



## Abstracts for 15th World Congress on Menopause

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# Abstracts for 15th World Congress on Menopause

## THE PIETER VAN KEEP LECTURE

### *Are we there yet?*

Rodney Baber (AU)  
University of Sydney, Australia

In June 1976 a group of friends, interested in the health and well-being of women in mid-life, organized The 1st International Congress on the Menopause in the French seaside resort of La Grande Motte. Held under the auspices of The American Geriatric Society and The University of Montpellier, this meeting of members of what was little more than a 'menopause club' heralded the beginnings of what is today The International Menopause Society. The 2nd International Congress on the Menopause, held in Jerusalem in June 1978, a timely meeting as the first of a seemingly never-ending series of menopausal 'controversies', endometrial hyperplasia following unopposed estrogen therapy, had broken out only recently. The 3rd International Congress, held in Ostend, Belgium, was the first conducted under the auspices of The International Menopause Society. Its theme was controversies, a prescient choice as each subsequent IMS Congress has had its own 'issues'.

The IMS was formed and registered in Switzerland in 1978 where it remained until its head office was relocated to the UK in 2014 under the Umbrella of The UK Charities Commission.

IMS' aim is to promote knowledge, study and research on all aspects of aging in women, to organize, prepare and conduct international meetings and congresses on the menopause and to encourage the interchange of research and experience between individual members.

In the 40 years since La Grande Motte, there have been 14 International or World Congresses on the menopause which have attracted not hundreds but many thousands of men and women from all corners of the globe with a common interest – the care and well-being of women. Our mission has always been to work with like-minded colleagues so that we can, together, meet our goals.

The details of those goals and challenges have changed over time as have many of the participants. This paper will celebrate their efforts and achievements on behalf of all of us and the women for whom we care.

## PLENARY LECTURES

### *Cardiovascular disease in women, is it different to men?*

Giuseppe Rosano (GB)  
Cardiovascular & Cell Science Research Institute, St George's Hospital Medical School, University of London

Cardiovascular diseases have become the principal cause of death in women and, unlike for men, mortality rates do not seem to be declining. Many factors are the causes of sex-based differences in incidence and outcome of cardiovascular diseases, including delays in recognizing symptoms, underutilization of diagnostic tests and treatments, as well as anatomic, physiological, and genetic factors.

Evidence of fundamental biological differences in vascular function and the underlying pathologic processes is only beginning to be elucidated, motivated by growing evidence of differences in clinical presentations and outcomes between men and women. Furthermore, the underlying mechanisms of ischemic heart disease in women remain to be elucidated as women have a higher prevalence of sub-endocardial myocardial infarctions, spontaneous arterial dissections, plaque erosion, increased vasospastic disorders, such as coronary microvascular disease, and pulmonary hypertension compared with men.

Conditions other than cardiovascular diseases like Takotsubo Cardiomyopathy and heart failure with preserved ejection fraction are more prevalent in women than in men. Also women have a different response to cardiovascular drugs that may explain the different results of therapeutic interventions in the two sexes.

Ovarian hormone deficiency has a pivotal role in the development of cardiovascular disease and time has come to take a critical look at the results of the randomized studies of hormone replacement therapy and cardio-protection in order to identify which women will benefit and which may receive harm from hormone replacement therapy.

Great progress has been made in understanding gender-related differences in cardiovascular diseases, but much remains to be done to optimize the prevention and treatment for both sexes.

### *Can we prevent the Alzheimer tsunami?*

Harald Hampel (FR)<sup>a</sup> and Simone Lista (FR)<sup>b</sup>

<sup>a</sup>Pierre and Marie Curie University (UPMC); <sup>b</sup>IHU-A-ICM – Paris Institute of Translational Neurosciences

During the past decade, conceptual shifts occurred in the field of Alzheimer's disease (AD) considering the disease as a slowly progressing, non-linear dynamic continuum, amongst a wide

spectrum of neurodegenerative diseases. The future with breakthrough discoveries in AD is likely to emerge through the beginning of transfertilization from more advanced research fields, such as oncology, through the precision medicine, systems biology, and complex network paradigms.

