD risk factors in this population.

P-82. The relationship between serum cystatin-C level and metabolic syndrome according to menopausal status in Korean healthy women
Jong Kii Jo, Sun Suk Kim, Si Eun Han, Ka Young Yoon, Kyu Sup Lee. Department of Obstetrics and Gynecology, Pusan National University, School of Medicine, Busan, Korea (the Republic of)
Objective: To assess the relationship between serum cystatin-C level and metabolic syndrome components in healthy Korean women.

Method: A total of 2,241 women who visited the health promotion center at Pusan National University Hospital from 2010 to 2014 were included in this cross-sectional study. Self-report questionnaires and interviews with healthcare providers were used to assess disease history, medication history, menstrual history, and hormone replacement therapy. Anthropometric measurements and laboratory results were compared as presence of metabolic syndrome and menopausal status by student-t test. Logistic regression analysis was performed between presence of metabolic syndrome and serum cystatin-C levels. For statistical analysis were used the Student-t, chi-square tests and logistic regression method (odds ratio-OR). Results: A higher percentage of women with polyps were obese (72%) compared to control (35%) (P = 0.0001). The WC was higher among patients with polyps (P = 0.0001). We observed a higher incidence of diabetes, hypertension and dyslipidemia in patients with endometrial polyps (P = 0.0001). According to the diagnostic criteria of the US National Cholesterol Education Program: Adult Treatment Panel III (NCEP/ATP III), 48.5% of women with polyps and 33.3% in the control group were classified as having metabolic syndrome (P = 0.004). Analysis of risk for endometrial polyp was higher in patients with BMI > 25 kg/m2 (Pop: 84.2%, CI95%: 16.10.0%); glucose >100 mg/dL (OR: 2.83; CI95%: 3.56.5.0); dyslipidemia (OR: 7.02; CI95%: 7.0.13.32); diabetes (OR: 5.62; CI95%: 0.6.6.2); and metabolic syndrome (OR: 7.78; CI95%: 5.18.6.6) compared to control. Conclusion: In postmenopausal women, obesity, dyslipidemia, hypertension, and the presence of metabolic syndrome were predictive factors for endometrial polyps.
P-88. Post-reproductive Aged Women: In Support of Health Screening Guidelines for Assisted Reproductive Technology (ART) Using Donor Oocytes
Taleen MacArthur, Gloria Bachmann, M.D., MMS, Charlotte Ayers, M.D., MPH, Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ
Objective: As more post-reproductive aged women opt to pursue pregnancy with advanced ART technologies, the menopausal practitioner will become more involved in counseling, screening and referral of menopausal women for these services. This review will evaluate current ART screening practices in the United States and propose discussion surrounding more universal guidelines for ART candidacy in post reproductive aged women using donor eggs/embryos. The review will also assess the similarities and guidelines in the adoption process of a postbirth child as compared to the process of "adoption" of a donor egg/embryo with ART. Design: A review of articles on PubMed and official websites pertaining to ART, advanced maternal age, and ART screening over the last twenty years was conducted. Results: Despite the increasing use of ART with donor eggs/embryos in post-reproductive aged women, there are no universal guidelines in use for determining candidacy with regard to maternal health. As national trends move towards women delaying childbearing, the cohort of post-reproductive age women looking towards ART using donor oocytes as a fertility option is expanding. The American Society for Reproductive Medicine (ASRM) states that healthy women over fifty who are prepared for parenthood are good candidates for ART through oocyte donation, but advises that older women be counseled as to the increased obstetric risk associated with advanced maternal age. This society recommends a thorough medical evaluation and appropriate health screening, and that women should be discouraged from pursuing pregnancy if they have a health condition that may increase maternal or fetal risk. However, the issue raised is whether more comprehensive guidelines that would be customized for all post reproductive aged women that address screening and advice for ART be developed with the assistance of practitioners caring for midlife and older women. That each older woman be screened by the same set of guidelines by all centers rather than guidelines that are individualized at each health center offering ART services. Further, a discussion that is initiated by the topic of donation is whether guidelines for potential patients who want to use donated oocytes more closely follow present adoption guidelines. In adoption, a postbirth child is brought into a family’s home while in ART a prebirth child is brought into a family’s or individual woman’s home. In both cases, a third party is enlisted to help facilitate parenthood. Despite the fundamental similarities between them, the screening processes for adoption are far more comprehensive than those for ART with a donor oocyte. Conclusion: A universal template of practice with input from practitioners caring for postreproductive aged women should be considered. Universal guidelines would create more consistency in care for this cohort of older women seeking ART services and utilizing oocyte donation.

