

Abstracts of Oral Communications

BEST ABSTRACTS FOR ROBERT GREENBLATT PRIZES

OC1.1

METFORMIN FOR THE MANAGEMENT OF INSULIN RESISTANCE IN OVERWEIGHT WOMEN AT MIDLIFE

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Aim: Evidence to support the use of metformin to treat insulin resistance (IR) and prevent progression to type 2 diabetes mellitus (T2DM) in its preclinical phase is lacking. The aim of this study was to determine whether metformin would reduce IR, weight and waist circumference and improve lipids and lower sex hormone binding globulin (SHBG) in obese, but not morbidly obese, euglycaemic women.

Methods: Obese women (body mass index (BMI) >30 and <40 kg/m² and/or waist circumference >88 cm), aged 35–65 were randomised (1:1) to metformin 850 mg, or identical placebo, twice daily for 26 weeks. The primary study outcome was the change in IR determined by the homeostasis model of assessment (HOMA-IR). Secondary outcomes included fasting insulin, glucose, weight, waist circumference and BMI. The trial was registered on ACTRN12610000836033.

Results: 125 women were screened, 117 enrolled and 100 women, mean age 53 years, were included in the primary intention to treat analysis. Metformin treatment resulted in statistically significant between group difference in the change in HOMA-IR (mean change -0.38; 95% CI of mean -0.54 to -0.22, vs placebo -0.13; 95% CI -0.50 to 0.24, $p=0.018$) and BMI (mean change -1.00 kg/m²; 95% CI of mean -1.37 to -0.62 vs placebo 0.00; 95% CI -0.29 to 0.28, $p<0.001$). Statistically significant reductions in HbA1C ($p=0.008$) and fasting insulin ($p=0.03$) and a borderline increase in HDL-C ($p=0.07$) were also observed for metformin, compared with placebo. No effects were seen for waist circumference, fasting glucose, other lipids or SHBG.

Conclusion: Treatment of euglycemic obese middle-aged women with metformin 1700 mg/day resulted in improved IR and weight loss compared with placebo. Our findings support the use of metformin as an intervention to prevent progression of IR to T2DM in obese, but not morbidly obese, middle-aged women.

This study was supported by the Bupa Health Foundation, Australia.

OC1.2

ISOLATION AND CHARACTERIZATION OF OOGONIAL (OOCYTE-PRODUCING) STEM CELLS FROM OVARIES OF PERI- AND POST-MENOPAUSAL WOMEN

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We and others have previously reported that the ovaries of reproductive-age mice and women contain a rare population of mitotically-active germ cells, termed female germline or oogonial stem cells (OSCs), that have the ability to generate functional oocytes and participate in de-novo follicle formation (Nature Medicine 2012 18:413–421; Nature Protocols 2013 8:966–988). When cultured ex vivo, these cells actively divide for months without losing germline characteristics, including the ability to spontaneously form in vitro-derived (IVD)-oocytes after each passage. However, it is not known whether these cells persist in the ovaries of women after menopause. Using a validated DDX4 antibody-based flow cytometric sorting approach (Nature Protocols 2013 8:966–988), we analyzed dissociated ovarian cortex from women in their 20s, 30s, 40s,

and 50s for the existence of OSCs. We found that OSCs were present in the ovaries of women in each indicated decade of life, without a significant decline in the percent yield of these cells with increasing age. Once established in culture, OSCs isolated from ovaries of women in their 40s and 50s proliferated, expressed germline markers, and routinely generated IVD-oocytes in a manner similar to their counterparts from ovaries of younger women in their 20s and 30s (Nature Medicine 2012 18:413–421). These findings raise the exciting possibility that ovaries of perimenopausal and post-menopausal women maintain the capacity to form new oocytes. Our current studies are directed at elucidating why ovaries of women lose the ability to support the oogenic function of these cells with age, and if this impairment in OSC function in aging human ovaries is reversible (Support: NIH R37-AG012279, Glenn Foundation for Biomedical Research).

OC1.3

ANDROGEN AND ESTROGEN FORMATION FROM DEHYDROEPIANDROSTERONE IN THE MONKEY VAGINA: POSSIBLE IMPLICATIONS FOR THE TREATMENT OF POSTMENOPAUSAL VULVOVAGINAL ATROPHY (VVA) AND SEXUAL DYSFUNCTION

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Intravaginal administration of dehydroepiandrosterone (DHEA, prasterone) has been found to improve VVA and sexual dysfunction in postmenopausal women. The distribution of the enzymes responsible for estradiol (E2) and androgen formation as well as their respective receptors within the monkey vagina, the closest model to humans, should help explain how DHEA improves VVA and sexual dysfunction. Objective: Determine the sites and level of expression of steroidogenic enzymes responsible for estrogen and androgen formation as well as the androgen receptor (AR) and estrogen receptors (ERs) in vaginal specimens collected from cynomolgus monkeys. Measurements and results: HSD3B1, HSD17B1, HSD17B3, HSD17B5, HSD17B12, HSD17B15, CYP19A1, SRD5A1, SRD5A2, Estrogen Receptors (ER α and ER β), AR and nerve fibers (PEP 9.5) were measured or localized by quantitative RT-PCR, immunohistochemistry and immunofluorescence. The above-mentioned steroidogenic enzymes are at the highest level in the cell-rich squamous epithelial layer of the vagina. ERs and AR are also mainly localized in the epithelium, especially near the basement membrane with modest levels also found in the lamina propria and muscularis. Immunostaining of the enzymes and sex steroid receptors is also seen around the blood vessels and zona muscularis of the deepest part of the tissue where nerve fibers are also mainly located. Conclusions: This study shows the distribution of the enzymes involved in sex steroid formation as well as their site of action (ERs and AR) in the various layers of the vagina, thus supporting the role of both estrogens and androgens in regulating epithelial cell maturation and fluid secretion, smooth muscle activity, blood flow regulation and neuronal activity.

OC1.4

HORMONE REPLACEMENT THERAPY REDUCES LIPID OXIDATION DIRECTLY AT THE ARTERIAL WALL: A DIRECT LINK TO ESTROGEN'S CARDIOPROTECTIVE EFFECT THROUGH ATHEROSCLEROSIS PREVENTION

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BACKGROUND: Post-menopausal women not only have an increase in oxidative stress, they also have a decrease in the antioxidant

mechanisms that protect them. The first step in atherosclerosis formation is the ingurgitation of an oxidized LDL molecule by a macrophage which then turns into a foam cell within the vascular wall and initiates a cascade of inflammatory responses. Estrogen has been shown to have antioxidant capacities in vitro and in vivo. Could it be, that the cardioprotective effect observed in women receiving HRT, is by estrogen's capacity to decrease LDL oxidation in the vascular wall and thus decrease atherosclerotic foam cells?

AIM: To determine HRTs' capacity to decrease lipid oxidation directly in the arterial wall. To establish a direct link that could possibly explain estrogens' mechanism as a cardioprotective molecule.

METHOD: 24 adult female Wistar rats were divided in 3 groups. All were double oophorectomized. After a week of recovery, Group 1 received Estradiol Valerate SC(2.5 mg/kg/week), Group 2 Estradiol Valerate SC(2.5 mg/kg/week) + Progesterone SC(10 mg/kg/48 hrs), and Group 3 Placebo SC. All conditions were the same for the groups. After 8 weeks all rats were sacrificed and a vascular dissection to include aorta, femoral and renal arteries was performed. Malondialdehyde (MDA) was measured directly in the vascular extract to determine lipid oxidative levels and HRTs' effect.

RESULTS: Vascular MDA levels for Group1 = 80.80(±16.8) µmol/ml/g, Group2 = 107.69(±24.9) µmol/ml/g, and Group3 = 140.96(±32.4) µmol/ml/g. ANNOVA (p<0.05), with a post-hoc Bonferroni corrective t-test, showed that both Group1 and 2 have statistically significant lower levels of MDA than Group3.

CONCLUSION: HRT statistically reduces lipid oxidation directly in the arterial wall. This is the first study to link estrogen's cardio protective effects directly to atherosclerosis' physiopathology.

OC1.5

PROGNOSTIC IMAGING AND LABORATORY PROPERTIES OF CYSTIC OVARIAN STRUCTURES IN THE PERI- AND POSTMENOPAUSE

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Aim: To determine the efficacy of ultrasound (US) examinations and CA-125 measurement in the diagnosis of peri- and postmenopausal ovarian cysts.

Materials and Methods: Imaging properties of peri- (PEM) and postmenopausal (POM) ovarian cysts were examined preoperatively. According to US findings two groups were made: (1) simple cysts: unilocular, anechoic cysts without papillarization, (2) complex cysts: cystic structures with different parameters. Imaging characteristics, size were matched with histology and CA125 levels.

Results: 379 cystic structures (PEM: N=195, average age: 45.6 yrs; range: 40–54 yrs, POM: N=184, average age 61.2 yrs; range: 41–88 yrs) were analysed. In the PEM group 75 simple ($\varnothing < 5$ cm N=32, $\varnothing \geq 5$ cm N=43) and 122 complex cysts ($\varnothing < 5$ cm N=29, $\varnothing \geq 5$ cm, N=93), while in the POM group 49 simple ($\varnothing < 5$ cm N=9, $\varnothing \geq 5$ cm N=40) and 135 complex cysts ($\varnothing < 5$ cm N=15, $\varnothing \geq 5$ cm N=120) were found. In the PEM group malignancy was detected in complex cysts larger than 5cm (N=16, 17.58%). In the POM group we found malignancy in 40 cases, three of them smaller than 5 cm. Majority of cysts were functional (54.36 %) in the PEM group. In the POM group serous cysts were the most frequent (38.04%), followed by malignant (21.74%) and mucinous cysts (13.04%). CA125 were elevated in 66 of 217 cases (30.41%), only 23 of these were malignant (NPV: 0.95, PPV: 0.35).

Discussion: Functional cysts are frequently found among peri menopausal ovarian cysts, but we detected malignancy only among complex cysts larger than 5 cms. However, complex cyst of any size carries significant risk of malignancy in the menopause, thus surgery is

recommended. Simple cysts can be followed by serial scan in both groups. CA-125 did not give added value to the detection of malignancy.

OC1.6

FRACTIONAL CO2 LASER IMPROVES SEXUAL FUNCTION IN WOMEN WITH VULVOVAGINAL ATROPHY

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Objective: To investigate the impact of fractional CO2 laser on sexual function of women with vulvovaginal atrophy (VVA).

Design: Prospective study performed between January 2013 and December 2013.

Materials and Methods: The criteria for inclusion in the study were: symptoms of VVA; menopausal age; absence of menstruation for ≥ 12 months; active sexual life or desire to resume sexual activity; dissatisfaction with hormonal therapy. The criteria for exclusion from the study were: use of hormonal therapies in the 6 months prior to inclusion in the study; prolapse staged \geq II according to the pelvic organ prolapse quantification system; acute or recurrent urinary tract infection; genital infection; previous reconstructive pelvic surgery; any serious disease or chronic condition that could interfere with study compliance; psychiatric disorders precluding informed consent. Women were treated with three applications of vaginal fractional microablative CO2 laser. The procedure was performed in the outpatient clinic, not requiring any specific preparation, analgesia or anaesthesia.

Results: The study included 50 patients. At baseline, 38 women (76.0%) were sexually active while 12 (24.0%) did not have sexual intercourse due to the severity of VVA. The FSFI score at baseline was 13.9 ± 7.3 . After one cycle of laser treatment, 10 patients (83.3%) resumed sexual activity. Two patients (16.7%) did not recover sexual activity due to the persistence of VVA. A significant improvement in FSFI score was reported among sexually active women (26.9 ± 5.7 ; $p < 0.001$). A significant amelioration in all FSFI domains was reported ($p < 0.001$ for all comparisons).

Conclusions: The treatment with fractional CO2 laser improves sexual function in women with VVA.

Support: none.

BEST ABSTRACTS IN SPANISH

OC2.1

A MULTICENTRIC STUDY REGARDING THE USE OF HORMONE THERAPY DURING MID-AGE (REDLINC VI)

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Background: The use of hormone therapy (HT) during the climacteric is low; despite the fact that it improves quality of life and decreases the risk of chronic diseases. Objective: To determine the prevalence of current HT use and the characteristics of women who have never used, have abandoned or are currently using HT; and the reasons for which they are not using HT. Method: This was a cross-sectional study that studied a total of 6,731 otherwise healthy women aged 45 to 59 years of 15 cities of 11 Latin American countries. Participants were requested to fill out the Menopause Rating Scale (MRS) and a

questionnaire containing socio-demographic data and items regarding the menopause and HT. Results: The prevalence of HT use was 12.5% (22.6% in 2006). The most frequently used HT was oral estrogens (43.7%) followed by transdermal (17.7%). Main factors related to the use of HT included: positive perceptions regarding HT (OR: 11.53, 95% CI, 9.41–14.13), being postmenopausal (OR 3.47, 95% CI, 2.75–4.36) and having a better socio-economical level. A 48.8% of surveyed women used HT, but abandoned it due to symptom improvement or being unconcerned; fear to cancer or any other secondary effects was reported but in less than 10%. Among women who never used HT, 28% reported the lack of prescription as the main reason followed by the absence of symptoms (27.8%). A 30.6% of those reporting lack of prescription as the main reason for not using HT had MRS scores defined as severe (MRS total score > 16). A 19.5% of women use alternative therapies “natural”, with 35.1% of them having severe menopausal symptoms against 22.5% observed among current HT users. Conclusion: The use of HT has not regained rates observed a decade ago. Positive perceptions regarding HT was related to a higher use. Non medical prescription was the main reason for not using HT among non users; many of them having severe menopausal symptoms.

OC2.2

UTERINE CERVICAL PATHOLOGY IN MENOPAUSE PATIENTS

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INTRODUCTION: The length of life in the women in Ecuador is 78 years, the average of the menopause is 46,5 years.

Statistics result of the invasive cancer is 17,3/100.000, the cancer in situ 30,4 and adenocarcinoma is 9,8%.

The average age of the invasive cancer on the cervix 53 years.

OBJECTIVE: Evaluate the procedures of biopsy and cone on the diagnostic of the pathology on the cervix and success.

MATERIALS AND METHODS: Descriptive transversal, epidemiological study on 2600 patients diagnosed with Cono Lletz between 2003/2013 at Oncological Hospital SOLCA QUITO-ECUADOR.

RESULTS: It was found 908 menopausers between 45 to 98 years (35%), with diagnosis in biopsy of CIN, cancer, persistent CIN, discordance and management “see and treat”.

Biopsy: Adenocarcinoma and invasive Adenocarcinoma 1(0,11%) each one; Adenocarcinoma in situ 3(0,33%); Ca in situ 87(9,58%); Ca invasive and Ca micro-invasive 12(1,32%) each one; Cervicitis 56(6,17%); Leiomyoma 6(0,66%); CINI 86(9,47%), CINII 301(33,15%); CINIII 308(33,92%); Polyps 7(0,77%); Sarcoma of the Endometrial Stroma 1(0,11%); see and treat 27(2,97%).

Cone: Invasive Adenocarcinoma 8(0,88%); Micro-invasive Adenocarcinoma 2(0,22%); Adenocarcinoma in situ 8 (0,88%); Ca in situ 88(9,69%); Invasive carcinoma 30 (3,30%); Micro-invasive Carcinoma 17(1,87%); Cervicitis 217(23,90%); CINI 96 (10,57%); CINII 170 (18,72%); CINIII 259(28,52%); Polyps and Leiomyoma 6(0,66%) each one; Endometrial stromal sarcoma 1(0,11%).

841(92,62%) cones present no residual tumor and 67(7,67%) residual tumor. In biopsy were detected 27 invasive neoplasms, and in cone 58 cases. 31 (53%) patients were rescued for protocol.

CONCLUSION: The diagnosis difficulty on menopausers with the technic used was surpassed when it was found 92,62% no residual tumor.

Comes out the increase of diagnosis on the most severe related the conization at the biopsy in 1 to 2,2%.