This reintegration of neuroscience and neurology into biological medicine is characterized by advancing biomarker research with substantial methodological developments and discoveries of the comprehensive pathophysiological profile of late-onset sporadic AD. This will allow identifying and characterizing the disease even at the preclinical stage, in which specific pathophysiological abnormalities precede overt clinical symptoms by many years to decades. In this respect, the AD preclinical stage has become a major research focus as the field postulates that early personalized intervention may offer the best chance of therapeutic success. Clarification is needed about comprehensive disease mechanisms, natural history, biomarkers of risk and progression, and the ethical consequence of detection at the asymptomatic stage. In this scenario, the role of neuroimaging and biological markers will become crucial for early individual detection in asymptomatic people at risk. Biomarkers are expected to guide selection for prevention trials and will be crucial as surrogate outcomes. To stop the global AD epidemic we need to move away from the classical "one size fits all" approach in drug development. We are heading towards a new age of prevention with molecularly tailored therapy combinations for biologically stratified preclinical disease subpopulations.

### *The evidence base for HRT – what can we believe?*

Robert Langer (US)

Jackson Hole Center for Preventive Medicine

Prior to the unexpected early termination of the Women's Health Initiative (WHI) trial of conjugated equine estrogens (CEE) and medroxyprogesterone acetate (MPA), the prevailing view was that HRT was a low-risk intervention with immediate value for symptom relief in recently menopausal women, and that it probably conferred long-term protection against the major chronic diseases that affect women after menopause. The widely publicized early WHI papers challenged that expectation.

Critically, the WHI was not designed to test outcomes of HRT initiated near menopause. Rather, it tested whether the associations consistently seen in women who started near menopause would be replicated in women starting long after menopause.

Views of the benefits and risks of HRT changed dramatically with the initial WHI publication. Use plummeted, driven by fear of breast cancer and skepticism about cardiovascular benefits. Stunningly, the contrasting findings of the WHI trial of CEE alone reported 2 years later – suggesting prevention of coronary heart disease in women who began HRT at age <60, and a reduction in breast cancer overall – were largely ignored.

Key lessons from the WHI are that the effects of HRT on most organ systems vary by age and time since last physiologic exposure to hormones, and that there are differences between regimens. In the years since the first WHI report, we have learned much about the characteristics of women who are likely to benefit from HRT. The range of HRT regimens has also increased. Not all women have indications for HRT, but for those who do, benefits are both short-term (vasomotor, dyspareunia), and long-term (bone health, possible coronary risk reduction, possible cognitive protection). Critically, the 'facts' that most women and clinicians consider in making the decision to use, or not use, HRT are frequently wrong or incorrectly applied.

### *Human obesity causes and consequences*

Stephen O'Rahilly (GB)

WT-MRC Institute of Metabolic Science

The genetic component of quantitative metabolic traits is complex with a mixture of common alleles of small effect and rarer alleles of larger effect. We have principally focused on finding the latter through the study of extreme human phenotypes of obesity and insulin resistance, including lipodystrophy. By applying both candidate and hypothesis-free genetic approaches we have identified multiple different genetic variants that cause highly penetrant forms of these diseases. Through detailed phenotypic studies in humans and relevant murine and cellular models, these disorders continue to provide new insights into the physiology and pathophysiology of energy balance and metabolism.

### *What is the role of bariatric surgery in the management of obesity?*

Eleftheria Panteliou (GB) and Alexander Miras (GB)

Imperial College London

Diet, exercise, cognitive behavioural therapy and pharmacotherapy are some of the means assisting patients to lose weight, with bariatric surgery being the most effective. Over the last two decades the increased awareness of the systemic benefits of bariatric surgery as well as the improved safety and the wider use of the laparoscopic approach has made bariatric surgery flourish. In the United Kingdom (UK), the adjustable gastric band (AGB) (10%), vertical sleeve gastrectomy (VSG) (37%) and Roux-en-Y Gastric Bypass (RYGB) (45%) are the three commonest procedures. Obesity associated mortality and co-morbidities such as Type 2 Diabetes, hypertension, dyslipidaemia, obstructive sleep apnoea, renal dysfunction and depression improve significantly with bariatric surgery. The mechanisms of weight loss extend beyond restriction and malabsorption and include changes in hunger and satiety, food preferences, and possibly energy expenditure. Despite its safety and efficacy, bariatric surgery is underutilised as less than 1% of adults with obesity receive it. In view of the evolution of obesity into a global threat access to bariatric surgery should be increased, whilst developing safer and less invasive weight loss treatments.