P-89. Evaluation of Shared Decision Making Between Patients and Providers to Improve Menopause Health Outcomes
Laura M. Borgelt, PharmD, FCCP, BCPS, NCMP2, Robin Liston, MPH1, Kelli Giacomin, BS, Miriam Dickinson, PhD1. National Research Network, AAAP, Leawood, KS; 1Clinical Pharmacy and Family Medicine, UCD, Aurora, CO; 2Family Medicine, UCD, Aurora, CO
Objective: The increasing use of ART with gestational carriers (GC), also known as third-party reproduction, incorporates SDM may lead to improved health outcomes and increased satisfaction with the healthcare experience. Given that approximately half of women between the ages of 45-60 years experience at least one menopausal symptom, it is important to offer individualized treatment options. Hormone therapy (HT) has been proven to be the most effective treatment for menopausal symptoms and is an acceptable option in many

P-86. Metabolic syndrome in Brazilian postmenopausal women
Benedito F. Reis, MD1,2, Layara S. Ribeiro, academic,1 Diego L. Aguiar, academic,1 Sonia Maria R. Rolim-Lima, MD1, Lyliana Coutinho R. Barbosa, PhD2, Antonio Marcos C. Francisco, PhD1. Obstetrics and Gynecology, FMCS, São Paulo, Brazil; 1Gynecology, UNIVAS, Pouso Alegre, Brazil
Objective: To compare the prevalence of Metabolic Syndrome (MS) according to the criteria of the National Cholesterol Education Program ATP III (NCEP) and the American Diabetes Association (ADA) in Brazilian postmenopausal women. Design: All 124 postmenopausal women attended from 2013 to 2014 in climacteric clinic in Vale do Sapucaí University (UNIVAS) were classified according to the MS criteria by the NCEP and ADA. Results: The prevalence of MS in the population of 124 women was 47.6% (59 cases) by the NCEP and 55.6% (69 cases) by the ADA. There was an accretion of the criteria of the National Cholesterol Education Programm ATP III (NCEP) and the American Diabetes Association (ADA) in Brazilian postmenopausal women. Conclusion: Metabolic syndrome is a common condition in postmenopausal women. Both criteria showed an increase in MS prevalence in postmenopausal women.

P-85. Differences of prevalence and components of metabolic syndrome according to menopausal status
Sung-Tack Oh, MD PhD1, Kyu-Sup Lee, MD PhD2, Jong-Kil Joo, MD, Jung-Bin Son1. Department of Obstetrics & Gynecology, Chonnam University Medical School, Gwangju, Korea (the Republic of)1; 1Department of Obstetrics and Gynecology, Pusan national university, Busan, Korea (the Republic of)2
Objective: Metabolic and endocrinologic alterations is developed at menopause transition of women and these alterations can have an effect on prevalence of metabolic syndrome (MS). The objective was evaluated the prevalence of metabolic syndrome components as menopausal status of women who visited our health screening clinic. Design: We surveyed body sizes, blood pressures and other several blood tests from January 2006 to December 2010 in University Hospitals by retrospectively reviewing medical records. Results: The results were compared according to the prevalence of metabolic syndrome and menopausal status. Differences of the components of metabolic syndrome as the menopausal status and occurrences of metabolic syndrome as the age and the menopausal status are investigated. Results: In menopausal and postmenopausal women, the prevalence of metabolic syndrome were 8.69% and 21.85%, respectively. More body weight, high BMI and cholesterol were checked in women who have metabolic syndrome irrespective of menopausal status. Low high density lipoprotein was most prominent component of metabolic syndrome irrespective of menopausal status. Hypertension and high blood sugar were showed meaningful proportions in postmenopausal women. The prevalence of metabolic syndrome was unrelated to the menopausal status by regressively analyze, but meaningfully increased related to aging. Conclusion: Metabolic alterations restrictively effect on occurrence of metabolic syndrome and aging is more effect. Further detailed and additional studies are needed about determining the relation of metabolic syndrome in women who surgically menopaused and receiving hormone therapy.