OC2.4

EVALUATING MENOPAUSE-RELATED SYMPTOMS IN MID-AGED WOMEN WITH THE ABRIDGED CERVANTES SCALE [EVALUACIÓN DE LOS SÍNTOMAS RELACIONADOS CON LA MENOPAUSIA EN MUJERES DE EDAD MEDIANA USANDO LA ESCALA CERVANTES ABREVIADA]

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The objective of the study was to develop an abridged version of the original 31-item Cervantes Scale (CS) to assess menopausal symptoms in short time. Reliability of the new short tool was assessed through internal consistency determination (Cronbach's alpha) and intra-class correlation coefficient (ICC) analysis. Ten items out of the 31 composing the original CS were selected according to their clinical relation with menopausal symptoms. The sum of scores obtained with each of the 10 graded items provides a global CS-10 score which can range from 0 to 50. This global score was correlated to the several studied variables. Subsequently the short tool was used to assess menopausal symptoms and related factors among 1739 mid-aged women. The abridged CS (CS-10) displayed a mean (\pm SD) ICC value of 0.45 (\pm 0.06) and a Cronbach's alpha of 0.778 suggesting good internal reliability. For the entire sample median [interquartile range] CS-10 global scores were 10.0 [12.0], and for pre-, peri- and postmenopausal women: 8.0 [9.2], 9.0 [9.0] and 14.0 [14.0], respectively. Median global CS-10 scores significantly increased with menopausal status, marital status and ethnicity. Multiple linear regression analysis determined that higher global CS-10 scores (worse quality of life) correlated with age, parity, years since menopause, body mass index, ethnics (black) and smoking habit. It can be concluded that the CS-10 seems to be a simple instrument that may aid everyday clinical consultation and help at performing an accurate diagnosis of menopause-related symptoms. Further studies are needed to confirm our findings.

OC2.5

BODY COMPOSITION, PREVALENCE OF LOW BONE MINERAL DENSITY AND OSTEOPOROSIS AND SOME ASSOCIATED DETERMINANTS OF RISK IN A PRIVATE CLINIC IN MEXICO CITY

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Overweight and obesity are mayor problems in Mexican women and has been associated with a lower risk of osteoporosis. It has also been linked breast-feeding and parity with BMD.

Medical history, anthropometric and bone mineral density BMD were collected from 511 women aged 30 to 87 years. Participants had a mean age of 59.4 years, a mean parity of 2.6 children, a mean BMI of 25.6 kg/m², 91 were premenopausal (17.8%) and 420 postmenopausal (82.2%); 12.32% had osteoporosis, 3.17% of those were premenopausal and 96.83% were postmenopausal. Frequencies of low BMD were 54.01%, 13.77% of those premenopause women and 86.23% postmenopausal.

In relation to BMI 12% of women in the underweight group had osteoporosis and 72% low BMD. Of the overweight patients 11% had osteoporosis and 52% low BMD. Out of the patients with obesity, 6% had osteoporosis and 49% low BMD.

Out of the patients who were below 34% of body fat, 11.6% had osteoporosis and 53.3% low BMD. On the group of patients above 34% of fat 14.4% had osteoporosis and 56% low BMD. 17.3% of

women with low muscle circumference had osteoporosis and 57% low BMD, while in the group of high muscle circumference 4.9% had osteoporosis and 53.6% low BMD.

Increasing age, post-menopausal status, and higher parity were significantly associated with low vertebral, hip, and femoral neck BMD. Increasing age increased the likelihood of low BMD at spine, while increasing height, muscle mass and BMI reduced the likelihood of low BMD. Increasing age increased the likelihood of low BMD at the hip and femoral neck, and increasing BMI and increasing muscle mass reduced the likelihood of low BMD.

It appears that increasing muscle mass is almost as protective for women at risk for low BMD as increasing BMI. The average values of weight, BMI and fat mass increases with aging, simultaneously we observed a decrease in muscle mass and BMD.

OC2.6

ASSESSING MENOPAUSAL SYMPTOMS IN MID-AGED ECUADORIAN WOMEN WITH THE 10-ITEM CERVANTES SCALE

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OBJECTIVE: To assess menopausal symptoms in mid-aged Ecuadorian women using the short 10 item version of the original menopause Cervantes Scale (CS-10).

METHODS: In this cross sectional study a total of 151 women (40 to 59 years) were requested to fill out the CS-10 and general socio-demographic questionnaire containing personal data.

RESULTS: Median age of the whole sample was 49 years. A 41.8% were postmenopausal, 25.8% abdominally obese (circumference > 88 cm), 6% diabetic, 17.2% hypertense, 13.9% smoked, 15.2% used hormone therapy (HT), 10.2% phytoestrogens, and 11.3% psychotropic drugs. For the entire sample median [interquartile range] total CS-10 scores were 10.0 [10.0], and for pre-, peri- and postmenopausal women: 5.0 [7.5], 9.0 [12.0] and 14.0 [8.0], respectively. According to the CS-10 the four most prevalent menopausal symptoms were: muscle and joint pains (96.8%), Anxiety and nervousness (93.7%), dry skin (88.9%) and hot flushes (84.1%). Median total CS-10 scores significantly increased with menopausal status and abdominal circumference.

CONCLUSION: In this Ecuadorian mid-aged female sample the CS-10 was a simple and easy to use instrument that gives a rapid overview of the prevalence and severity of menopausal symptoms. Analysis in a larger sample is required in this population to validate and confirm our preliminary findings.

HORMONES AND HORMONE ACTION

OC3.1

THE INFLUENCE OF DANAZOL ON ANGIOGENESIS AND INFLAMMATORY RESPONSE

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Aims: Danazol, a drug launched in the 1980s, is a cheap and easily available therapeutic alternative in endometriosis and some other diseases. By acting in the anterior pituitary, the drug has an antagonistic effect. The precise mechanisms of drug activity in vivo on angiogenesis and inflammatory response in endometriosis still have not been fully elucidated. The aim of the study was to

evaluate Ca125, VEGF, IL-1 β and CRP concentration in plasma in patients with endometriosis and after treatment of the disease with danazol.

Design and methods: 103 Caucasian women diagnosed laparoscopically for endometriosis were divided in study and comparative group. The analysis of markers in plasma was conducted before laparoscopy and after 3 and 6 months of treatment with danazol. Endometrium biopsy was taken to establish cycle phase. Pain accompanying endometriosis was assessed in VAS scale. Full study protocol (two follow-up visits) completed 35 patients.

Results: Endometriosis was confirmed in 68,9% women (n=71). The study group presented significantly higher concentration of Ca125 and significantly lower of VEGF. Statistically significant regression of pain measured in VAS scale (p<0,001) and fall in Ca125 concentration (p<0,001) was observed during and after danazol treatment. VEGF plasma concentration rose significantly in the first period of treatment (from baseline: 73,33 pg/ml \pm 61,53 vs 141,69 \pm 94,18; p = 0,009). Il-1 beta and CRP concentration did not changed during treatment.

Conclusions: Danazol treatment is highly effective in alleviating pain symptoms measured objectively in VAS scale. Ca125 could be a useful test in follow-up since its concentration drop significantly during danazol treatment. The therapy influences VEGF plasma concentration but has no impact on inflammatory markers.

OC3.2

EVALUATION OF EFFICACY AND SAFETY OF CONJUGATED ESTROGENS/BAZEDOXIFENE (CE/BZA) IN A LATIN AMERICAN POPULATION

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Introduction: The tissue selective estrogen complex pairing conjugated estrogens (CE) with bazedoxifene (BZA) has proven efficacy for menopausal symptoms and prevention of osteoporosis. CE/BZA was evaluated in a subpopulation of Latin American (LA) participants from the Selective estrogens, Menopause, and Response to Therapy (SMART) series of multinational trials.

Methods: Data for LA subjects assigned to CE 0.45 mg/BZA 20 mg (n = 227), CE 0.625 mg/BZA 20 mg (n = 222), or placebo (PBO; n = 193) were pooled from 3 randomized, double-blind, phase 3 studies in non-hysterectomized postmenopausal women (2-year SMART-1; 1-year SMART-4 and -5). Efficacy outcomes from SMART included week 12 hot flush (HF) frequency (in women with \geq 5 moderate/severe HFs/day at baseline; n = 39); bone mineral density (BMD) for lumbar spine (LS) and total hip (TH) at month 12 (each n = 381); and vulvovaginal atrophy (VVA) at month 12 (in women with baseline VVA; n = 189).

Results: At week 12, the average number of moderate/severe HFs/day decreased with CE 0.45 mg/BZA 20 mg (-7.0) and CE 0.625 mg/BZA 20 mg (-8.0) vs PBO (-3.1), indicating 4 to 5 fewer HFs with CE/BZA vs PBO. At month 12, % change from baseline BMD with CE 0.45 mg/BZA 20 mg, CE 0.625 mg/BZA 20 mg, and PBO were as follows: LS: 1.2, 1.6, and -1.1; TH: 1.1, 1.2, and -0.3, respectively; VVA also was improved at month 12, marked by greater % changes from baseline in vaginal cells vs placebo (superficial: 4.5, 7.4, vs 2.0; parbasal: -9.3, -27.8 vs 2.8, respectively). Results in the LA subpopulation were similar to those in the global population, with no apparent differences in safety trends.

Conclusion: In generally healthy nonhysterectomized postmenopausal LA women, CE/BZA treatment improved VMS, VVA, and BMD with no new or unexpected safety trends. CE/BZA is expected to behave similarly in LA populations as in the global trial population.

OC3.3**ESTRADIOL AND SKELETAL MUSCLE STRENGTH**

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The loss of skeletal muscle strength is an undesirable consequence of aging leading to frailty, disability, and loss of independence for aged individuals. Skeletal muscle of females is additionally affected due to the reduction of ovarian hormone production with the onset of menopause. By meta-analysis we showed that women on estrogen-based hormone therapy were stronger than those not taking. Using an ovariectomy mouse model, we showed that 17 β estradiol (E2) is a key hormone because strength loss was prevented or reversed by treatment with this hormone. Furthermore we showed that a decrement in myosin strong-binding to actin was the molecular mechanism of strength loss with E2 deficiency. Our goal now is to determine how E2 impacts myosin and muscle (dys)function in females. We are testing the hypothesis that E2 deficiency affects the structure-function of the myosin through estrogen receptor-mediated post-translation modifications of contractile proteins. To do this, soleus and EDL muscles from sham-operated and ovariectomized mice with and without E2 treatment were analyzed for contractility and phosphorylation of the myosin regulatory light chain (RLC). Phosphorylation of RLC was ~40% lower in muscle from ovariectomized mice than those treated with E2 or sham operated and force potentiation was also lowest in those muscles from E2 deficient mice ($p < 0.05$). A 30 min incubation of soleus muscles from ovariectomized mice increased RLC phosphorylation and improved force (< 0.050). Blocking phosphorylation of RLC by various kinase inhibitors indicates that E2 modulates kinase pathways differentially in slow- and fast-twitch muscles. A skeletal muscle specific estrogen receptor a knock out mouse has been developed and is being used utilized to determine if E2's effects on myosin and muscle functions are mediated through this receptor in skeletal muscle.

OC3.4**DIFFERENCE OF VITAMIN D RECEPTOR EXPRESSION IN COMPARISON OF HORMONE THERAPY AND ESTROGEN VAGINAL TABLETS FROM VAGINAL SMEAR SAMPLES OF POSTMENOPAUSAL WOMEN**

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Tae-Hee Kim was awarded the IMS Research Bursary in 2011.

Objectives: To study the effect of the local or systemic hormonal therapy on the expression of vitamin D receptor (VDR) in the vaginal epithelium.

Materials & Methods: This study was approved by the Institutional Review Board of Soonchunhyang University Bucheon Hospital. Informed consents were obtained from all participating women. From June 21, 2012 to January 9, 2014, 60 subjects had finally enrolled in the current study, because of follow-up loss, insufficient medical record or survey (Kupperman's Index) reply, and inappropriate quality of specimens. The enrolled patients were grouped by method of hormonal therapy and degree of improvement of postmenopausal symptoms. Vaginal epithelial cells were obtained by vaginal swab. Swabbed cells were prepared for immunocytochemistry (ICC) and Western blot analysis. By ICC and Western blot, we could evaluate an expression of vitamin D receptor on the vaginal epithelium.

Results: In ICC study, we confirmed the cytoplasmic expression of VDR in vaginal epithelial cell. By Western blot analysis, we could find that

VDR expression was increased in the group which showed improved postmenopausal symptoms after local estrogen treatment. There was no significant change in systemic hormonal therapy group.

Discussion: Postmenopausal symptoms could be improved by local estrogen treatment. Furthermore, it seems that estrogen, contained in vaginal tablet, affected vagina via VDR receptor. However, local estrogen therapy could not affect to some patients in the respect of VDR expression and symptom relief. It suggested that there would be various factors related with estrogen-VDR interaction, and we thought that VDR polymorphism could be related with VDR-mediated estrogen effect.

SPANISH ORAL COMMUNICATIONS**OC4.1****PREVALENCE OF SEXUAL DYSFUNCTION AND HYPOACTIVE SEXUAL DESIRE DISORDER IN INDIGENOUS WOMEN IN CLIMACTERIC FROM TWO LATIN-AMERICAN COMMUNITIES**

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Introduction: The change in the menopausal status is associated to deterioration of quality of life. There are few studies about Sexual Dysfunction (SD) and Hypoactive Sexual Desire Disorder (HSDD) in indigenous from Latin-American. **Objective:** To estimate the prevalence of SD and HSDD in Latin-American indigenous women in climacteric. **Methods:** Cross-sectional study carried out Zenúes (Colombian) and Quechua (Peruvian) indigenous aged between 40 and 59 years who had sexual partner and regular coital activity. The Female Sexual Function Index (FSFI) evaluated 6 domains (Desire, arousal, lubrication, orgasm, satisfaction and pain). Score ≤ 26.55 indicates presence of SD. The scale allows establishing the presence of HSDD when the score of the desire domain is ≤ 5 . They were assessed in their own communities. Data analysis was performed using the EPI-INFO-7. $p < 0.05$ was statistically significant. **Results:** 466 women were included, 157 (33.7%) Zenúes and 309 (66.3%) Quechuas. Age: 47.0 ± 6.3 years, BMI: 23.6 ± 2.8 , offspring: 4.0 ± 1.7 , diabetes: 2.7%, arterial hypertension: 0.6%, Never smokers: 96.7%, hormonal therapy: 3.8%. The average age of the last menstruation in postmenopausal women 43.0 ± 2.9 and the number of years in postmenopause: 9.7 ± 4.8 . The most damaged domain was sexual satisfaction, followed by the desire and lubrication. The average score of FSFI: 22.7 ± 3.9 . SD: 87.1% [CI95%:83.6–89.9%] and HSDD: 93.9% [CI95%:91.3–95.9]. DS appeared in 52.4% [CI95%:47.4–57.4] of women premenopausal and 47.5% [CI95%:42.6–52.5] postmenopausal. The HSDD was observed in 52.5% [CI95%:47.7–57.2] of premenopausal, and 47.4% [CI95%:42.7–52.8] of postmenopausal women. **Conclusions:** The prevalence of SD and HSDD in a group of Colombian and Peruvian indigenous in climacteric was high. For both sexual disorders, significant differences were not observed with the change of the menopausal status.

OC4.2**PREVALENCE OF SEXUAL DYSFUNCTION, INSOMNIA AND DETERIORATION OF THE QUALITY OF LIFE IN HYSTERECTOMIZED WOMEN**

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Introduction: the hysterectomy is a surgical procedure used for the treatment of uterine pathologies.

Objective: to assess the female sexual function, insomnia and QoL in a group of hysterectomized women.

Methods: cross-sectional study carried out with three scales: The short 6-item Female Sexual Function Index, the Athens Insomnia Scale and the Menopause Rating Scale; in women with one or more years since the hysterectomy, aged 40–59 years, belonging to afrodescendant and mestizo ethnic groups, who were from the Colombia.