### *Future strategies for fracture prevention*

Tobias De Villiers (ZA)

Stellenbosch University

Osteoporosis-related fractures are common, age-related and a huge burden on healthcare resources. The impact of currently available agents is limited by poor uptake, side effects and high cost. There is a need to develop better drugs to address these limitations. Odanacatib (ODN) is an inhibitor of cathepsin K, the main osteoclast-derived protease involved in the resorption of bone. Inhibition of bone resorption is achieved without decreasing the numbers or activity of osteoblasts. In a phase 3 trial, ODN 50 mg given orally once weekly increased bone mineral density and significantly reduced the risk of vertebral, hip and non-vertebral fractures compared to placebo.

Abaloparatide is a new synthetic peptide analog of human parathyroid hormone-related protein, a naturally occurring bone anabolic hormone. In an 18-month phase 3 placebo-controlled trial, abaloparatide significantly increased bone mineral density from baseline at the lumbar spine by 9.2%, the total hip by 3.4% and the femoral neck by 2.9%. Abaloparatide also reduced new vertebral fractures by 86%, nonvertebral fractures by 43% and major osteoporotic fractures by 70%. Compared to teriparatide, abaloparatide reduced major osteoporotic fractures by 55%, without causing hypercalcemia.

Romosozumab and blosozumab are two sclerostin inhibitors in clinical development. Sclerostin is an osteocyte-derived inhibitor of osteoblast function. Natural sclerostin deficiency results in a phenotype of high bone mass and excellent bone quality. A phase III study in postmenopausal women with osteoporosis showed that the percent change from baseline in BMD at the total hip was significantly greater when treated with romosozumab compared with teriparatide. Fracture prevention studies are underway.

It is hoped that these novel therapies will have a significant impact on the prevention of fractures.

### *Lifestyle approaches to prevent falls, fractures and frail bones: an update of the evidence*

Robin Daly (AU)

Deakin University

Regular exercise combined with adequate nutrition are regarded as important lifestyle approaches to prevent and manage osteoporosis (low bone strength) and sarcopenia (low muscle mass, muscle strength and/or impaired function). Both these conditions often coexist (hence the term 'osteosarcopenia') and have similar health consequences with regard to disability, falls, frailty and fractures. While exercise is one of the few strategies that can simultaneously have a positive effect on all these parameters, not all forms are equally effective, with the benefits being modality and intensity-dependent, and reliant upon adequate nutrition, particularly with regard to vitamin D, calcium and protein. This presentation will provide an overview of the facts, myths and truths about the role of different types of exercise and nutritional factors for optimizing musculoskeletal health and function during ageing. The specific objectives are to: 1) describe the clinical consequences of osteosarcopenia and frailty and how it can be assessed; 2) review the latest evidence with regard to the optimal type and dose of exercise to prevent osteosarcopenia, falls, frailty and fractures; and 3) outline exercise-nutrient interactions that may optimize musculoskeletal health and function to reduce falls and fracture risk in the elderly.

## **CONTROVERSIES**

### **Can women at risk of cardiovascular disease be treated with hormone therapy?**

**Yes**

Mary Ann Lumsden (GB)

University of Glasgow

After the publication of WHI in 2002, it became accepted that HRT should not be used to treat women who were at increased

risk of heart disease. This was because the original publication suggested that it increased the risk of CVD as compared with placebo. This presented a problem for many doctors working in communities where the risk of CVD is very high, e.g. the West of Scotland, as an overwhelming majority of women have some increase in cardiovascular risk which may be due to hypertension, abnormal lipids, Type 2 Diabetes or obesity.