POSTER PRESENTATIONS
women up to 59 years; however, long-term use appears to impose greater risks than benefits. It is equally important to ensure that women between 60-65 years stop using HT unless deemed appropriate. Other treatments, including non-prescription therapies, may be more appropriate for individual situations. Breast cancer risk increases with age and is the most significant concern for women age 60-65 years. Therefore, women coming in and out of the menopause transition require individualized evaluation and management. The primary objectives are to evaluate the impact of SDM among health care providers and women age 45-65 years regarding menopause, postmenopause breast cancer risk, life transitions and improved quality of life. We also hope to collect information related to these issues. Design: Using a stepped wedge randomized design, 9 primary care practices throughout the U.S., located in varied geographic areas (e.g., rural, suburban, urban) were enrolled, with 1 to 4 participating providers per site. Up to 650 peri- and post-menopausal women aged 45-65 years seen at a routine appointment between August 2014 and August 2015 were recruited to participate. Tablet technology incorporated surveys, health assessment tools with scoring algorithms, and educational videos. The Menopause Rating Scale and Breast Cancer Risk Assessment Tool were combined into a Menopause Health Assessment report which was printed, saved to a secured server for uploading into an electronic health record (EHR) and available on the tablet at point-of-care. Videos provided women guidance on how to enhance discussions about SDM with their provider. Patients completed surveys of selected domains (e.g., whole-person orientation) from the Ambulatory Care Experiences Survey (ACES). Providers completed pre- and post-assessments for a webinar that included: menopause terminology; physiologic changes that occur in perimenopause and through menopause; assessment tools for menopausal symptoms and breast cancer risk; clinical trials and position statements that have provided evidence to influence clinical practice; therapeutic options to manage the symptoms of menopause; and communication strategies to discuss symptoms and treatment options with patients. Providers also completed a modified version of the ACES survey. Baseline and end of study EHR data will be utilized at each participating practice to: evaluate changes in rates for diagnosis of menopause and/or postmenopausal status; use of therapies for menopausal symptoms for women age 45-59 years; and women age 60-65 years with a menopause diagnosis or postmenopausal disorder prescribed HT. Evaluation of the data will describe gaps that may exist in the assessment and appropriate treatment. Provider satisfaction with communication, interpersonal treatment, patient trust, whole person orientation, health promotion, and satisfaction with SDM will be included. An assessment of provider knowledge will also be included. Conclusion: Conclusions will be determined with completion of data analysis. P-90. Perceptions and attitudes towards menopausal hormone therapy (HT) amongst family physicians attending a mature women’s health conference in Ontario, Canada Kelsey E. Mills, MD, FRCS, FRCSC, NCMP, Michelle Jacobson, MD, FRCS, NCMP, Wendy L. Wolfman, MD, FRCS, FRCSC. Obstetrics and Gynecology, University of Toronto, Toronto, ON, Canada Objective: The goal of this study was to evaluate the perceptions and attitudes towards menopausal HT, as well as the prescribing practices, of family physicians attending a mature women’s health conference in Ontario, Canada. Design: A paper survey was included in the orientation package of all registered participants attending a mature women’s health conference in April 2015 in Toronto, Ontario, Canada. Attendees were invited to complete the survey, which was anonymous and did not collect identifying demographic information. Completion of the survey was voluntary. Survey questions evaluated the perceptions of primary care providers towards duration of use of HT, prescription preferences for types of systemic estrogens and progestogens, and preferences for the management of genitourinary syndrome of menopause (GSM). We assessed these providers’ comfort levels with managing menopausal symptoms and with prescribing hormonal and non-hormonal treatments for menopausal issues. We also evaluated their current prescribing practices with regards to compounded bioidentical hormone therapies. Results: The response rate for this survey was 59.4% (n=164) and the average length of time in practice for responders was 19.8 years (range 0.5-43). 75.0% of these family physicians perceived that they were “comfortable” or “very comfortable” with managing menopausal symptoms. Of the 8 physicians (3.6%) who felt “uncomfortable” or “very uncomfortable” managing menopause, four had been in practice for more than 30 years. Non-hormone therapy for menopause management was used by 58.5% of clinicians who reported that they were comfortable managing menopausal symptoms of respondents, 61.5% of physicians prescribed system HT for the indication of GSM. Conclusion: Family physicians are the first-line providers of menopause management for Canadian women. This is the largest study to provide information about the perceptions and attitudes of Ontario family physicians towards menopausal medicine, as well as delineating the prescribing practices of this group. Despite the majority of the highly motivated group (by virtue of their attendance at a mature women’s health conference) rating themselves as comfortable managing