Results: 202 women were included in the study. Age: 50 ± 5.0 years. 85.1% were in free union. 69.8% were mestizo. The average score in the sexual grade between women with sexual partner was 11.3 ± 4.0 (Range from 0 to 20, the higher the score, the better satisfaction). 29.7% had bilateral oophorectomy, 28.7% had unilateral oophorectomy and 41.5% kept the two ovaries. The sexual dysfunction was presented in the 71.7% of women, with disorder in orgasm in the 50.9%. 71.2% of women presented insomnia with an average score of 8.1 ± 4.5 . 28.6% expressed night awakenings. 42.5% of women manifested severe deterioration of the quality of life, 22.7%, 37.6% and 52.9% expressed deterioration of the somatic, psychological and urogenital domain, respectively. 90.4% had vasomotor symptoms and 25.7% reported to have severe or very severe sexual disorders. Sexual dysfunction and insomnia had OR for severe deterioration of the quality of life of 2.1 and 2.4, respectively. There were not significant differences in the presence of sexual dysfunction, insomnia and severe deterioration of the quality of life between women with or without hormonal therapy.

Conclusions: sexual dysfunction and insomnia was high; both of them increased the risk of severe deterioration of QoL. Four of each ten had severe deterioration of the QoL with predominance in the urogenital area.

OC4.3

INCREASE IN WEIGHT IN MID-AGED WOMEN COULD BE DUE TO A SEDENTARY LIFESTYLE LINKED TO DEPRESSED MOOD

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Background: During the menopause women increase weight. **Objective:** To determine whether the increase in weight observed during mid-age is associated to sedentary lifestyle and depressed mood. **Material and Methods:** A total of 6,079 women aged 40–59 of eleven Latin American countries were invited to fill out the Menopause Rating Scale (MRS), the Goldberg Depression Scale and a general socio-demographic questionnaire. Physical activity was recorded and women performing at least 30 minutes of activity three times a week were defined as active. Overweight was defined as body mass index (BMI) ≥ 25 . **Results:** Compared to active women, those with no physical activity had a higher BMI (26.8 ± 4.8 vs. 25.9 ± 4.1 kg/m², $p < 0.0001$), abdominal circumference (86.2 ± 12.4 vs. 84.3 ± 11.8 cm, $p < 0.0001$) and prevalence of overweight (60.7% vs. 53.4% [OR: 1.35, 95% CI, 1.20–1.50]); there were no differences in age among them. While 60.1% of women without depressive mood (MRS) were sedentary, 85.5% were sedentary in those displaying severe depressive symptoms (OR: 3.93, 95% CI, 1.98–7.96). The prevalence of overweight was higher among women presenting severe depressed symptoms (76.3% vs 52.7%, [OR: 2.89, 95% CI, 1.64–5.15]). By means of the Goldberg Depression Scale it was found that 61.9% of women without depressive symptoms were sedentary as compared to 67% among those depressed (OR: 1.25, 95% CI, 1.09–1.44). The prevalence of overweight was higher among those depressed (62.2% vs 48.5% [OR: 1.75, 95% CI, 1.53–2.00]). **Conclusion:** Depressive symptoms are associated with

greater physical inactivity and body weight and may be an important factor affecting weight gain observed during mid-life.

OC4.4

SEXUAL BEHAVIORS, SATISFACTION AND EXPECTATIONS OF SEX LIFE IN CLIMACTERIC STAGE COUPLES

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Objective: To analyze behaviors, expectations and satisfaction regarding sexual life in climacteric stage couples. **Methods:** cross-sectional and correlational research. Study a population of 142 couples (women from 40–60 years old and men from 40–65 years old) obtained by stratified sampling of family health centers in Concepción, Chile. Each member of the couple independently responded to the Couple Relationship, Sexual Practices and Satisfaction Questionnaire. Ethical aspects were considered. **Results:** The average age was 49.1 (SD 5.8) for women, and 51.5 (SD 6.8) for men; the average relationship time was 24 years. 64.1% of women vs. 80.3% of men said to be in love with their mates. The average sexual relations frequency was 6.3 (SD 6.8) for women, and 7.7 (SD 6.64) for men ($p < 0.05$), and mostly men were the ones who took the sexual initiative (61.9% vs. 7.3%; $p = 0.0000$). 66% of women and 74.6% of men say they talk about sexual topics with their mates. 37.3% of women and 45.8% of men have erotic dreams and fantasies with their mates; 17.7% of women vs. 31.2% of men masturbated during last month. 70.2% of women and 91.5% of men had an orgasm during their last sexual relation ($p < 0.000$). 66% of women and 84% of men said to be very or somewhat satisfied with their sexual life ($p < 0.01$), however, 83.8% of women and 88% of men wish they could change something in their sexual live and 46.5% would like to feel more emotional intimacy with their mates. Regarding infidelity, 5.8% of women and 9.4% of men declared they had cheated during last 12 months. **Conclusion:** During climacteric stage, couples continue sexual activity and are very or somewhat satisfied. However, most of them wish they could change something in their sexual life. Health care providers are suggested to include sexual health topics among their priorities.

BONE HEALTH

OC5.1

THE VITAMIN D STATUS ANALYSIS IN ROMANIAN MENOPAUSAL WOMEN WITH OR WITHOUT NORMAL DXA

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Introduction: Vitamin D is essential in bone assessment, especially in menopausal women.

Aim: 25-OH vitamin D relationship to risk factors and bone turnover markers in women \pm normal DXA.

Material and Method: A transversal study (Parhon National Institute of Endocrinology, Bucharest, Romania, 2008–2013) has inclusion criteria: menopause, age > 40 yrs, informed consent; exclusion criteria: previous osteoporosis therapy. DXA (GE Lunar Prodigy), years since menopause (YSM), body mass index (BMI), 25-OH D, bone markers: alkaline phosphatase (AP), osteocalcin (OC), CrossLaps (CL) were assessed. Statistics (SPSS21) included statistical significance (SS) at $p < 0.05$.

Results: 471 women were included: non-normal DXA group or studied group ($n = 328$; T-score ≤ -1) + control group with normal DXA ($n = 143$). Age (between 41–82 years) was 59.35 versus 54.08 yrs;

BMI: 27.98 vs. 30.22 kg/m²; YSM: 12.9 vs. 7.54; AP: 78.65 vs. 74.75 U/L; OC: 0.52 vs. 0.41 ng/mL; CL: 25.51 vs. 20.88 ng/mL; 25-OH D: 15.16 vs. 14.81 U/L. Except for 25-OH D and AP, all the parameters were SS different between groups.

BMI based sub-groups had 25-OH D distribution in studied group: normal BMI (≤ 24.9 kg/m²) 15.45 ng/mL (n = 99); overweight (BMI: 25–29.9 kg/m²) 15.22 ng/mL (n = 127); obese (BMI ≥ 30 kg/m²) 14.82 ng/mL (n = 102). For the control group: 19.69 ng/mL (n = 22); 15.11 ng/mL (n = 56); 12.89 ng/mL (n = 65).

25-OH D distribution based on YSM decades was for studied group: 1–10 YSM (n = 149) 15.64 ng/mL, 11–20 YSM (n = 119) 15.56 ng/mL; 21–30 YSM (n = 51) 13.18 ng/mL, 31–40 YSM (n = 9) 13.15 ng/mL; for control group 1–10 YSM (n = 104) 14.59 ng/mL, 11–20 YSM (n = 33) 15.09 ng/mL; 21–30 YSM (n = 5) 18.4 ng/mL, 31–40 YSM (n = 1) 11.95 ng/mL. The linear regression coefficient r between 25-OH D and YSM, OC, CL was not SS in either group; between 25-OH D and AL was -0.14 ($p = 0.01$) in studied group.

Discussion: We had limited number of patients in the control groups with >20 YSM.

Conclusion: 25-OH D has a homogenous pattern of distribution in BMI sub-groups and YSM decades. D hypovitaminosis in menopausal Romanian women is frequent. In patients with low bone mineral density, a negative SS correlation was found between 25-OH D and AP.

OC5.2

THE ROLE OF ISOFLAVONES IN MENOPAUSAL BONE LOSS

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Background: Isoflavones found abundantly in soybeans are structurally similar to estrogen and thus able to exert weak estrogenic effects. Fermentation of soymilk with probiotic bifidobacteria metabolises daidzein into equol. Findings from earlier clinical studies on the potential positive effects of isoflavones on cardiovascular and osteoporosis risk factors in postmenopausal women have been highly variable and inconclusive.

Aim: The objective of this study was to examine the effects of ingesting a fermented soymilk containing viable bifidobacteria on serum lipid profiles, bone turnover markers and levels of FSH, LH and SHBG in postmenopausal women.

Methodology: Thirty-six post-menopausal women were involved in a randomised, double-blind, placebo-controlled, parallel study involving a 12-week supplementation of fermented soymilk (FS), non-fermented soymilk (NFS) and casein-milk (CAS). Subjects in the FS and NFS group ingested the same dosage of isoflavone at 80 mg per day. Populations of *B. animalis* in fermented soymilks were 107 to 108 viable cells per mL. At baseline and endpoint, hormones, lipids, osteocalcin and β -CrossLaps were analysed in serum and deoxypyridinoline in urine.

Results: There was no significant differences in either BMI ($P = 0.24$) or bodyweight ($P = 0.14$) between the three groups. After 12 weeks of milk supplementation, there was no significant change in mean bodyweight from baseline measurements for any of the groups. Supplementation of FS and NFS caused a decrease in the levels of FSH and LH ($P > 0.05$). Moderate rises in SHBG were observed in the groups consuming the NFS and FS. There were no significant differences between baseline and endpoint means of total cholesterol, triglyceride and LDL-cholesterol ($P > 0.05$). Ingestion of FS showed a trend toward a reduction in bone resorption, with urinary DPD decreasing by 2.4 nmol/mmol of CRE, but no significant difference was evident between baseline and endpoint means of the FS group ($P = 0.16$). In contrast to the increase in DPD excretion shown by women in the NFS and CAS group (10.3% and 3.3%, respectively), women consuming fermented soymilk showed a 17.3% reduction in the urinary excretion of DPD ($P = 0.05$).

Conclusion: Preliminary findings show that FS may prevent bone loss in postmenopausal women. However, further studies with a larger number of subjects per group are required to evaluate trends showing a positive effect on hormones, bone formation and cardiovascular disease risk.

OC5.3

OSTEOCYTE-SECRETED PROTEINS AND BONE MINERAL DENSITY IN WOMEN WITH AMENORRHEA

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Objective. To evaluate osteocyte-secreted proteins and molecular-genetic markers in relation to bone mineral density in women with amenorrhea. Materials and Methods. 110 women with amenorrhea living in Russian Federation enrolled in the cross-sectional study. Levels of reproductive hormones, osteocyte-secreted proteins were evaluated, as well as DXA. SNPs were genotyped by PCR for SOST (sclerostin) (rs1107748), LEPR (leptin receptor) (rs1805094, rs8179183). Results. Low bone mineral density (BMD) (Z-score ≤ -2.0) in L1-L4 was found in 33.6% of women with amenorrhea (23.2% in premature ovarian insufficiency, 47.5% in hypogonadotropic amenorrhea, 45.5% in gonadal dysgenesis, 46 XX); in femoral neck - in 8.9% (all cases refer to hypogonadotropic amenorrhea). Sclerostin (Scl) in women with amenorrhea was lower than in postmenopausal women ($p = 0.02$), osteoprotegerin (Opg) in POI was higher in normal vs. low BMD ($p = 0.02$), RANKL in gonadal dysgenesis was lower in normal vs. low BMD ($p = 0.04$). There was a moderate positive correlation of Scl to the age of beginning of amenorrhea ($p = 0.04$) and a moderate negative correlation of Opg to the duration of amenorrhea ($p = 0.01$). ROC-analysis showed levels of Opg (AUC 0.759 ± 0.089 , sensitivity 87.8%, specificity 69.2%, cut-off 1.6 pmol/l, $p = 0.001$) and RANKL/Opg ratio (AUC = 0.672 ± 0.081 , sensitivity 92.3%, specificity 51.0%, cut-off 0.07, $p = 0.002$) to be diagnostic markers of low BMD in these patients. T/T genotype in SOST (rs1107748) was associated with 3-fold increase in risk of low BMD in femoral neck ($p < 0.05$); C/C genotype in LEPR - with 3-fold increase in risk of low BMD in L1-L4 ($p < 0.05$). Conclusion. The age of beginning of amenorrhea and its duration influence the concentration of osteocyte-secreted proteins and BMD. Several SNPs of genes coding SOST and LEPR have shown to influence risks of low BMD in different skeletal sites.

OC5.4

WHEN AND WHICH LIFESTYLE FACTORS SHOULD BE MORE EFFECTIVE FOR THE PREVENTION OF POSTMENOPAUSAL OSTEOPOROSIS?

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Background: A higher calcium intake and exercise in adolescence and menopause should play important roles for the prevention of osteoporosis. However, vital timing for the prevention at either hip or spine has not been clarified.

Objective: To investigate the association between food intake and duration of exercise, age at menarche or menopause and bone mineral density (BMD) in adolescent and menopausal women. To determine when and which lifestyle factors should be more important to prevent osteoporosis.

Methods: Cross-sectional measurements of lumbar spine and hip BMD by dual energy x-ray absorptiometry (DXA), and body weight, menstrual function, current and past food intake and physical activity were assessed by questionnaires. Subjects were 127 adolescents, 176 young adults and 133 premenopausal and 123 postmenopausal women. Single and multiple regression analyses were used to examine the relationships between BMD and menstrual function or life style variables by SPSS 9.0.

Results: Higher dairy intake was associated with spine and hip BMD in adolescents and young adults, but not spine BMD in menopause. Past and current physical activities were associated with spine and hip BMD in adolescent, but current physical activity was not associated with spine BMD at menopause. The spine BMD was associated with body weight and menstrual function such as age at menarche and menopause, although hip BMD was not associated with the menstrual functions.

Thus increased intake of calcium in adolescents should be extremely important to accumulate higher peak bone mass in spine which might be effective throughout their life. Higher calcium intake and physical activity in adolescent and also menopause should be effective for the higher hip BMD.

Conclusions: Adolescent should be the vital period for the prevention of postmenopausal osteoporosis. Higher intake of calcium and physical activity at adolescent should be important, especially in spine BMD. These lifestyle factors in menopause could be still effective for hip BMD.

HORMONES AND METABOLISM

OC6.1

HORMONAL AND METABOLIC EFFECTS OF POLYUNSATURATED FATTY ACID (OMEGA-3) ON POLYCYSTIC OVARY SYNDROME INDUCED RATS UNDER DIET

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Objective: PCOS (polycystic ovary syndrome) produces symptoms in approximately 5% to 10% of women of reproductive age (12–45 years old). It is thought to be one of the leading causes of female subfertility. To confirm the role of nutrition with omega-3 (polyunsaturated fatty acid) on control of experimental PCO induced by estradiol-valerate (PPA) in rats, this study was done.

Material and Methods: Wistar female rats ($n = 40$) were allocated into control ($n = 10$) and test groups ($n = 30$), test group subdivided into 3 groups: G1, received omega-3 (240 mg/kg/orally/daily), G2 and G3 groups were induced PCO by single injection of estradiol-valerate (4 mg/rat/IM). Group 3 received omega-3 (240 mg/kg/orally/daily) and low carbohydrate feeding for 60 subsequent days. In sixtieth day 5cc blood samples and ovarian tissues of Rats in whole groups were removed and prepared to biochemical and hormonal analysis.

Results: Catalase, GPX (Glutathione peroxidase), SOD (Superoxide dismutase) in groups that received omega-3 were shown higher levels, but MDA (malondialdehyde) level was significantly decreased ($p < 0.05$) in comparison to other experimental groups. Ovarian weights in both experimental and control groups were similar ($p < 0.05$). Level of serum FSH (follicle stimulating hormone) was decreased, but level of Testosterone was significantly increased ($p < 0.05$) in PCO group in comparison to control and omega-3 groups.