However, the results have now been reanalysed and reviewed several times and in the final paper from 2013, it was concluded that these results were misleading and resulted from the fact that 2/3rds of the women were over 60 and thus not representative of those who usually take HRT, i.e. symptomatic women in their early 50s. Although sub-group analyses need to be treated with caution, further evidence has emerged to suggest that there is a 'window of opportunity' and if women are commenced on HRT around the age of the menopause, then it may even offer a degree of protection.

Type 2 Diabetes is a major risk factor for cardiovascular disease. Synthetic steroids, such as those found in the combined oral contraceptive pill, may have a detrimental effect on disease control. However, this does not appear to be true for HRT where systematic review and meta-analysis demonstrate improved control. In addition, cohort studies in the US have documented a delay in onset in women taking HRT. Hypertension is another significant risk factor in women and overall, HRT does not lead to an increase in blood pressure. The beneficial effect of oestrogen on lipid profiles is also well known.

Thus, it is only possible to conclude that women should not be denied HRT. In fact, it is not just those who are strong advocates of HRT who would argue to the contrary

**No**

Richard Santen (US)

Division of Endocrinology and Metabolism, University of Virginia Health Science System, Charlottesville, Virginia, USA

Extensive biologic studies of the effects of menopausal hormone therapy (MHT) on cardiovascular disease (CVD) have led to the hypothesis that the effects differ, depending on the age of the patient. In younger women with minimal coronary artery plaque formation, estrogens enhance endothelial function and reduce the formation of early atheroma through induction of Cox-2, prostacyclin, and other factors. In older individuals who have developed coronary plaques, estrogens destabilize the plaques resulting in plaque rupture, local site thrombosis and acute coronary syndrome. Inflammation and matrix metalloproteinases have been suggested to contribute to this process. Based on an understanding of the underlying biology, the "timing hypothesis" has been put forward suggesting that treatment of young women with MHT may reduce the risk of myocardial infarction and overall cardiac events whereas MHT increases the risk in older women. Trends reported from the intervention phase of the WHI study support this concept as benefit gradually shifts to risk in women as they start MHT at increasingly longer times after menopause. WHI data compared women starting MHT <10 years after menopause onset, 10–20 years after, and >20 years after. For use of conjugated estrogen plus medroxyprogesterone acetate the CVD hazard ratios were: 0.90 (0.56–1.45), 1.19 (0.83–1.70), and 1.52 (1.07–2.17) respectively and for conjugated estrogen alone 0.50 (0.22–1.18), 1.0 (0.60–1.40) and 1.08 (0.83–1.40) respectively. The methods to predict cardiovascular risk in women (i.e. Framingham, Reynolds, ATPIII, and AHA-ACC-ASCVD risk models) are likely evaluating the underlying development of plaque present. This hypothesis is based on the fact that the percentage of plaque increases with age from 10% at ages 35–44, to

18% at 45–54, to 40% at 55–64, to 62% at 65–74 and to 81% at 75–84 as does the age incidence of coronary artery disease. These considerations led the Endocrine Society in its guidelines to advise avoidance of MHT in women with a high 10-year predicted risk of cardiovascular disease of >10% and to suggest the choice of transdermal in those with a moderate risk of 5–10%. In those with a low risk of <5%, MHT was recommended in those with symptoms. A modulating factor is that estrogen alone generally appears to have less risk of increasing coronary events than does estrogen plus a progestogen. It should be noted that the various risk models vary in predictive accuracy and are likely country and population specific. A simplified methodology is proposed in this presentation to guide decision making, the use of the calculated cardiovascular age of a patient. With younger cardiovascular ages, MHT is reasonable in symptomatic patients but gradually becomes contraindicated with older ages. Methodology for calculating cardiovascular age will be presented. Conclusion: MHT should not be prescribed in women with advanced cardiovascular age (CVA) but is reasonable in those with younger CVA.