menopausal symptoms, this survey demonstrates the variety of evidence and non-evidence based practices occurring amongst these physicians. Results from this study indicate that opportunities for continuing medical education with a specific focus on the prescription of menopausal HT may be beneficial to family physicians to provide the best possible care to menopausal women. P-91. The Clinical Utility of a Blood Test Incorporating Age, Sex, and Gene Expression Scores in the Evaluation of Women Presenting with Symptomatic Obstructive Coronary Artery Disease in a Large Primary Care Registry (PRESET): Subgroup Analysis of the PRESET-4 Endpoint Gregory Pokvorkya, MD, FACCP, FNLA, NCMCP, Joseph A. Ladapo, MD, PhD, Richard Wright, MD, FACCP, Paul McLaughlin, MD, Bruce Maniet, DO, David Sharp, DO, Linda Ross, MPH, Lin Huang, PhD, Mark Monane, MD, MS, Matthew Budoff, MD, ‘Johns Hopkins University School of Medicine, Baltimore, MD, ‘NYU Langone Medical Center, New York, NY; ‘Pacific Heart Institute, Santa Monica, CA; ‘Paul E White Memorial MD, Mount Sterling, KY; ‘Bells Medical Clinic, Belts, TX; ‘Doctors for Health, Omaha, NE; ‘CardioDiDs, Inc., Redwood City, CA; ‘UCLA Community Medical Center, Los Angeles, CA Objective: Better methods are needed for the evaluation of women presenting to the primary care physician (PCP) with symptoms of obstructive coronary artery disease (CAD), as current methods are characterized by test overutilization, high costs, patient exposure to appreciable risks from radiation and contrast-dye reactions, and diagnostic uncertainty. A previously validated blood-based test combining age, sex, and gene expression levels into an algorithmic score has been shown to have a 96% negative predictive value in a combined population of men and women in determining a patient’s current likelihood of obstructive CAD, thereby helping primary care clinicians rule out obstructive CAD diagnosis in low-to-intermediate risk symptomatic patients. We hypothesized that information from the age/sex/gene expression score (ASGES) would change medical decision making during the evaluation of patients presenting with stable chest pain or anginal equivalent symptoms. The primary outcome of this analysis was the association between ASGES and referrals for further cardiac evaluation in women. Design: The prospective PRESET Registry (NC1056771156) enrolled stable, non-acute adults evaluated for obstructive CAD from 21 US primary care, community-based practices over a one-year period. Primary care physicians, nurse practitioners, and physician assistants at primary care practices were educated and trained on the use and interpretation of the ASGES through a standardized in-service program. The laboratory reported the patient’s ASGES to the primary care provider within a median of three days from the blood draw, who were then able to incorporate the ASGES test results, in conjunction with other clinical information, into their medical decision-making process for further diagnostic evaluation. Data collected included the patient demographics, comorbidities, and clinical presentation, and the clinician’s treatment plan before vs. after receiving the ASGES results. We evaluated the relationship between the ASGES results (predetermined as low [ASGES ≤15] or elevated [ASGES >15]) and decision-making, including cardiology referrals and downstream cardiac diagnostic tests. Results: Endpoint analysis was the association between ASGES and referrals for further cardiac evaluation. Data collected included the patient demographics, comorbidities, and clinical presentation, and the clinician’s treatment plan before vs. after receiving the ASGES results. We evaluated the relationship between the ASGES results (predetermined as low [ASGES ≤15] or elevated [ASGES >15]) and decision-making, including cardiology referrals and downstream cardiac diagnostic tests. Of 21 primary care practices, 19 (90.5%) participated in the study. Of the 718 evaluable patients in the final analysis, 369 (51%) were female participants with a median age of 59 years, median BMI of 29, and median ASGES of 9 (range, 1-40). The ASGES test showed that 272 of 369 patients (74%) had low scores. With regard to further diagnostic evaluation, which included either referral to cardiology and/or advanced cardiac testing (MPI, ECHO, CCTA, ICA), 21 of 272 (8%) of women with low ASGES and 31 of 97 (32%) of women with elevated ASGES were referred to cardiology or advanced diagnostic testing (OR 0.18, p<0.0001). The overall MACE event rate for the female cohort was 0.5% (2/369; both events were judged to be unrelated to the investigational agent or procedure) at 30-days post-ASGES. Conclusion: A blood test incorporating age, sex, and gene expression was adopted into clinical practice and showed clinical utility in helping clinicians rule out obstructive CAD as the cause of women’s symptoms in this large community-based primary care patient population presenting with typical and atypical symptoms suggestive of obstructive CAD. There was a statistically significant and clinical relevant reduction in referral to cardiology and advanced cardiac testing among low ASGES women who have a low current likelihood of obstructive CAD, thus preventing unnecessary—and potentially harmful—and invasive—downstream cardiac testing. The ASGES blood test may help address an important diagnostic challenge in cardiovascular medicine in the care of mid-life women.
**P-92.**
An Approach to Improving the Care of Women Aged 45 to 64 through the Implementation of a Women’s Health Assessment Tool and Clinical Decision Support Toolkit (WHAT/CDS)