Conclusion: Results revealed that administration of omega-3 plus lower carbohydrate food significantly controlled PCO syndrome with balanced FSH and testosterone.

OC6.2

MENOPAUSE IN WOMEN WITH MORBID OBESITY

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The aim of this study was estimate the peculiarities of menopausal syndrome and hormonal changes in menopausal women with morbid obesity.

The study included 60 patients with morbid obesity (I group) and 60 nonobese women (II group) in the perimenopause and postmenopause. BMI in group I was 42.8 ± 0.8 kg/m², in group II $- 26.6 \pm 0.9$ kg/m² ($p < 0.001$). We used clinical methods, evaluation of modified Kupperman index (KI), determination of hormonal levels by Immunoassay method, densitometry.

The results of this study showed that women with morbid obesity had significantly higher KI than women from group II, respectively -48.8 ± 9.2 and 28.6 ± 10.2 points ($p < 0.001$). The severity of menopausal disorders in patients from group I was due primarily to the neuroendocrine and metabolic disorders. Body weight change in postmenopausal patients with morbid obesity varied from -18 to $+40$ kg, averaged increase 11.1 ± 17.3 kg. Psycho-emotional disorders were similar in both groups. Patients with morbid obesity in postmenopausal women had a higher bone mineral density (BMD) than nonobese women. Only 2 patients with morbid obesity and severe diabetes mellitus had osteoporosis. Women with morbid obesity in 46–55 years had significantly higher levels of cortisol, estradiol, testosterone, and leptin and lower levels of SHBG, progesterone and T4 relatively perimenopausal women without obesity. Postmenopausal women with morbid obesity have higher levels of estradiol, leptin, insulin, and lower levels of FSH, LH, SHBG, TSH, T3, T4.

Thus, women with morbid obesity have more severe menopausal symptoms and peculiarities of the metabolic changes regarding nonobese women.

OC6.3

ARE HOT FLASHES RELATED TO ADIPOKINES OR CELL ADHESION MOLECULES?

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Objectives: To analyze the association between climacteric vasomotor symptoms (VMS) and adiponectin, plasminogen activator inhibitor 1 (PAI-1), intercellular adhesion molecule 1 (ICAM-1), vascular cell adhesion molecule 1 (VCAM-1), lipid profile and nutritional status. Methods: This was a cross sectional study with 102 peri- and postmenopausal women from 40 and 65 years old that evaluated VMS, body mass index (BMI), waist circumference (WC), body fat percentage (BF%), adiponectin, PAI-1, ICAM-1 e VCAM-1, lipid profile, and glycemia. Results: Mean age 53.8 (± 5.4) years, median 48 (10–96) months from the last menstrual period. Overweight was observed in 41.2% of women, very high cardiovascular risk ($WC \geq 88$ cm) in 50.0%, and BF% (mean \pm standard deviation) was $33.3 \pm 5.3\%$. Mean values were 22.5 (± 11.8) ng/dL for adiponectin, 284.9 (± 134.1) ng/dL for PAI-1, 457.0 (± 210.6) ng/dL for ICAM-1, 202.0 (± 61.3) ng/dL for VCAM-1, 214.4 (± 42.3) mg/dL for total cholesterol, 51.0 (± 2.8) mg/dL for high-density level cholesterol (HDL-c), 138.8 (± 2.2) mg/dL for low-density level cholesterol (LDL-c), and 129.4 (± 67.8) mg/dL for triglycerides. No significant relationship was observed between adipokine or cell adhesion molecule levels and VMS. Adiponectin was negatively inversely associated with BMI. There was a statistically significant inverse correlation between age

and hot flash intensity. Conclusions: VMS intensity was inversely related with age, and VMS were not associated with adiponectin, PAI-1, ICAM-1 and VCAM-1. Changes in several study parameters, such as presence of overweight/obesity, increased WC and BF%, and hypercholesterolemia contribute to a higher risk for cardiovascular disease in this sample of climacteric women.

OC6.4

CONTRIBUTION OF OBESITY AND INSULIN RESISTANCE ON BRAIN RESPONSES VISUAL FOOD CUES

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Introduction: Women with Polycystic Ovary Syndrome (PCOS) exhibit high rates of obesity and insulin resistance. Obesity is associated with abnormal brain responses to food cues. Central insulin resistance may contribute to this abnormal response. Alternatively, adiposity may affect neural responses to appetitive stimuli by a mechanism independent of insulin signaling. We determined the contributions of adiposity and insulin sensitivity to appetite regulation by comparing the neural responses to food cues in obese and non-obese women with PCOS while controlling for insulin sensitivity. Methods: Women with PCOS (n=19) underwent functional magnetic resonance imaging while viewing pictures of food. Subjects were scanned on two occasions; once during an oral glucose challenge and once during a water control. Scans were conducted mid afternoon following a 6 hour fast. The glucose to insulin ratio at 2 hours of a fasting oral glucose tolerance test performed on a separate occasion was used as an index of insulin sensitivity. Results and Conclusions: A glucose challenge reduced reactivity to food pictures in the cingulate, parahippocampus, and insula of insulin sensitive subjects (n=11), whereas reactivity was increased in insulin resistant subjects (n=8). In contrast, when patients were partitioned into non-obese (n=6) and obese (n=13) groups, glucose increased reactivity in the cingulate, caudate, and insula in the non-obese group, but reduced brain reactivity in the obese group. We conclude that insulin sensitivity and adiposity independently affect the responsiveness of brain regions involved in reward evaluation, food motivation and cognitive control to metabolic and visual food cues. Knowledge about the neural substrates affected by insulin sensitivity and adiposity are needed to develop more effective strategies for obesity treatment and prevention.

MENOPAUSE MOOD AND MENTAL DISORDERS

OC7.1

TO EXERCISE, OR NOT TO EXERCISE: MENOPAUSAL EXPERIENCE OF PHYSICAL ACTIVITY

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Background: Menopausal symptoms in women can be severe and disruptive to overall quality of life. Hormone replacement therapy, is known to be effective in ameliorating symptoms, however, reporting of side effects has resulted in alternative treatment options. Exercise has been assessed as an alternative treatment option for alleviating menopausal symptoms, including, psychological, vasomotor, somatic and sexual symptoms. Maintaining an active lifestyle can delay the onset of most conditions associated with ageing and with menopause.

Aim: To identify what it means for women to exercise during the menopause, and whether this is affected by the severity of their menopausal symptoms.

Methods: Interpretative phenomenological analysis was employed as the theoretical and methodological framework in this qualitative study.

Semi-structured interviews were carried out with twelve women with different levels of exercise participation and menopausal symptom severity. Results: Women associate various meanings with the experience of exercise during menopause. Regardless of exercise behavior and symptom severity, the participants associated exercise with both physical and physiological benefits. The women with high-severity symptoms valued the role of exercise in fighting ageing, whereas the 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. Exercisers enjoyed exercise more than non-exercisers, and exercise participation was found to have more influence in the perception of symptom severity as a barrier to exercise than symptom severity itself.

Conclusion: Findings of this study will contribute in the development of tailored interventions to enable women to overcome personal obstacles to exercise throughout menopause, regardless of the severity of their symptoms.

OC7.2

DEPRESSIVE SYMPTOMS IN THE POSTMENOPAUSAL YEARS: THE SECOND DECADE OF FOLLOW-UP IN THE WOMEN'S HEALTHY AGEING PROJECT

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Background: Postmenopause represents a period of distinct biological, psychological and social changes. During early postmenopause, hormone levels fluctuate and vasomotor symptoms are most likely to be present. Whilst studies of the menopausal transition and ageing population exist, data exploring depressive symptoms across the early and late postmenopause are sparse. The current project examines data from an ongoing epidemiological study spanning two decades to provide insight into the pattern and characteristics of depressive symptoms across the postmenopause.

Methods: The Women's Healthy Ageing Project (WHAP) is an ongoing longitudinal prospective study involving a cohort of 438 women, which began recruitment in 1991. Measures include biological, cognitive, lifestyle and psychological assessments. Prevalence rates of depressive symptoms over ten years (CESD) and lowered mood over twenty years (Affectometer 2) were examined.

Results: Preliminary analysis revealed that mild to moderate rates of depressive symptoms on the CESD were present in 3.7%, 4.2% and 12% of the cohort in 2002, 2004 and 2012 respectively. Negative mood rates improved over twenty years based on the results of the Affectometer 2 with significantly lowered mood reported in 2012 compared to 1991.

Conclusions: Preliminary data demonstrated an increase in depressive symptoms over time despite a reduction in lowered mood. Items on the CESD that are somatic in nature and associated with ageing may have led to the increased prevalence rates. Consideration of somatic complaints associated with ageing and the specific assessment of lowered mood for this population will be discussed.

OC7.3

HORMONE REPLACEMENT THERAPY AND KAMPO THERAPY SIMILARLY IMPROVE ANXIETY AND DEPRESSION IN MENOPAUSAL WOMEN

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Background: In Japan, Kampo therapy is very common used in treatment for menopausal symptoms. And more, it is well known that hormone replacement therapy (HRT) and Kampo therapy can improve depression in menopausal women. However, few reports have compared the effects of these two therapies; particularly, very few reports has examined their effects on anxiety in women. Here, we studied the efficacy of both therapies in treating depression and anxiety in menopausal women.

Method: The subjects included 49 women who visited the menopause clinic and were treated by either HRT (HRT group) or Kamishoyosan (Kampo group), which is a typical Kampo therapy for menopausal disorders. After obtaining informed consent, the patients answered a questionnaire based on the Hospital Anxiety and Depression Scale (HADS) before and 4 weeks after the treatments. We examined differences in the HADS total scores, anxiety scores, and depression scores between the HRT group and Kampo group and analyzed them.

Results: No differences were observed between the 2 groups for age or the pretreatment HADS score. After 4 weeks of treatment, the total HADS score and anxiety score were significantly decreased in the HRT group ($p < 0.05$); further, in the Kampo group, the total HADS score, anxiety score, and depression score were significantly decreased. No statistical differences were noted between the HRT and Kampo groups with regard to the change ratios in the HADS score before and after treatment.

Conclusion: We found that both HRT and Kampo therapies could improve the symptoms of anxiety and depression in menopausal women in a short 4-week period with similar efficacy.

OC7.4

DEPRESSION IN MIDLIFE WOMEN: UNDERSTANDING THE CRITICAL WINDOW AND ITS CLINICAL IMPLICATIONS

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Objectives: The menopausal transition and early postmenopausal years have been characterized as a 'window of vulnerability' for some women for the development of depressive symptoms or depression (new, recurrent). This presentation aims to review contributing factors to the emergence of menopause-related depression, some of the key challenges for its proper identification and management and the evidence on effective treatment strategies.

Methods: A body of evidence (animal data, epidemiologic and clinical studies) will be reviewed to disentangle some of the complex interactions between changes in sex hormones and reproductive function, physical health and mood in midlife women. A special focus will be given to the 'window of vulnerability' framework.

Results: Despite the evidence of a critical window for new onset of depression, a prior depressive episode – particularly if related to reproductive events – remains the strongest predictor of mood symptoms or depression during midlife years. Vasomotor symptoms and other health-related issues also modulate the risk for depression. Mechanistically, estrogen plays an important role in mood and cognitive regulation. Transdermal estradiol, as well as serotonergic and noradrenergic antidepressants, have shown efficacy in the management of depression in this population. Other evidence-based treatment options (hormonal, pharmacological, behavioural) are available to clinicians and health professionals.

Conclusions: A more comprehensive diagnostic approach should be given to symptomatic midlife women. Ultimately, preventative strategies and treatments should be tailored to address multiple symptom domains and improve overall functioning.

GYNECOLOGICAL ISSUES AT MENOPAUSE

OC8.1

ER:YAG LASER TREATMENT FOR EARLY STAGES OF STRESS URINARY INCONTINENCE (SUI) IN WOMEN: A CONTROLLED CLINICAL TRIAL

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Objective: The objective of this open-labeled, prospective pilot study was to assess the efficacy and safety of the novel minimally invasive non-ablative laser treatment in the early stages of SUI.

Methods: 33 female patients suffering from stress urinary incontinence were recruited for this study. 22 of them underwent treatment with Er:YAG (2940 nm) laser, while 11 patients were scheduled for pelvic floor muscle training (PMFT). All patients were assessed with ICIQ-UI SF and PISQ-12 questionnaires, Q-tip test, perineometry and residual urine volume (RUV). Follow ups were done after 1, 2 and 6 months for laser group and at 6 months for PFMT group.

Results: Laser treatment was significantly ($p < 0.05$) more effective than PFMT in all the domains tested: ICIQ-UI score reduced for more than 6 points at all follow ups ($p < 0.01$). PISQ-12 scores increase after 6 months was 5.5 points ($p < 0.03$). All three perineometric parameters (max. pressure, average pressure and duration of squeeze) showed significant increase ($p < 0.02$). Q-tip angle significantly decreased for 4.8° in restful and for 14.1° in strain position at 6 months and RUV was significantly ($p < 0.03$) reduced as well. Laser treatment had no adverse effects.

Conclusion: This study showed statistically significant improvements in all outcome measures used in the study. Our data revealed that the improvement of incontinence achieved with laser therapy was also associated with significant improvements in sexual function. Er:YAG laser therapy is another possible minimally invasive option for treating premenopausal and postmenopausal women with SUI symptoms.

OC8.2

CO2 FRACTIONAL LASER FOR THE TREATMENT OF VAGINAL ATROPHY

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Introduction and aim: Symptoms of vaginal atrophy include vaginal dryness or itching and dyspareunia that may impact on sexual life. The first line treatment for vaginal atrophy is the use of local estrogen. However, due to different factors, only a small proportion of postmenopausal women, despite symptomatic, are on treatment. Alternative therapies have therefore been proposed, such as lubricant or moisturizing creams. Fractional CO2 laser has shown regenerative tissue properties in many other body districts, such as the skin and the oral mucosa.

The aim of our study was to assess the efficacy of fractional CO2 laser in the treatment of symptoms of vaginal atrophy.

Methods: Women with symptoms of vaginal atrophy not tolerant or willing to take estrogens were included. Women were treated with an outpatient CO2 laser procedure without the use of any analgesia or anaesthesia. Three treatment sessions were always performed with an interval of 30 days. Each woman was assessed objectively and subjectively at baseline and 30 days after each single treatment using the Vaginal Health Index (VHI), a 10-point Visual Analogue scale for each single symptom of vaginal atrophy, the FSFI and the SF12.

Pearson and Signed Rank Tests were used and a p value <0.05 was considered significant.

Results: Fifty postmenopausal women with a mean age of 59.6 years were included. Laser treatment improved significantly all vaginal atrophy symptoms in 100% of patients included in the study at 12-week follow-up. Compared to the data on entry we found the following significant differences in terms of mean values \pm SD after 3 laser treatments: VHI from 13.1 ± 2.5 to 23.1 ± 1.9 , Vaginal Dryness from 8.3 ± 2.1 to 2.7 ± 1.9 , vaginal itching from 6.1 ± 3.0 to 1.5 ± 1.7 , dyspareunia from 8.1 ± 2.8 to 3.3 ± 2.3 , dysuria from 5.0 ± 2.4 to 1.1 ± 1.1 , FSFI from 24.6 ± 18.2 to 53.4 ± 26.2 , PCS12 from 44.6 ± 11.0 to 50.0 ± 5.9 , MCS12 from 42.6 ± 10.6 to 47.0 ± 6.9 . Concluding message: We showed that 3 sessions of fractional CO2 laser determine a highly significant improvement in symptoms of vaginal atrophy.