## Can we effectively treat menopausal symptoms without hormones?

### *A non-hormonal pollen extract for VMS: is there credible data?*

Santiago Palacios (ES)

Palacios Institute of Women's Health

Women around the world experience vasomotor symptoms when they start and complete the menopausal transition, these being recognized by patients and physicians as the most characteristic and troublesome menopausal symptoms.

Hormone therapy for menopause (THM) is the most effective treatment. However, given its potential adverse effects and contraindications, many symptomatic women are unable or unwilling to take THM. Therefore, natural products without any estrogenic action are a new option in the great stockpile of handlings for menopausal symptoms.

Purified and specific pollen cytoplasm (PSCP) are extracted from selected species (Poaceae, grasses). The cultivation and harvesting are carried out in fields that are separated by types of plants according to the recommendations of the European Medicines Agency.

Its mechanism of action is probably through CNS due to tryptophan content of pollen, it has been shown to have no estrogenic effect and does not interfere with tamoxifen metabolism.

It has been evaluated in several studies including three double-blind, placebo, compared clinical trials to where it has demonstrated its value in the treatment of menopausal hot flashes and night hot flushes. In one controlled trial, double-blind, randomized, compared with placebo, conducted in a period of three months showed a statistically significant difference ( $p < 0.006$ ) in favor of EPCP compared to placebo and a significant improvement ( $p < 0.031$ ) in all parameters of quality of life of women who received treatment. These results have been confirmed in two randomized, placebo-controlled trials with 32 and 101 women. In all studies EPCP has proven to be well tolerated and as safe as placebo.

PSCP can be used as non-hormonal treatment for relief of hot flashes in women with breast cancer in addition to showing a good tolerance and significant increase in the quality of life and sleep.

## *Other herbal preparations for the menopause (beyond isoflavones and black cohosh)*

Herman Depypere (BE)

University Hospital

The fruit-oil of the *Vitex agnus-castus* binds to the estrogen receptor is attributed to the presence of linoleic acid which induces certain estrogen-dependent genes. This substance seems to exert some dopaminergic action, but a favorable effect on menopausal symptoms could not be evidenced. The most important flavonoid extracted from hop (*Humulus lupulus*) is 8-pregnylnaringenin(8-PN). In vitro this molecule has an up to 100-fold stronger estrogenic action than the soy isoflavones. There is some evidence that 8-PN may be efficacious against vasomotor complaints. Diosgenin is the saponine extracted from the *Dioscorea villosa* (wild yam) and does not bind to the human estrogen receptor. *Dioscorea* may be given to women who have been treated for breast cancer. A significant favorable effect of *Dioscorea* extract on menopausal symptoms has been observed. Linseed or flaxseed (*Linum usitatissimum*) extract was moderately effective on menopausal vasomotor symptoms. Linseed extract increases the 2OH/16OH-oestrogen ratio more effectively than the soy-isoflavones. The extract of the bark of the (Mediterranean) pine tree is rich in anthocyanidins with antioxidant effect, and it reduces inflammatory reaction through the inhibition of the Cyclooxygenase (COX) enzymes 1 and 2 and of the Nuclear Factor kappa B (NF-kB). In 3 randomized double-blind trials PycnogenolR was found to significantly reduce vasomotor symptoms. Also, Broccoli extract is an important source of sulforafane that has a demethylating effect, influences the epigenoma, and protects against (breast) cancer. *Lepidium meyenii* has been tested against menopausal symptoms, and was found to reduce the Kupperman Menopausal Index and the Greene Climacteric Score in a controlled trial. Tolerability is excellent.

## *Is there a place for isoflavones and black cohosh in menopausal management?*

Mohamad Darmasetiawan (ID)

Pembangunan National University/UPN

Menopause is a natural phenomenon for every woman. Due to reaching such menopausal age, in conjunction with the decrease of estrogen, starting from climacteric symptoms related to the quality of life to osteoporosis fracture which is a quite serious long term complication. The best choice as well as the gold standard management of climacteric symptoms and osteoporosis prevention is an HRT. The misperception of developing breast cancer and the contra-indication for HT make Phytoestrogen as the alternative of choice. Phytoestrogen is known to be divided into many groups, such as Genistein and Black Cohosh, among others, which work at different receptors.