Terry Silvestrin1, Karin Coyne, MPH2, PhD2, Anna Steenrod, MPH2, David Gross, Pharm D2, Canan Esindury, MD3, Angela Koishi, Pharm D, Gayle Slika, Pharm D, CPEHR3, Lucy Abraham1, Anna Araiza, MPH1, Andrew Bushmakin1, Xuemei Luo, PhD3, MultiCare Tacoma Women’s Specialists, Tacoma, WA; 1Evidera, Bethesda, MD; 2Pfizer, Inc, New York, NY

**Objective:** To describe the Women’s Health Assessment Tool (WHAT) and Clinical Decision Support (CDS) toolkit implementation process within an integrated delivery system (IDS) and to assess patients’ and providers’ perceptions about the WHAT/CDS toolkit. **Design:** The WHAT/CDS toolkit comprised of two components: 1) The WHAT, a 35-item, web-based patient-reported questionnaire to assess four health conditions (depression, UI, VMS, and VVA); and 2) The CDS, a toolkit built into the electronic health record (EHR) to support the delivery of evidence-based care. The WHAT/CDS toolkit was piloted over a 4-month period through an IDS in the South Puget Sound area of Washington State. Women, aged 45-64, scheduled for an annual well-woman visit, were asked to complete the WHAT questionnaire online through their MyChart patient portal prior to their appointment. A provider received a summary of the patient’s responses, which were uploaded into the EHR and triggered the CDS toolkit to support clinical decision-making during the patient’s visit (Figure 1). Patients’ and providers’ perceptions of the WHAT/CDS toolkit were collected through surveys and qualitative interviews. **Results:** Over the 4-month pilot period, 110 women (mean age: 54.3, SD=5.9) completed the WHAT questionnaire (30% response rate) and 12 providers used the WHAT/CDS toolkit. A third of the women (n=37, 33.6%) had at least one new diagnosis of UI, VVA, depression, or VMS during the well-woman visit. Two-thirds of patients (n=76) and providers (n=8) completed the feedback surveys and five providers participated in a qualitative interview to discuss the implementation process. The majority of the patients (69.8%) agreed that they felt more prepared for their annual visit and that the WHAT questionnaire helped their discussions with their provider. Most women (59.2%) felt the WHAT/CDS toolkit improved their quality of care and 70% agreed they would use the WHAT questionnaire again. Most provider survey responses were neutral although 50% agreed that the WHAT/CDS toolkit captured pertinent information. Qualitative interviews provided additional insight and support for the WHAT/CDS toolkit with providers reporting that the WHAT/CDS toolkit streamlined patient visits, improved communication between the provider and patient, and allowed patients to feel more ownership over their healthcare. Most interviewed providers indicated that they would use the WHAT/CDS toolkit again (60%). **Conclusion:** Patients and providers’ perceptions of the WHAT/CDS toolkit provide evidence to support the use of the toolkit to improve the care of mid-life women during their annual well-woman visits.