OC8.3

ER:YAG LASER TREATMENT OF CYSTOCELES – NEW NON-SURGICAL MINIMALLY INVASIVE POP THERAPY

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OBJECTIVE: The objective of this study was to evaluate new minimally invasive, non-ablative Er:YAG laser technique for prolapse reduction. **METHOD:** During 15 months period (between March 2012 and June 2013) 65 patients (average age 55.1 yrs, parous status 2.2 and BMI of 24.9) with cystoceles of grades II–IV were treated with new non-ablative Er:YAG laser treatment. Preoperative evaluation included history and physical examination and classification of cystocele grades using Baden-Walker scale. Patients received between one and three treatment sessions with intervals of 2 months in between the sessions. Pain during the treatment was measured at every session with 10 point VAS pain scale. Digital photographs of prolapses were obtained at every visit. Follow-ups were performed at 2, 4, 6 and 12 months. At each follow-up aside of physical examination and prolapse photographing cystoceles grading by two physicians were performed and patients were interviewed about post-op adverse effects, degree of improvement of their cystocele and satisfaction. **RESULTS:** Before the treatment there were 44 patients with cystocele of grade II, 14 of grade III and 7 of grade IV. At last follow-up the large majority of patients (63 or 97%) reduced their prolapse grades for at least one grade, 33 of them (51%) for two grades and 6 (9%) even for three grades. Treatment discomfort was very low (average score of 0.34 on 10 grade scale) large majority of patients assess their satisfaction as satisfied or very satisfied and their subjective assessment of improvement was also very positive. There were no adverse effects of this treatment reported. **CONCLUSIONS:** This study of efficacy and safety of a new non-invasive Er:YAG laser treatment for higher-grade cystocele demonstrated good efficacy in improvement of cystocele with minimal patients' discomfort during the treatment and no adverse effects.

OC8.4

REACHING THE UNREACHED: MOBILE SURGICAL CAMPS IN A REMOTE VILLAGE OF HIMACHAL PRADESH

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Aims: To study the epidemiological factors responsible for pelvic organ prolapse in poor women of remote village Shillai, do their POPQ staging, to study the variety of surgeries conducted in Mobile Surgical Camps in this area.

Methods: Retrospective analysis of surgeries conducted in five Mobile Surgical Camps in Shillai, Himachal Pradesh from 2009 to 2013, under "Project Prolapse".

Results: Total number of surgeries conducted in five camps from 2009 to 2013 was 490 including 192 gynecological surgeries. Eighty two percent of gynecological surgery was conducted for pelvic organ prolapse. Poor nutritional status (mean weight 41.1kg), multiparty (mean 3.5), early marriage (mean age 18.2 years), unassisted home deliveries (100%), premature bearing down (23.8%), early post partum resumption of strenuous activity (54.7%) and smoking (33%) contribute to high incidence of POP. Anterior compartment prolapse was seen in 99% of patients undergoing surgery while posterior compartment prolapse was seen in 4% of patients. Vaginal hysterectomy with anterior repair with culdoplasty was the most common procedure performed (73.4%). Vault prolapse was seen in 3.6% subjects otherwise the complication rate was negligible.

Conclusion: Uterovaginal prolapse is not only socially embarrassing & disabling; its surgical treatment is complex and costly too. The free mobile surgical camps under "Project Prolapse" in Shillai, Himachal Pradesh has provided relief to old neglected, disabled women suffering from prolapse in this remote village. Parallel counseling of women & dais for safe hospital delivery and training subordinates in prolapse surgery may help in addressing the problem of pelvic organ prolapse in this area in the long run.

Key words: Pelvic organ prolapse, UV prolapse, menopausal problems, multiparty.

MENOPAUSE GENERAL

OC9.1

JOINT PAIN IN URBAN PERIMENOPAUSAL HISPANIC WOMEN: A PILOT STUDY OF CULTURAL INFLUENCES

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Hispanic women exhibit elevated rates of obesity, chronic pain, and menopause symptoms compared to non-Hispanic US groups. Data from large longitudinal studies suggest that joint pain is one of the most common symptoms of menopause, second only to hot flashes, but in-depth assessments are lacking. To describe the symptom experience and coping strategies for managing joint pain attributed to the perimenopause in urban Hispanic women, we conducted focus groups in a predominantly Hispanic neighborhood of New York city. Subjects, recruited through flyers and snowball sampling, were compensated \$25 cash and given the NAMS guidebook on menopause. Focus group interviews were audiotaped, transcribed and analyzed by a bilingual research team, using NVivo software (QSR International) to organize and code themes. Common themes included the lack of knowledge/preparation about menopause symptoms; fears about future health and relationships, the importance of social support as a coping strategy.

Salsa dancing was an important social and physical therapy and the use of Spanish cable TV fitness shows as a way to make time for exercise. Most women had extensive histories of pain conditions which emerged or were magnified with menopause; many suffered through it, were not satisfied with health care options and relied on alternative medicine or home remedies purchased online or in neighborhood bodegas for hot flashes, sleep and pain relief; fear of estrogen treatment was common.

CONCLUSION: Middle-aged urban Hispanic women are at high risk for health disparities in pain management.

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OC9.2

PERCUTANEOUS ESTRADIOL/ORAL MICRONIZED PROGESTERONE GIVES CONSIDERABLY LESS MAMMARY TUMOR INCREASING GENE EXPRESSIONS THAN ORAL CONJUGATED EQUINE ESTROGENS/MEDROXYPROGESTERONE ACETATE IN THE BREASTS OF HEALTHY WOMEN IN VIVO: RESULTS FROM MICRO-ARRAY AND PCR DATA FROM CORE NEEDLE BIOPSIES

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77 healthy women were randomized to sequential hormone therapy with two 28 day cycles of either oral 0.625 mg Conjugated Equine Estrogens (CEE) or 2,5 g 0.06% (1.5 mg E2) percutaneous E2- gel daily, with the addition of 5 mg of oral Medroxyprogesterone acetate (MPA), or 200 mg of oral micronized P, daily, 14/28 days per cycle. Micro-array analysis was done on Core needle biopsies from 8 patients before and after 2 months. IPA analysis found 225 genes to be involved in mammary tumor development, 198 genes for CEE/MPA and 34 for E2/P. The IPA database found 14 genes of them to be regulated to increase mammary tumor significantly more for CEE/MPA than for E2/P v.s. 4 genes more for E2/P than CEE /MPA. In 30 patients, (15 + 15) with sufficient mRNA, RT-PCR was performed from the biopsies before and after 2 months to assess the change in expression of 16 genes. Results: PCR analysis showed a significant increase in MKi-67 gene expression ($p < 0.05$) in the CEE/MPA but not the E2/P group where the Prolactin gene was down-regulated ($p < 0.05$) as well as the Bcl-2 gene ($p = 0.05$). For CEE/MPA but not for E2/P, there was a positive correlation between IGF1 gene expression and Ki-67 MIB1 protein during treatment as well as a marked activation of the PGR B gene in cases with high % pos Ki-67 MIB1 cells, while there was a tendency for down-regulation of protective genes as Cav-1 and FBX-4. Conclusion: PCR analysis confirms micro-array data of an increase in MKi-67 gene expression ($p < 0.05$) concomitant with an increase in Ki-67 protein ($p < 0.05$) in the CEE /MPA but not the E2/P group. A reduction in the Bcl-2 gene and proliferative Prolactin gene in the E2/P group, adds to data showing that treatment with percutaneous E2 in combination with oral micronized P induces less proliferation and adverse expression of important genes regulating proliferation, apoptosis and tumor inclination in vivo.

OC9.3

WORK, WOMEN AND THE MENOPAUSE: AN AUSTRALIAN EXPLORATORY STUDY

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We present the findings of an exploratory study into the relationships between menopausal symptoms and work outcomes. The data form part of a wider investigation into women's health and well-being at work conducted in 2013 at two Australian universities. The study targeted women ($n = 583$) aged 40–70 years (mean age: 51.7 years), in both academic and professional & administrative staff

roles, working full-time, part-time and casually. Questions derived from the STRAW + 10 staging system (Soules et al., 2001; Harlow et al., 2012), and the MENSI scale (Sarrel et al., 1990), as well as a self-classification question, were used to assess menstrual status and menopausal symptoms. Work outcomes were captured via four commonly used, validated scales: work engagement (Schaufeli et al., 2002); job satisfaction (Cammann et al., 1983); intention to leave (Cammann et al., 1983); and organizational commitment (Meyer et al., 1993).

Overall, none of the reported work outcomes differed significantly by menopausal status. However, there were significant differences in work outcomes for those women who reported that particular menopause symptoms (notably headaches, sleep disturbance, weakness or fatigue, and anxiety) were a problem for them compared to women who reported that these particular symptoms were not a problem. For example, women who reported that anxiety was a problem for them indicated greater intention to leave, less job satisfaction, were less engaged at work, and showed less organizational commitment, than those who did not report anxiety as a problem. The frequency of all menopause symptoms was negatively related to work engagement, job satisfaction, and organizational commitment and positively related to intention to quit. Similar relationships were found for symptom bothersomeness.

OC9.4

NORMATIVE VALUES OF SERUM ANTI-MULLERIAN HORMONE (AMH) IN DIFFERENT AGE GROUPS AND CORRELATION WITH MENOPAUSAL SYMPTOMS – AN INDIAN PILOT STUDY

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Introduction: Anti-mullerian hormone (AMH) is a homodimeric glycoprotein linked by disulphide bond belonging to the transforming growth factor beta (TGF-b) superfamily, known to play important role in embryogenesis and follicular development. Serum AMH levels are mostly considered for measuring the ovarian reserve.

Objective: To determine the normative values of serum anti-mullerian hormone in Indian women of different age groups and to predict menopausal transition based on its values.

Material and Methods: Study enrolled healthy women with no apparent complaints ($n = 114$) from various departments at Sir Ganga Ram Hospital, New Delhi (INDIA), irrespective of their profession. The study group was divided into 20–29 years ($n = 20$), 30–39 years ($n = 56$), 40–49 years ($n = 35$) and postmenopausal ($n = 3$). Based on their response to a set of questions (medical/social/obstetric history), they were grouped as symptomatic ($n = 53$) and asymptomatic ($n = 61$). Menopausal symptoms such as Vasomotor, Genitourinary, Musculoskeletal, Menstrual irregularities were correlated with sAMH by ELISA assay as per manufacturer's protocol (AMH Gen II ELISA Kit, BD Coulter). Correlation of sAMH levels was also done with BMI. Statistical analysis was performed by the SPSS program for Windows, version 17.0.

Result: In the present study, serum AMH levels were inversely proportional to the advancing age in healthy women ($p < 0.001$), but the early premenopausal group of women (age 30–39 years) showed statistical significant higher variations than the late premenopausal group of women (age 40–49 years, $p = 0.016$). Majority (63%) of the women categorized under symptomatic subgroup presented with either musculoskeletal symptom or related to the group labelled as others (insomnia, mood changes, depression, dry/wrinkled skin, decreased libido). Noteworthy, were the findings that women age.

HORMONES, MENOPAUSE AND CARDIOVASCULAR SYSTEM

OC10.1

VENOUS THROMBOEMBOLISM (VTE) AND CARDIOVASCULAR DISEASE (CVD) COMPLICATIONS IN POSTMENOPAUSAL WOMEN USING TRANSDERMAL VS ORAL ESTROGEN THERAPY

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Objective: To evaluate the risk of VTE and CVD and compare health-care costs in postmenopausal women using estradiol transdermal system (ETS) relative to oral estrogen therapy (OET).

Design: Insurance claims from 60 US companies from 01/1999–09/2011 were analyzed. Women ≥ 35 y, newly initiated on ETS or OET were included. Women with a history of VTE or CVD, or using any estrogen within 180 days of starting ETS or OET were excluded. Incidence rates of VTE or CVD were calculated. The incidence rate ratio, assessed through both unadjusted and conditional Poisson models was used to compare the event rates for ETS or OET cohorts. Healthcare costs in USD were assessed.

Results: 7,552 users (each cohort) were matched to form the study population. Mean age for both cohorts was 50 y, mean estrogen exposure was 533 (ETS) and 532 (oral) days; progestin use was 12.4% (ETS) and 11.7% (oral). A total of 718 ETS users developed VTE or CVD compared to 828 OET users (adjusted IRR: 0.79; 95% CI: 0.70–0.89, $P < 0.001$). ETS users had significantly lower risk of VTE and/or CVD, as well as hospitalization-related events, relative to OET users. ETS users also incurred significantly lower adjusted all-cause and VTE/CVD-related healthcare costs relative to OET users (all-cause difference [95% CI] = \$56 [4–109], $P = 0.026$; VTE/CVD-related cost difference [95% CI] = \$24 [2–51], $P = 0.024$) per member per month. **Conclusion:** This matched-cohort study of $> 15,000$ women suggests that women receiving ETS have significant lower incidences of VTE and CVD compared to women receiving OET, and incur significantly lower healthcare costs.

OC10.2

MENOPAUSAL WOMEN WITH SEVERE HOT FLUSHES HAVE ENHANCED MICRO-VASCULAR PERFUSION BUT UNCHANGED MACRO-VASCULAR REACTIVITY COMPARED WITH NON-FLUSHERS

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Introduction: Hot flushing is a common feature of menopause among women from different ethnic backgrounds affecting significantly their general wellbeing and quality of life. There are recent data linking hot flushing with metabolic profile and altered vascular reactivity. The aim of our study was to assess the vascular reactivity in different vascular beds of women with severe hot flushes compared with non-flushers in relation to metabolic risks profile.

Methods: Micro-vascular perfusion was assessed using Laser Doppler Imaging (LDI) and macro-vascular reactivity using Peripheral Arterial Tonometry (EndoPAT). Routine metabolic features were measured too.

Results: 28 healthy women with severe hot flushes of a mean age of 55.9 (SD 5.8) years and mean BMI of 27.8 (SD 4.5) kg/m^2 were compared with 25 non flushers of similar age and BMI. Central adiposity, blood pressure and fasting blood sugar did not differ between the groups. The response of the subcutaneous micro-vessels was greater in

women who flushed following administration of the endothelium-dependent vasodilator Acetylcholine (972.4 v 703.1, $p < 0.001$). However, the reactive hyperaemia index (RHI) measured by the EndoPAT did not differ between the two groups (2.6 v 2.8, $p = 0.23$). **Conclusion:** In our study, women with severe hot flushes demonstrated improved cutaneous perfusion but similar metabolic features and macro-vascular reactivity with non-flushers. Greater micro-vascular perfusion of the cutaneous circulation among the women with severe hot flushes may be associated with peripheral vasodilation which enables more efficient heat loss, as opposed to a favourable metabolic profile.

OC10.3

MINIMAL IMPACT ON THROMBOPHILIA MARKERS WITH CONJUGATED ESTROGENS/BAZEDOXIFENE: SUMMARY OF POOLED COAGULATION DATA FROM THE SELECTIVE ESTROGENS, MENOPAUSE, AND RESPONSE TO THERAPY (SMART) TRIALS

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Objective: The effects of conjugated estrogens (CE)/bazedoxifene (BZA) on coagulation parameters were assessed based on SMART-1, -4, and -5 trial pooled data.

Methods: The randomized, double-blind, placebo (PBO)- and active-controlled, phase 3 SMART trials in postmenopausal women with a uterus assessed mean changes in coagulation parameters at 12 months (SMART-4 and -5) and 12 and 24 months (SMART-1); data were analyzed for women who received CE 0.45 or 0.625 mg/BZA 20 mg or PBO.

Results: Pooled data were available for 1978 subjects. At 12 months, CE 0.45 and 0.625 mg/BZA 20 mg had antithrombin III decreases vs an increase for PBO (-0.05 , -0.06 , and 0.02 L/L, respectively; all $P < 0.01$ vs baseline). At 24 months, the CE/BZA doses and PBO had similar decreases in antithrombin III (-0.27 , -0.26 , and -0.21 L/L; all $P < 0.001$ vs baseline). Protein C activity changes at 12 and 24 months were -0.01 to -0.03 and 0.05 L/L for the CE/BZA doses vs -0.02 and 0.04 L/L for PBO (all $P < 0.01$ vs baseline except CE 0.625 mg/BZA 20 mg and PBO at 12 months). For the CE/BZA doses and PBO, Protein S activity changes were -0.02 to -0.03 and -0.02 L/L at 12 months and 0.06 to 0.08 and 0.15 L/L at 24 months (all $P < 0.05$ vs baseline except PBO at 12 months). There were no changes in fibrinogen, prothrombin time, partial thromboplastin time, PAI-1 activity, plasminogen, and D-dimer between groups. Venous thromboembolic and cerebrovascular events were low ($\leq 0.2\%$) and similar among groups.