*Material and method:* The aim of the study is to find the role of phytoestrogen (combination of Genistein + Black Cohosh) at climacteric symptoms and bone strength and to find out whether there is a possibility of synergism between these two phytoestrogens. The research is conducted as RCT study using a Factorial Design and multivariate analysis of variance (statistic analysis). The independent variables are made into 4 groups and conducted by giving 4 kinds of research tablets in the same and identical packaging. The dependent variables are

Menopause-Quality of Life, Bone Turn-Over, N-Mid-Osteocalcyn, CTX, RANKL, Osteoprotegerin, and Bone Mineral Density.

**Result and Conclusions:** This research failed to show that both agents could improve climacteric symptoms ( $p > 0.05$ , Friedman Rank). It also cannot prove synergism process by giving the combination of Genistein and Black Cohosh. Genistein does not show any benefit in reducing climacteric symptoms. In vasomotoric symptom, Genistein tends to increase the complaint significantly. This phenomenon is reminiscent of the SERM mechanism. The Genistein can lower down the bone resorption through a suppressed mechanism of coupling osteoclast activity

## Common vulval conditions in peri- and postmenopausal women

### *Vulvar lichen sclerosus – early recognition and treatment*

Faustino Perez-Lopez (ES)

University of Zaragoza and Lozano-Blesa University Hospital, Zaragoza, Spain

Vulvar lichen sclerosus (VLS) is a chronic and inflammatory skin condition of unknown origin highly prevalent during low-estrogen physiological states, such as perimenarch and the postmenopause. During the second half of life it affects one out of 70–90 women. It can cause itching, pain, bruising, and scarring. In its most severe forms, pain is continuous or exacerbated by micturition or defecation, and sexual intimacy is very painful. Despite this, women can also be completely asymptomatic, and the anogenital area be thin and white and skin be wrinkled. During the early phase of the disease the vulvar anatomy may be preserved; however, as the disease progresses the distinction between the labia majora and minora becomes difficult and the clitoris may present phimosis. The coexistence with pre- or malignant conditions increases with years of evolution. The presence of such lesions may require specific surgical management. Differential diagnosis also includes lichen planus and lichen simplex chronicus and local infections. The management of VLS includes corticosteroids or calcineurin inhibitors. Topical androgens, progesterone or estrogens have not shown benefit for VLS. Long-term preventive topical treatment of VLS aiming at reaching the normality of skin color and texture may reduce symptoms, scarring, and vulvar carcinoma risk.

### *Vulvodynia – causes and management*

Hope Haefner (US)

University of Michigan Health System, USA

**Objectives:** To understand the current classification system for vulval pain (2015 Consensus Terminology and Classification of Persistent Vulvar Pain) developed by the International Society for the Study of Women's Sexual Health, International Society for the Study of Vulvovaginal Disease, and the International Pelvic Pain Society with support from the National Vulvodynia Association; To explore the various causes of vulvodynia; To gain knowledge on the treatments utilized for localized and generalized vulvodynia.

**Methods:** A review of the basic science behind vulvodynia will be provided. New thoughts on potential causes will be discussed. Routine, as well as some investigative treatments for vulvodynia will be explored.

**Results:** A number of subcategories of vulvodynia exist. Treatment for the various subcategories differs.

**Conclusions:** Vulvodynia is a condition that is challenging for patients and health care providers. The pain and discomfort of vulvodynia affects the quality of life of many women. Pain can be continuous or intermittent, often aggravated by activities such as sitting at a desk, bicycle riding, and sexual intercourse. While research in this topic has increased over the last 40 years, further investigation is needed to optimize the care of women with vulvodynia.