**Figure 1. Women’s Health Assessment Process**

**P-93.**
Outcomes Assessment of Implementing the Women’s Health Assessment Tool and Clinical Decision Support Toolkit (WHAT/CDS) within an Integrated Delivery System

Terry Silvestrin1, Anna Steenrod, MPH2, Karin Coyne, MPH, PhD2, David Gross, Pharm D2, Canan Esindury, MD3, Angela Koishi, Pharm D, Gayle Slika, Pharm D, CPEHR3, Lucy Abraham1, Anna Araiza, MPH1, Andrew Bushmakin1, Xuemei Luo, PhD3, 1MultiCare Tacoma Women’s Specialists, Tacoma, WA; 2Evidera, Bethesda, MD; 3Pfizer, Inc, New York, NY

**Objective:** To evaluate outcomes after implementing a newly developed Women’s Health Assessment Tool and Clinical Decision Support Toolkit (WHAT/CDS) toolkit during annual well-woman visits and to compare patients’ health resource utilization pre and post implementation. **Design:** This observational project recruited women aged 45 to 64 attending one of three medical sites in an Integrated Delivery System (IDS) in the South Puget Sound area of Washington State for an annual health visit. Prior to their visit, women were asked to complete the Women’s Health Assessment Tool (WHAT), a 35-item web-based patient-reported health questionnaire to assess four highly prevalent health conditions in mid-life women: depression, urinary incontinence [UI], vasomotor symptoms [VMS] and vulvovaginal atrophy [VVA]. A physician received a summary of the patient’s responses to the questionnaire which were uploaded into the patient’s electronic health record (EHR) and triggered a clinical support decision (CDS) toolkit to support the physician’s clinical decision making during the patient’s annual visit. Data from the WHAT questionnaire and patients’ annual visits were collected over a 4-month period and analyzed using descriptive statistics. Change in healthcare resource utilization including referrals, lab orders, diagnostic procedures, and follow-up visits were analyzed using retrospective analysis of the EHR data from the past 12 months prior to the patient’s visit. **Results:** 110 women (mean age: 54.3, SD=5.9) completed the WHAT questionnaire (30% response rate). The majority of women had entered menopause (77.3%) and rated their overall health as “good”, “very good”, or “excellent” (88.0%) WHAT questionnaire results showed that most women had experienced depressive mood (63.6%), hot flashes (61.9%) or anxiety (60.9%) in the last three months. About half of the women indicated that they had experienced sexual problems (51.2%), dryness or discomfort of the vagina (52.7%), or bladder problems (55.5%). A third of the women (44.5%) had at least one diagnosis of UI, VVA, depression, or VMS during the well-woman visit. There was a 72.2% increase in the number of diagnoses for all four conditions made during the patient’s annual visit (n=31 new diagnoses) vs. previous 12-month period (n=18 diagnoses). Most new diagnoses were for VMS (n=15) or VVA (n=11). Fifty-nine laboratory tests were ordered during the well-woman visit compared to 37 during the previous 12-months for patients diagnosed with UI, depression, VVA or VMS. Similarly, 32 procedures or diagnostic test were ordered during the well-woman visit compared to 20 during the previous 12-months for patients diagnosed with UI, depression, VVA or VMS. **Conclusion:** There was a 72.2% increase in the number of diagnoses for all four conditions made during the patient’s annual visit when using the WHAT which indicates that the WHAT questionnaire can help identify conditions relevant to mid-life women. There was also an increase in the number of diagnoses and laboratory tests ordered after the implementation of the WHAT/CDS toolkit.

![Figure 1. Women’s Health Assessment Process](image_url)