Conclusion: CE 0.45 and 0.625 mg/BZA 20 mg showed a favorable coagulation profile in postmenopausal women, with changes in coagulation parameters generally comparable with PBO over 2 years. Combined with the demonstrated efficacy and safety of CE/BZA in treating menopausal symptoms and preventing osteoporosis, these findings show that CE/BZA may be a promising alternative for nonhysterectomized women.

OC10.4

POOLED CARDIOVASCULAR (CV) SAFETY RESULTS FROM PHASE 3 TRIALS OF CONJUGATED ESTROGENS/ BAZEDOXIFENE (CE/BZA)

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Objective: The CV safety of CE/BZA was evaluated using pooled data from the Selective estrogens, Menopause, And Response to Therapy (SMART) trials.

Design: Data were summarized using a meta-analysis from 5 phase 3 studies of 12 wk to 2 yr, conducted in generally healthy, nonhysterectomized postmenopausal women, including SMART-1 (N = 3397), -2 (N = 318), -3 (N = 652), -4 (N = 1061), and -5 (N = 1843). CV, cerebrovascular, and venous thromboembolic (VTE) adverse events (AEs) were reviewed by 3 independent adjudication committees; adjudicated results are presented for CE 0.45 mg/BZA 20 mg, CE 0.625 mg/BZA 20 mg, and PBO.

Results: The incidence (per 1000 woman-years) of CV risks were: VTEs, 0.30 (95% confidence interval [CI], 0.00–2.02) for CE 0.45 mg/BZA 20 mg, 0.00 (0.00–1.54) for CE 0.625 mg/BZA 20 mg, and 0.59 (0.00–2.89) for PBO (relative risk of VTEs vs PBO was 0.86 [0.18–4.14] for CE 0.45 mg/BZA 20 mg and 0.50 [0.09–2.65] for CE 0.625 mg/BZA 20 mg); deep vein thrombosis, CE 0.45 mg/BZA 20 mg (0.30 [0.00–2.02]), CE 0.625 mg/BZA 20 mg (0.00 [0.00–1.54]), and PBO (0.59 [0.00–2.89]); superficial thrombophlebitis, CE 0.45 mg/BZA 20 mg (0.17 [0.00–1.80]), CE 0.625 mg/BZA 20 mg (0.41 [0.00–2.32]), and PBO (0.59 [0.00–2.89]); adjudicated fatal and nonfatal coronary heart disease (CHD)-related AEs, CE 0.45 mg/BZA 20 mg (2.57 [0.00–5.55]), CE 0.625 mg/BZA 20 mg (1.41 [0.00–3.91]), and PBO (2.01 [0.00–5.15]); nonfatal myocardial infarction, CE 0.45 mg/BZA 20 mg (1.83 [0.00–4.45]), CE 0.625 mg/BZA 20 mg (0.41 [0.00–2.32]), and PBO (1.40 [0.00–4.17]); and ischemic stroke, CE 0.45 mg/BZA 20 mg (0.44 [0.00–2.37]), CE 0.625 mg/BZA 20 mg (0.20 [0.00–1.86]), and PBO (0.00 [0.00–1.74]).

Conclusions: CE 0.45 mg/BZA 20 mg and CE 0.625 mg/BZA 20 mg had an acceptable CV safety profile in postmenopausal women, with incidence of CV risks comparable with that of PBO.

OC11.1

CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS OF WOMEN WITH MENOPAUSE IN A PRIVATE INSTITUTION IN THE CITY OF MEDELLÍN, COLOMBIA

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Menopause represents a variety of physiological changes that can affect the quality of life and women's health. Objective: To determine the clinical and epidemiological characteristics of patients with menopause treated in the outpatient department in a private institution in the city of Medellín. Materials and Methods: A retrospective descriptive study with a study population of menopausal women who consulted in a private institution between 2002 and 2012 was performed. Results: 123 charts of menopausal women who met eligibility criteria were reviewed. The average age of participants was 54.4 ± 6.5 years, and the age of onset of menopause was 48.8 ± 3.7 . 21.1% had a history of hysterectomy. The most common clinical manifestations of menopause were: heat (63.4%), menstrual disorders (36.6%) and headache (35.0%). The most frequent medical history was hypertension (39.4%) and dyslipidemia (28.5%), 6.5% had a history of stroke, angina and / or myocardial infarction. In the category of body mass index, 6.7% were normal weight, 75.0% overweight and 18.8% obese. 70.7% of women receiving treatment for menopause. Conclusion: the clinical and epidemiological characteristics of women in the study are similar to those reported in the literature.

SPANISH ORAL COMMUNICATIONS

OC11.2

IDENTIFICATION OF CARDIOMETABOLIC RISK FACTORS ASSOCIATED THYROID STATUS IN WOMEN PERIMENOPAUSIC. UBACYT PROJECT 2012–2015

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Introduction: Hypothyroidism is associated with cardiometabolic risk factors such as hypertension (HTN), dyslipidemia, systemic inflammation and insulin resistance (IR), considered this thyroid dysfunction independent factor for development of cardiovascular disease.

Objectives: Identify in perimenopause women cardiometabolic risk factors associated with thyroid status.

Methodology: Cross-sectional observational design where a nonrandom sample of adults (40–65 years) attending Endocrine Center of Buenos Aires was studied. Were randomized according to thyroid function in two groups: Group A (levothyroxine-treated hypothyroid cases considered: 46.2%) and Group B (euthyroid considered controls: 53.8%). The following cardiometabolic risk factors were evaluated: Body Mass Index (BMI) ≥ 25.0 kg/m², waist circumference (WC) > 88 cm; Biological stage (pre-and postmenopausal), smoking, sedentary lifestyle, altered lipid profile (Colt > 200 mg/dl, LDL > 130 mg/dl, Tg > 150 mg/dl, HDL < 40 mg/dl), HTN $\geq 120/80$ mmHg and increased fasting glucose (> 100 mg/dl). Statistics with SPSS 15.0 establishing measures of central tendency, OR with 95% confidence intervals (CI) and difference of proportions with p value < 0.05 .

Results: On a sample of 316 women (53.9 DS 6.6 years, 35.8% premenopausal and 64.2% postmenopausal). The average BMI was 27.8 DS 4.8 kg/m² and WC 87.9 DS 10.3cm. In the cases group risk factors more prevalent were sedentary lifestyle (84.9%), altered BMI (79.4%) and total cholesterol increased (73.9%).

The cases had significantly altered risk of BMI (OR = 2.77; 95% CI = 1.67–4.59; p = 0.0001) and altered WC (OR = 1.85; 95% CI = 1.18–2.90; p = 0.0068) than controls.

Conclusions: We found significant association between hypothyroidism and altered nutritional status but not with other cardiometabolic risk factors studied was found.

OC11.3

EFFECTS OF A NURSING INTERVENTION ON CARDIOVASCULAR HEALTH IN HYPERTENSIVE, DYSLIPIDEMIC AND OVERWEIGHT POSTMENOPAUSAL WOMEN

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OBJECTIVE: To examine the effects of a 6-month nursing intervention on cardiovascular risk factors and health-related quality of life (HRQOL) in hypertensive, dyslipidemic and overweight postmenopausal women in Concepcion, Chile. METHODS: Experimental design with pre and post tests. 55 women (mean age 57.8 SD 4.2 years) were recruited from 6 community health centers and were randomly assigned to the intervention (n = 27) or control (n = 28) groups. The patients in the intervention group participated in face to face and telephone counselling sessions. The nursing intervention included health monitoring, counseling, health education. Before the intervention, HRQOL, Systolic Blood Pressure (SBP), Diastolic Blood Pressure

(DBP), Body Mass Index (BMI), Waist Circumference (WC), Total Cholesterol (TC), Low Density Lipoprotein-Cholesterol (LDL-C), High Density Lipoprotein-Cholesterol (HDL-C), Triglycerides (TG), and the TC/HDL ratio levels were measured as pre-test data and completion the intervention. Ethics requirements were incorporated. RESULTS: Compared with the control group, the nursing intervention group showed significantly reductions in SBP ($p < 0, 05$) and WC ($p < 0, 05$). Women's within intervention group at 6 month compared with the baseline showed: HRQOL significantly greater increased, DBP and WC significantly greater decreased and significant mean decrease in TC, LDL-C, BMI, WC and TC/HDL ratio. Womens within control group at 6 month compared with the baseline showed: HRQOL significantly increased, DBP significantly greater decreased. The mean changes within the intervention and control group were not significant in SBP, HDL-C and TG. CONCLUSIONS: The results indicate that nursing intervention on cardiovascular risk factors and HRQOL may be an effective strategy for managing hypertensive, dyslipidemic, overweight postmenopausal women at a primary health care level.

OC11.4

ASSESSING QUALITY OF LIFE AND SEXUAL FUNCTION IN MIDDLE-AGED WOMEN USING THE CERVANTES SCALE (CS) AND THE FEMALE SEXUAL FUNCTION INDEX (FSFI)

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In the present investigation we assessed menopause-related quality of life and female sexual function using the 31-item CS and the 19-item FSFI (Cronbach's alpha 0.896 and 0.983, respectively), and a questionnaire about socio-demographic data. Median [interquartile range] results were: age 47[9] years, parity 3[2], year of formal education 11[8]. A 69.8% of women were Mestizo and 30.2% Black. They were 26.3% peri- and 35.4% postmenopausal, and 52.9% had increased body mass index. A 54.7% had a total FSFI scores ≤ 26.55 , which suggests sexual dysfunction. To avoid colinearity with the FSFI score, sexuality and partner relationship CS sub-domains were not included in the combined analysis; thus, total FSFI scores were inversely correlated with total ($\rho = -0.137$), somatic ($\rho = -0.354$) and psychological ($\rho = -0.380$) CS ($P < 0.001$). Multiple linear regression was used to obtain a reduced best-fit model predicting total FSFI scores which were positively correlated (better sexual function) to female education and parity, and inversely correlated to age, years since the menopause and both somatic and psychological CS scores.

BREAST AND UTERINE CANCER

OC12.1

BREAST SAFETY OF CONJUGATED ESTROGENS/BAZEDOXIFENE (CE/BZA): POOLED ANALYSIS OF THE SELECTIVE ESTROGENS, MENOPAUSE, AND RESPONSE TO THERAPY (SMART) TRIALS

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Objective: The breast safety profile of CE/BZA was assessed based on pooled data from the SMART 1 to 5 trials. Design: Data for CE 0.45 mg/BZA 20 mg ($n = 1585$), CE 0.625 mg/BZA 20 mg ($n = 1583$), CE 0.45 mg/medroxyprogesterone acetate (MPA) 1.5 mg ($n = 399$ [SMART-4 and -5 only]), raloxifene (RLX) 60 mg ($n = 423$ [SMART-1 only]), and placebo (PBO; $n = 1241$) were

pooled from the randomized, double-blind, PBO- and active-controlled, phase 3 SMART trials in postmenopausal women with a uterus. Breast procedure incidence (biopsies, aspirations, nipple discharge cytology), mammography data, breast pain/tenderness (measured by daily diaries), and breast-related adverse events (AEs) were assessed; breast cancer incidence was determined from cumulative meta-analysis with inverse variance weighting.

Results: Overall incidence of breast cancer per 1000 woman-years was 1.00 (95% CI 0.00–3.21) for CE 0.45 mg/BZA 20 mg, 0.00 (0.00–1.54) for CE 0.625 mg/BZA 20 mg, 1.05 (0.00–6.89) for CE/MPA, 0.00 (0.00–2.20) for RLX, and 1.40 (0.00–4.17) for PBO. Incidences of abnormal mammograms were similar for both CE/BZA doses vs PBO and CE/MPA and significantly lower vs RLX. Percentage of subjects who had follow-up breast procedures was similar for CE 0.45 mg/BZA 20 mg (0.76%), CE 0.625 mg/BZA 20 mg (0.88%), and PBO (0.89%); percentage of subjects was numerically higher for CE/MPA (1.50%) and RLX (1.33%). Incidence of breast pain/tenderness for CE 0.45 mg/BZA 20 mg (9.8–11.5%) and CE 0.625 mg/BZA 20 mg (9.8–10.2%) was similar to PBO (8.1–11.2%) and RLX (6.2–8.7%) and significantly lower vs CE/MPA (21.6–29.1%; $P < 0.001$). Incidence of breast-related AEs was low and similar among groups.

Conclusions: Pooled SMART trial data showed that both CE/BZA doses were associated with an acceptable breast safety profile with no increase in breast-related tolerability concerns.

OC12.2

WHICH ENDOMETRIAL POLYPS SHOULD BE RESECTED?

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Objective: To estimate the prevalence of malignant and premalignant lesions among endometrial polyps and correlate this prevalence with risk factors for endometrial neoplasms.

Methods: Review of clinical and histopathological data on polyps resected during hysteroscopic polypectomies performed from January 2005 through July 2013 at Hospital de Clínicas de Porto Alegre (HCPA), Brazil.

Results: The sample comprised 359 patients who underwent hysteroscopic polypectomy. Overall, 87.2% of patients had benign polyps and 9.9% had hyperplasia without atypia. Polyps with atypical hyperplasia were found in 2.6% of patients, and endometrial adenocarcinoma, in 0.3%. Polyp malignancy/premalignancy correlated with patient age, menopausal status, and presence of abnormal uterine bleeding. All women with malignant/premalignant lesions had abnormal uterine bleeding. The rate of polyp malignancy was higher among tamoxifen users, although the difference did not reach statistical significance ($p = 0.059$). There was no correlation with hypertension, diabetes mellitus, obesity, hormone replacement therapy, endometrial thickness, or polyp diameter.

Conclusion: The prevalence of malignancy/premalignancy among endometrial polyps is low; no cases were identified in patients without uterine bleeding. Routine excision of asymptomatic polyps cannot be recommended.

OC12.3

THE RELATIONSHIP BETWEEN PAPILLARY SEROUS ENDOMETRIAL CANCER AND BRCA 1 AND BRCA 2 MUTATIONS IN A COMMUNITY CARE SETTING

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Objective: The purpose of this study is to quantify the relationship between papillary serous (PS) endometrial cancer and deleterious BRCA 1 & BRCA 2 mutations within a community care setting.

Methods: Demographic, surgicopathologic, and BRCA status were retrospectively collected on 368 endometrial cancer patients seen in Aventura, Boca Raton, Boynton Beach and Delray Beach, Florida from January 1, 2000 to May 31, 2013. Endometrial cancer histologic subtypes were obtained from original surgicopathologic reports and BRCA mutation status was obtained from Myriad Genetics, Salt Lake City, Utah. Statistical analyses were performed using X2 and Fisher's exact.

Results: PS accounted for 23.6%, endometrioid adenocarcinoma (EM) 59.8%, non-characterized adenocarcinoma 6.5%, and sarcoma 10.1% of endometrial cancer cases as determined by original surgicopathologic reports. Excluding the sarcoma subtype, BRCA testing was completed in 8.96% of patients, this includes 26.4% of PS, 4.2% of non-characterized adenocarcinoma 4.1% of EM subtypes. Of those completing testing, deleterious BRCA 1 or BRCA 2 mutations were found in 17.4% (4 out of 23) PS cases, and 0% (0 out of 9) EM cases ($P = .159495$). Further analysis of the 4 BRCA positive PS patients was completed to evaluate for prior history of breast cancer and tamoxifen therapy. Two of these 4 patients had a history of breast cancer, one had a history of tamoxifen therapy, the other a history raloxifene therapy. Two patients had no prior history of breast cancer or tamoxifen therapy.

Conclusion: Within our community care setting the PS subtype accounted for more than 23% of endometrial cancers. While not statistically significant, due in part to the limited patients having initiated and completed BRCA testing, all patients with a deleterious BRCA mutation and primary endometrial malignancy were found to have the PS histologic subtype.

OC12.4

TREATMENT OF CLIMACTERIC SYMPTOMS IN BREAST CANCER PATIENTS: A RETROSPECTIVE STUDY FROM A MEDICATION DATABANK

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INTRODUCTION: Women affected by breast cancer (BC) will often go through menopause at an earlier age and display more frequent and severe symptoms than women who have a natural menopause. The safety of hormone replacement therapy (HRT) and vaginal estrogens for BC survivors has been debated over time and remains unclear. Non hormonal therapies such as antidepressants, gabapentine and clonidine may be useful for those patients but there are few data about their safety. AIM This retrospective study analyses, in a medication databank, the use by BC patients of treatments known to alleviate climacteric symptoms.

MATERIAL AND METHOD: Post-menopausal Estrogen Receptors positive (ER+) BC patients, aged 45 to 69, were identified as having bought, at least once, an aromatase inhibitor (AI) or Tamoxifen between the years 2000 and 2012. Among them, we defined users of a climacteric treatment those who bought, at least once, either HRT, vaginal topical estrogens, antidepressants, clonidine and gabapentine.

RESULTS: Among ER+ BC patients, 42.9% were buying a treatment known to alleviate menopausal symptoms. The majority of these treatments were non-HRT therapies. HRT and vaginal estrogens were seldom bought (respectively 1.1% and 6%), but 2.4% bought vaginal estrogens while buying AI. About 7.3% BC patients bought antidepressants implicated in tamoxifen metabolism at the same time as tamoxifen.

CONCLUSIONS: Most BC patients follow current guidelines contra-indicating the use of HRT after BC, they use non hormonal therapies. In some cases they use unfortunately antidepressants that may alter the metabolism of tamoxifen.

HORMONES, MENOPAUSE AND THE BRAIN OC13.1

MELATONIN IN PERIMENOPAUSAL AND POSTMENOPAUSAL WOMEN: ASSOCIATIONS WITH MOOD, SLEEP, CLIMACTERIC SYMPTOMS AND QUALITY OF LIFE

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Objective: Melatonin synthesis and secretion are partly modulated by estrogen and progesterone. Changes in melatonin concentrations, possibly related to the menopausal transition, may be associated with climacteric mood, sleep and vasomotor symptoms. The aims of this study were to compare the serum concentrations of melatonin in perimenopausal and postmenopausal women, and to evaluate its influence on mood, sleep, vasomotor symptoms and quality of life.

Methods: We analyzed data of 17 perimenopausal (43–51 years) and 18 postmenopausal (58–71 years) healthy women who participated in a prospective study. During the study night (21:00–09:00 hr) serum melatonin was sampled at 20-minute (21:00–24:00 hr; 06:00–09:00 hr) and one-hour (24:00–06:00 hr) intervals. Questionnaires were used to assess depression (Beck Depression Inventory, BDI), anxiety (State-Trait Anxiety Inventory, STAI), insomnia and sleepiness (Basic Nordic Sleep Questionnaire, BNSQ), subjective sleep quality, vasomotor symptoms, and the quality of life (EuroQoL).

Results: Postmenopausal women had lower nighttime serum melatonin concentrations than perimenopausal women. The duration of melatonin secretion tended to be shorter in postmenopause, while the melatonin peak time did not differ. Mean melatonin concentrations and exposure levels did not correlate with FSH or E2, BMI, BDI, STAI, BNSQ insomnia, BNSQ sleepiness, subjective sleep, climacteric vasomotor score or the quality of life. In perimenopause, the later the melatonin peak, the higher the level of anxiety ($p = 0.022$), and the longer the melatonin secretion, the better the quality of life ($p < 0.001$).

Conclusions: Longitudinal research is needed to better understand the possible contributive role of menopause on lower melatonin levels.

Key words: melatonin, perimenopause, postmenopause, mood, sleep, quality of life.

OC13.2

CONTRIBUTION OF THE NUCLEAR PROGESTERONE RECEPTOR TO BREATHING STABILITY DURING SLEEP AND RESPIRATORY CHEMOREFLEX IN ADULT FEMALE MICE

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We tested the hypothesis that the nuclear progesterone receptor (PR) is involved in respiratory control, and mediates the respiratory stimulant effect of progesterone. Adult female mice knocked-out for PR (PRKO) and wild-type controls (WT) were implanted with an osmotic pump delivering vehicle or progesterone (4 mg/kg/day), and instrumented with EEG and neck EMG electrodes connected to a telemetry transmitter. Seven days after the surgery the animals were placed in whole body plethysmograph to record ventilation, metabolic rate, EEG and neck EMG during 4 consecutive hours, then the animals were exposed to

hypercapnia (5% CO₂), hypoxia (12% O₂) and hypoxic-hypercapnia (5% CO₂ + 12% O₂ – 5 min each) to assess chemoreflex responses. EEG and EMG signals were used to characterize sleep-wake states. Compared to WT, PRKO mice had: - similar level of minute ventilation during non-REM and REM sleep, - higher frequency of sighs and post-sigh apneas during non-REM sleep, and - reduced ventilatory response to hypoxic-hypercapnia. Progesterone treatment increased minute ventilation and metabolic rate in both WT and PRKO mice during non-REM sleep. In PRKO mice (but not in WT) the response of respiratory frequency to hypercapnia and hypoxic hypercapnia was reduced after progesterone treatment. We conclude that the nuclear PR helps stabilizing the respiratory pattern during non-REM sleep and enhances chemoreflex responses to hypoxic-hypercapnia. These results also suggest that mechanisms other than activation of the nuclear PR are able to increase minute ventilation and metabolic rate in response to progesterone treatment in adult female mice.

OC13.3

THE INFLUENCE OF GRANDPARENTING ON POSTMENOPAUSAL WOMEN'S COGNITION: RESULTS FROM THE WOMEN'S HEALTHY AGEING PROJECT

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Background: Participation in cognitively stimulating activities has been found to maintain cognition in later life, which may prevent or delay the development of mild cognitive impairment or dementia. These activities are particularly important in the postmenopausal period as the critical window to influence early dementia development is 20–30 years prior to onset. Social engagement is a form of daily activity that has been shown to influence cognition in older adults. Grandparenting is one important example of social engagement that is increasingly popular as a form of childcare. This study investigated the effects of grandparenting on cognition in postmenopausal women.

Method: Participants were 186 women (mean age = 60) from the longitudinal prospective Women's Healthy Ageing Project (WHAP). Participants completed the core questionnaire which included grandparenting and reported feelings of demand. Working memory and processing speed were assessed using the Symbol-Digit Modalities Test (SDMT).

Results: Subjective memory complaints were not significantly associated with having or minding grandchildren. The amount of time spent minding grandchildren was significantly associated with differences in SDMT scores ($p < 0.05$). Participants who spent one day per week minding their grandchildren performed significantly better on the SDMT than those who minded more than one day per week ($p < 0.05$). This coincided with an increase in reported feelings of demand.

Conclusion: The results suggest that highly frequent grandparenting is associated with poorer working memory and processing speed performance, which may be linked to stress. Further research is required to deepen understanding of this association and apply these findings to the broader social context.

OC13.4

SURGICAL MENOPAUSE LEADS TO HIPPOCAMPAL ESTROGEN SIGNALING DEFICIT: ROLE OF ESTROGEN RECEPTOR CO-REGULATOR PELP1

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Prematurely menopausal women have an enhanced risk of neurological disease. Prolonged loss of ovarian 17 β -estradiol (E2) is thought to be crucial, as timely replacement of E2 normalizes the risk, but the molecular mechanisms underlying this phenomenon remain unknown. Previously, we observed degradation of ER α , basal elevation of the neurodegenerative Wnt antagonist Dkk1, and loss of E2's neuroprotective ability in the hippocampus of long-term ovariectomized rats. As such, we hypothesized that surgical menopause leads to a neural E2 signaling deficit. To investigate, we used a rat model of surgical menopause (10-week ovariectomy) to observe changes in hippocampal E2 signaling machinery. Interestingly, we observed a 40% decrease of the ER co-regulator PELP1 in the hippocampus of ovariectomized rats. To further determine the consequences of reduced PELP1 expression, we knocked down neural PELP1 in E2-treated rats with intracerebroventricular anti-sense oligonucleotides prior to inducing 10-min global cerebral ischemia (GCI). Missense oligos served as a control. Intriguingly, 40–50% knockdown of hippocampal PELP1 prevented E2 from suppressing activation of c-Jun N-terminal kinase (JNK), downstream activation of c-Jun, and elevation of Dkk1 in the hippocampus after GCI, similar to events seen in long-term ovariectomized females. Mass spec and Co-IP studies revealed that PELP1 was capable of binding to JNK and several upstream signaling effectors in the brain. Furthermore, E2 neuroprotection status was reversed in PELP1 knockdown animals, suggesting that PELP1 is a critical mediator of E2's neuroprotective signaling. Collectively, these studies suggest that the decrease in hippocampal PELP1 expression observed following surgical menopause indicates an E2 signaling deficit and may underlie the enhanced risk of neurological disease seen in prematurely menopausal women.

SEXUAL FUNCTION

OC14.1

IMPROVEMENT IN FEMALE SEXUAL DYSFUNCTION AS MEASURED BY THE FEMALE SEXUAL FUNCTION INDEX (FSFI): RESULTS OF A RANDOMIZED PLACEBO-CONTROLLED TRIAL WITH OSPEMIFENE

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Objective: To assess the effect of ospemifene 60 mg/day on female sexual dysfunctions (FSDs) by a widely used 19-item patient-reported questionnaire, the Female Sexual Function Index (FSFI), in a postmenopausal vulvar and vaginal atrophy (VVA) population.

Design: A randomized, double-blind, Phase 3 trial assessed the efficacy and safety of daily oral ospemifene 60 mg vs placebo for 12 weeks (wks) in 919 women. Participants were assigned to one of 2 self-reported VVA most bothersome symptom (MBS) strata: dyspareunia or dryness. Data were analyzed separately for each stratum. Co-primary endpoints were change from Baseline to Wk 12/LOCF in: Maturation Index (MI), vaginal pH, and MBS. FSFI score was analyzed as a secondary efficacy endpoint and results are reported here. The FSFI was used to assess change from Baseline to Wks 4 and 12/LOCF for ospemifene vs placebo for the 6 domains (arousal, desire, orgasm, lubrication, satisfaction, and pain) and total score according to an article by Rosen et al (2000); data were analyzed by ANCOVA model.

Results: Statistically significant ($p < 0.05$) improvements for ospemifene 60 mg vs placebo were seen for every FSFI domain score (desire, arousal, lubrication, orgasm, satisfaction, and pain) and the total score at Wk 12 (LOCF). At Wk 4, every domain was significantly improved except for orgasm ($p = 0.0820$) and satisfaction ($p = 0.3206$). **Conclusions:** Ospemifene 60 mg was shown to significantly improve sexual function as reflected in the total FSFI score. Significant improvement was also seen in 4 of the domains at Wk 4 and in all 6 domains at Wk 12 of treatment. Consistency of effect was observed in all

domains, distinguishing ospemifene from other agents that treat dyspareunia. Confirmation of this data and assessment as to whether these effects are related solely to the improvement in dyspareunia remains to be elucidated.

Support: Funding was provided by QuatRx Pharmaceuticals Company.

OC14.2

OVER ACTIVE BLADDER AND SEXUAL HEALTH OF MENOPAUSAL WOMEN

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INTRODUCTION: Overactive bladder (OAB) significantly affects the sexual health of menopausal women but this area is often overlooked as diminished sexuality is taken granted for menopause. OAB is increasingly recognized in menopause as more common than was once thought. Proper attention to OAB may improve the sexual health of menopausal women.

AIM: The study was conducted to give a thorough understanding of impacts of OAB on sexual health of menopausal women.

METHOD AND MATERIAL: Total 130 menopausal women were recruited, 65 women with OAB grouped A ,and 65 women without OAB grouped B from gynae and urology clinics . Questionnaires were filled by them. Data were analyzed using SPSS. Women with Psychiatric illness and severe medical diseases were excluded from the study.

MAIN OUTCOME MEASURE: To review the association between sexual health and OAB in menopausal women.

RESULT: Results of total 111 women (Group A=48 and Group B=63) obtained which reflected group B had better sexual life than group A. Decreased libido was found (29.2 vs 1.6 p =.0001), decreased coitus practice was in (12.5 vs 42.9 p =.0001), complains of dyspareunia (37.5 vs 22.2 p =.0355), wants to get sexual pleasure (18.8 vs 33.3 p =.0329) were found in group A and B respectively. Again interruption of sex and sleep disturbances were more complained (10.4 vs 36.5 p =.0001), (31.3 vs 6.3 p =0001) by group A than group B. Interestingly both group wanted emotional closeness rather physical (37.5 vs 42.9 p =ns) and reluctant to have HRT (14.6 vs 14.3 p =ns).

CONCLUSION: Menopause itself hampers the sexuality. Moreover OAB negatively affects the sexual health of menopausal women. Given the impact of OAB this area need to be routinely assessed and treated by clinicians and should be addressed by researcher with more attention.

OC14.3

THE PERIMENOPAUSAL AND POSTMENOPAUSAL CHINESE WOMEN SURVEY: SEXUAL FUNCTION AND PERCEPTIONS

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Objective: to assess the sexual function of Perimenopausal and postmenopausal Chinese women, to determine if there is an association between menopausal symptoms and sexual function, to determine the some factors affect sexual function.

Material and method: This study was a cross-sectional, descriptive analysis of the sexual function in a sample of 251 women performed between January 2012 and June 2013. Inclusion Criteria of study: Women with natural menopause \geq 12 months since last menstrual period or amenorrhea < 12 months and serum follicle stimu-

lating hormone levels above 30 IU/L, Women had intact uterus and both ovaries, No hormone therapy, Women whom were not undergoing psychiatric treatment or taking antidepressant or sedative medications. Sexual function and menopausal symptoms were evaluated by an anonymous questionnaire developed by HU Lei al for Chinese women. who demonstrated its reliability and Validity. The instrument used for collection of data was Sexual Quality of Life Questionnaire for Women 38 items was established, which had six domains: satisfaction, communication, anxiety, sexual response, attitude and selfimage. The Kupperman Menopausal Index was used to evaluate the severity and intensity of the menopausal symptoms.

Results: The average age of 251 women was 53.09 ± 4.83 years old (42–60), years of marriage was 27.91 ± 5.55 years (12–54 years). 218 of all were postmenopausal, 33 were perimenopausal. 26.0% now had no intercourses, 30.0% had it for only once a month, 32.0% once or twice a month, 7.0% once or twice a week. As for the sexual attitudes, 5.0% thought it very important in marriage, 12.0% quite important, 42% not essential, 14.0% not important. 62.0% of women reported hypoactive sexual desire, while only 13.0% reported normal. The overall sex satisfaction score (total 10 points) was 5.84 ± 2.60 , which was significantly lower than their score before perimenopause (7.18 ± 2.27)($t = -5.17$, $P < 0.05$). For those who still had sexual activities, 197 finished the Chinese Sexual Quality of Life Questionnaire (with full score 190 points), the total score (median) was 121.0, sexual satisfaction 34.0, sexual communication 17, sexual anxiety 29.0, sexual response 17.0, sexual attitude 14.0, sexual image 19.0. Kupperman index 20.0. Multivariable analysis showed female sexual total scores in perimenopausal and postmenopausal women was negative related to age, the number of children, spousal relationship, KMI ($r = -0.922$, $P = 0.023$; $r = -6.319$, $P = 0.074$; $r = -10.280$, $P = 0.087$; $r = -0.484$, $P = 0/003$).

Conclusion: Menopause affected in a negative manner some domains of female sexual function.

There was a negative association between age, the number of children, spousal relationship, KMI and female sexual total scores in perimenopausal and postmenopausal women.

OC14.4

ASSOCIATION BETWEEN HYPERTENSION AND RISK OF SEXUAL DYSFUNCTION IS MODIFIED BY DEPRESSIVE SYMPTOMATOLOGY IN MIDDLE AGE WOMEN

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OBJECTIVE: To assess the association between hypertension and sexual dysfunction (SD) in Peruvian middle age women. **METHODS:** We carried out a cross sectional study among middle age women (40 to 59 years) residents in Piura, Peru. Individuals filled out the Female Sexual Function Index (FSFI) and the Beck Depression Inventory (BDI) for defining SD (IFSF > 26.55) and risk of depression (RD: BDI > 13), respectively; also a questionnaire assessing demographical, clinical and partner variables. To evaluate the association between hypertension and SD, Generalized Linear Poisson Models with robust variance were used for analyses reporting prevalence ratio (PR). **RESULTS:** We included 260 women with hypertension and 257 with normal blood pressure. Total FSFI scores were lower in hypertension group as compared to normotensive group (19.2 ± 4.9 vs. 27.3 ± 2.25 , $p < 0.01$). 70.7% women in hypertensive group

and 35.4% in non-hypertension group had SD ($p < 0.001$). On multivariable analysis, we found that RD modified the effect of the association between hypertension and SD. Thus, two different models were constructed, one for women with RD and another for those without RD. In depressive women, only asthma [PR:1.42, 95%CI:1.14–1.77] and currently smoking [PR:1.39, 95%CI:1.17–1.73] were associated to SD whereas in non-depressive women, hypertension [PR:2.0, 95%CI:1.64–2.44], postmenopausal status [PR:1.46, 95%CI:1.19–1.79], partner premature ejaculation [PR:1.49, 95%CI:1.26–1.77] and good couple relationship [PR:0.63, 95%CI:0.47–0.83] were significantly associated to SD. CONCLUSION: Hypertension and sexual dysfunction are associated in middle age women, which is dependent on depressive symptomatology.

OTHER ONCOLOGY

OC15.1

THE EVALUATION OF THE ROLE OF IL-6 AND IL-8 IN THE COMPLEMENT INHIBITORS EXPRESSION WITH OVARIAN CARCINOMA ESTABLISHED CELL LINE NON-PRODUCING INTERLEUKINE-6 (A2780), BUT IL-6 RECEPTOR POSITIVE

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Dynamic development of immunology, molecular biology and genetics provides to increase resources of information about ovarian cancer biology. It creates new opportunities of treatment. The aim of this study was to evaluate effect of interleukin 6 (IL-6) and 8 (IL-8) to expression of soluble form complement system' inhibitors: factor H and factor H like protein 1. The ovarian cancer cell line A2780 were incubated with medium containing various concentrations of two interleukin IL-6 alone and IL-6 with IL-8 together (1, 10 and 100 ng/ml). After 4, 12 and 24 hours of incubation the supernatant were analyzed by ELISA test and the cells were lysed by RIPA cell lysis buffer. Isolated protein was subjected to western blot analysis using anti-FH and anti-FHL-1 antibodies. The level of soluble form of FH in medium of cell culture after incubation with various concentrations of IL-6 and IL-8 was the same in the test samples as in control. We didn't observe any significance differences. The level of intracellular form of FH was the highest after 24 hours incubation with 100 ng/ml concentration of IL-6 and 4 hours incubation with 100 ng/ml concentration of IL-6 and IL-8 together. While the level of intracellular form of FHL-1 was the highest after 4 hours incubation with 10 ng/ml concentration of IL-6 and after 4 hours incubation with 10 ng/ml concentration of IL-6 and IL-8 together. Generally IL-6 and IL-8 in our research affect to expression of intracellular form of factor H and factor H like protein. It seems that IL-6 and IL-8 together have a stronger effect than IL-6 alone. Unfortunately IL-6 and IL-8 not affect to expression of secreted form of this protein.

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OC15.2

THE EXPRESSION OF COMPLEMENT INHIBITORS IN OVARIAN AND CORPUS UTERI CANCERS - A NEW PERSPECTIVE FOR IMMUNOTHERAPY

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One of the potential therapeutic methods of cancer treatment is immunotherapy with monoclonal antibodies. This therapy, although devoid of serious side effects, it has insufficient efficacy. One of the main reasons for the inefficiency is the presence on the cancer cells of complement inhibitors which are able to inactivate complement-mediated immune response. In our studies we investigated the expression of the main complement regulators: CD55, CD59 and factor H/factor H-like in tumour samples of ovarian and corpus uteri cancer. Tumor samples were collected from 50 patients and stained immunohistochemically, with peroxidase-based immunodetection. The most prominently expressed complement inhibitor in both ovarian and endometrial cancer was factor H/factor H-like. Immunoreactivity was mostly marked within tumor stroma and within vascular structures. Membrane bound complement inhibitors are less prominently expressed by cancer cells. CD55 was detected in low percentage of cells, predominantly within cancer tubules. CD59 was detected in a subpopulation of both ovarian and corpus uteri cancer, often localized at the margin of tumor masses. It appears that the main complement inhibitor, present within tumors of the ovary and corpus uteri is soluble factor H/factor H-like. Accumulation of factor H/H-like within tumor stroma surrounding cancer cells indicates that tumor cells can possibly recruit this factor in order to defend itself from the complement-mediated cytotoxicity.

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OC15.3

EFFICIENT AND EFFECTIVE CERVICAL CANCER SCREENING IN LOW RESOURCE SETTINGS

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Introduction: Cervical cancer is a largely preventable disease which remains a significant cause of morbidity and mortality worldwide. It is usually characterised by a long pre-clinical phase of several years during which it is possible to detect cytological abnormalities which may develop into cancer if untreated. If identified at the pre-cancer stage of cervical intraepithelial neoplasia (CIN), the abnormal cells are usually treatable to prevent the development of cancer.

In India so far no organized community based screening program by Government of India are in place. Though Cervical cancer registries are there no documentation of cervical cancer screening being done. Cervical cancer screening is not a primary objective of Health Care Providers.

This project was started with the aim of converting opportunistic screening and camp based screening to organized screening and establishing a robust, economical, effective community based, acceptable cervical cancer screening programme with the help of concerned NGO.

Niche Foundation and Niche Theranostic Lab were main contributors.

The data was collected as per The Bethesda System along with clinical details as per TRF of Niche Theranostics over period of 15 months.

Total cases analysed so far are 1000, and included camp based approach for population based screenings, the sample accepted were Conventional pap smear on slide, Liquid Based Cytology and HPV HR DNA (Qiagen). This is still an ongoing project.

The results will be discussed after compilation and cytological abnormality correlated with age, HPV DNA status and P 16 wherever required.

Methods: The project was designed looking at various options available to Indian women in the context of diagnostics and management, currently Pap and HPV testing is out of reach.

OC15.4

MANAGEMENT OF OVARIAN CYST IN POSTMENOPAUSAL WOMEN IN LOW RESOURCE COUNTRIES

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AIM: The aim of this study is to see how can we manage ovarian cyst in postmenopausal women.

DESIGN: Prospective study of 600 postmenopausal women with ovarian cyst, were recruited since July 2011–July 2013, from Gynaecology department of Sikder medical college Hospital.

METHODS: All postmenopausal women with ovarian cysts were examined thoroughly and investigated mainly by TVS, Doppler and CA125 to assess the risk of malignancy. CT scan MRI or PET were done in selected cases as they are very expensive in Bangladesh. Women who had simple cyst, size <5 cm, painless and normal CA125 were posted for conservative treatment. They were followed every 4 months upto 1 year. If cyst was complex, large with high CA125, or if the cysts were increasing and becoming painful during follow up Surgery was offered. Laparotomy or laparoscopy was chosen according to patient's wish. Histopathology reports were documented and malignant cases were referred to oncology department.

RESULT: Results obtained from total 500 women. 99% of cysts were found benign and 1% was malignant, Unilocular cysts were found in 30%, 55% cysts resolved spontaneously within 6 months and 10% persisted even after 1 year. Surgery were carried out for 35% cases where serouscystadenoma and mucinouscystadenoma were found in 58% and 25% respectively. 5 among 500 women were found having malignant cysts, 2 of them were borderline serouscystadenocarcinoma, 1 was having granulosa cell tumour and 1 was mucinouscystadenocarcinoma.

CONCLUSION: Majority of cysts of postmenopausal women were benign. Though small but there is a risk of malignancy. MRI, CT SCAN or PET are not always feasible because of cost so a very careful assessment of malignant risk, strict follow up for them who are on conservative treatment and proper counseling is mandatory during the management of postmenopausal women with ovarian cysts.

MENOPAUSE THERAPY

OC16.1

EFFICACY OF ORAL OSPEMIFENE 60 MG: COMPARISON IN SUBPOPULATIONS

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Objective: Oral ospemifene, a tissue selective estrogen agonist/antagonist, is approved for the treatment of moderate to severe postmenopausal dyspareunia, a symptom of vulvar and vaginal atrophy (VVA). The objective of this analysis was to assess ospemifene 60 mg/day on the efficacy on the vaginal epithelium and self-identified most bothersome symptoms (MBS) of VVA in the overall population as well as subpopulations.

Design: Data from 4 randomized, double-blind placebo-controlled trials were analyzed for the co-primary endpoints of change in percent-

age of cells (superficial, parabasal) in the Maturation Index (MI) and in vaginal pH from Baseline to Week 12/LOCF. Change in severity for MBS from Baseline to Week 12/LOCF (dyspareunia, vaginal dryness) was analyzed in the two trials which included MBS as a co-primary endpoint. To assess population effects, pooled data from the placebo-controlled trials were analyzed for age, race, prior HRT use and uterine status of participants.

Results: Changes from Baseline to Week 12 in the % of superficial cells, % of parabasal cells and vaginal pH demonstrated statistically significant improvement vs placebo in each trial ($p < 0.05$). For MBS, ospemifene demonstrated significant improvement in severity at Week 12 for dyspareunia in both trials ($p < 0.05$); and in one trial for dryness with numerical improvement in the other.

At Week 12, for all subpopulations numerical improvements in all endpoints were observed in the ospemifene group compared to placebo.

Conclusion: Overall, ospemifene provided significant and reproducible benefit for physiological changes and symptoms associated with VVA and improvements remained consistent between and within the subpopulations of age, race, prior HRT use and uterine status. Oral ospemifene 60 mg is an effective treatment option for postmenopausal women with symptoms (ie, dyspareunia) of VVA.

OC16.2

IMPROVEMENT IN MENOPAUSAL SYMPTOMS WITH LYCORED: RANDOMIZED DOUBLE BLIND PLACEBO-CONTROLLED TRIAL

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Introduction: The onset of menopause and loss of ovarian function are associated with increased prevalence of menopausal symptoms. With the loss of antioxidant activity of estrogen, the redox imbalance is postulated to be involved. Objective: To investigate the relation between menopausal symptoms, cardiovascular & osteoporosis risk and supplementation with lycopene, the most biologically potent free-radical quencher. Methods, conclusion: This multicentric study screened 198 women, recruited 176 postmenopausal women at 19 centers across 12 cities in India for baseline data. 50 women did not enroll and 40 were excluded. These women were randomly assigned to 8mg of Lycopene or placebo supplementation. 8 women did not complete the study. Ethical Committee clearance for the study was taken and informed consent was obtained from each subject prior to enrollment. Demographical details and menopausal symptoms were recorded using a questionnaire. Fasting blood samples were obtained from each subject to analyze blood lycopene levels, lipid markers, CAD marker i.e. High sensitivity C-reactive protein (hs-CRP) and bone markers [aminoterminal propeptide of type 1 procollagen (P1NP) and Beta C-terminal telopeptide (β -CTX-1)] at pre and post supplementation. Blood lycopene levels were lower among symptomatic women, however the difference was statistically not significant. Women with depressive moods, bladder problems and joint & muscular discomfort had significantly higher BMI. In general all symptomatic women had higher hsCRP levels and particularly, those with symptom of bladder problem and vaginal dryness were statistically significant. While for bone turnover markers, β CTX-1 was not associated with symptoms, P1NP was significantly higher in symptomatic women with heart discomfort and depressive moods. After 6 months, percent improvement was better due to Lycopene for symptoms.

OC16.3**ENHANCED CUTANEOUS MICROVASCULAR PERFUSION AS THAT SEEN IN FLUSHING POSTMENOPAUSAL WOMEN IS ALSO SEEN IN HYPOGONADAL MEN WITH FLUSHING**

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Background: Vasomotor symptoms are the most commonly reported symptoms by women in the climacteric and are reported to cause significant morbidity in 25%. A centrally controlled mechanism is proposed, with narrowing of the thermoneutral zone, however, the trigger, as well as full understanding of the mechanisms responsible are still uncertain. We have shown that peripheral vascular reactivity is enhanced in women who flush, and there is work in men with flushes, demonstrating alterations in skin blood flow at the time of a flush; and in both, symptoms are improved with hormone replacement. This suggests that the mechanism may be similar.

Aim: To determine if a peripheral contribution to the mechanism of flushing, as determined by altered skin blood flow in postmenopausal women, is also found in men.

Methods: Skin blood flow was measured using laser Doppler imaging and endothelial function was assessed by iontophoresis (administration of vasoactive agents through the skin by an electric current) of acetylcholine (ACh – endothelium dependent) and sodium nitropruside (SNP – endothelium independent). 10 men (aged 55 to 75) with a new diagnosis of prostate cancer, for whom GnRH agonists are prescribed, had baseline perfusion measurements and measurements after 8 weeks of treatment. 6 men developed flushes and 4 did not. Results: 6 men developed flushes with treatment and 4 did not. At baseline, there was no difference in cutaneous microvascular perfusion in those that went on to develop flushing, when compared to those who did not. However, at 8 weeks, those with flushing had an increased perfusion response compared to non-flushers (ACh, $p < 0.001$ and SNP, $p = 0.005$).

Conclusions: Flushing in hypogonadal men seems to involve enhanced microvascular perfusion, similar to that seen in flushing postmenopausal women.

OC16.4**COGNITIVE BEHAVIOUR THERAPY FOR HOT FLUSHES AND NIGHT SWEATS: PRIMARY AND SECONDARY ANALYSES OF THREE RANDOMISED CONTROLLED TRIALS**

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There is a need for effective and acceptable interventions for women with vasomotor symptoms for whom hormonal treatments are contraindicated and for those with a preference for self management approaches. The results of three recent randomised controlled trials of cognitive behaviour therapy (CBT) for hot flushes and night sweats (MENOS1, MENOS2 and EVA) will be described. These trials include samples of well women (MENOS2 N = 140) and breast cancer patients (MENOS1 N = 90 and EVA N = 422). Results provide consistent evidence of the effectiveness of the interventions (effect sizes 1.19 MENOS1; 1.18–1.41 MENOS2; 0.39–0.56 EVA) upon the problem rating of HFNS. Secondary analyses include the impact of CBT upon physiological HFNS (Sternal skin conductance); the results of qualitative interviews with the women following the final 6 month assessment, as well as secondary analyses of moderators and mediators of treatment effects, which show for whom and how treatments work. Group and Selfhelp forms of CBT had similar positive effects on HFNS (MENOS2) and physiological HFNS significantly reduced for well women but not for breast cancer patients. CBT was more effective in reducing HFNS interference than exercise or usual care for breast cancer patients (EVA). These interventions offer women who have problematic hot flushes and night sweats a safe and acceptable treatment choice. Ayers et al. MENOS 2 trial. *Menopause* 2012;19,7:749–759; Duijts et al. EVA trial *J Clin Oncol* 2012; 30 [33]: 4124–4133; Mann et al. MENOS 1 trial *Lancet Oncology* 2012;13 (3):309–318.