Additional information available at: <http://pelvicpain.org/getattachment/703546fa-a1c6-435c-8e8c-1c8300f43187/Consensus-terminology-of-persistent-vulvar-pain.pdf.aspx>; <http://obgyn.med.umich.edu/patient-care/womens-health-library/vulvar-diseases/information>

## Do hormones cause thrombosis?

### *Can the menopause cause thrombosis?*

Jan Rosing (NL)

Cardiovascular Research Institute Maastricht, Maastricht University

Venous thrombosis (VT) is associated with genetic risk factors (affecting the haemostatic system) and acquired risk factors (e.g. age, trauma, immobilisation, changes of female sex hormones). The incidence of VT is higher in women at childbearing age than in men of similar age, while at higher age the incidence in men is higher. The higher incidence in young women is likely caused by changes in female sex hormone levels during oral contraceptive (OC) use and pregnancy. A biological explanation for the thrombotic risk associated with changes of female sex hormone levels has been lacking for a long time.

This changed when in the 1990s several new risk factors for thrombosis were discovered. At the same time it was reported that women using OC containing third generation progestagens were exposed to an ~1.5 to 2-fold higher VT risk than users of second generation OC containing levonorgestrel. Since then a large number of studies were published on the effect of female sex hormones on haemostasis parameters. These studies showed that OC, HRT and pregnancy have similar effects on coagulation parameters and cause acquired APC resistance, elevated levels of clotting factors and decreased levels of anti-coagulant proteins, together resulting in a prothrombotic condition that can explain the increased risk of VT associated with OC use, HRT and pregnancy. The studies further indicated that the estrogen component of hormonal preparations has a prothrombotic effect and that progestagen actually has an antithrombotic effect that partially counteracts the prothrombotic effect of estrogen. Furthermore, it appeared that third generation progestagens were less antithrombotic than second generation progestagens which resulted in more pronounced unfavorable effects on the haemostatic parameters explaining why third generation OC expose women to a higher VT risk than second generation OC.

### *Do progestogens influence the risk of thrombosis?*

Marianne Canonico (FR)

Center for Research on Epidemiology and Population Health (UMR-S 1018), Inserm and Paris-Sud 11 University, Villejuif Cedex, France

Despite a decrease in postmenopausal hormone therapy (HT) use over the last decade, this treatment, which remains the most effective for correcting climacteric symptoms, is still used by million women worldwide. HT initially consisted of estrogens alone and progestogens were secondly added to estrogens for preventing the risk of endometrial cancer associated to estrogens use. Venous thromboembolism (VTE), including deep vein thrombosis and pulmonary embolism, is a major harmful effect of HT.

There is now strong biological, clinical and epidemiological evidences for a safety of transdermal, but not oral, estrogens on VTE risk. Nevertheless, progestogens may also be an important determinant of VTE risk among postmenopausal HT users.

Comparison of VTE risk among users of estrogens and estrogens plus progestogens shows that adding progestogens significantly increases the thrombotic risk in both oral and transdermal estrogens.

In addition, data have suggested that the VTE risk associated with progestogens is different according to the pharmacological classes of progestogens. Norpregnanes derivatives, but not other groups, are associated with an increased risk of thrombosis.

With respect to the different molecules within pharmacological classes, data are scarce and concern micronized progesterone, the natural molecule, and medroxyprogesterone (MPA), a specific pregnane derivative mostly used in USA. While micronised progesterone seems to be safe with respect to VTE risk, MPA, which has been evaluated within direct and indirect comparisons, may be associated with an increased thrombotic risk.

In conclusion, both the route of estrogen administration and the progestogens are important determinants of VTE risk among HT users.

## Contraception during female midlife

### *The impact of hormonal contraception over bone mass*

Martin Birkhäuser

Professor Emeritus of Gynaecological Endocrinology and Reproductive Medicine, University of Berne, Switzerland

Mean endogenous oestradiol (E2) is decreasing during menopausal transition. As a consequence, bone remodelling is changing and the increasing dominance of bone resorption over bone formation resulting in bone loss. There is evidence from observational studies that bone loss due to oestrogen deficiency can be prevented by combined oral hormonal contraceptives (COC) delivering 30–35 µg ethinylestradiol (EE) per day. Still controversial is the effect of low-dose COC (20 µg and 15 µg EE per day) in women aged  $\geq 45$  years. There are data from adolescents (aged 16–19 years) suggesting that low-dose EE might be insufficient in presence of low endogenous E2 levels or/and an instable hypothalamic pulsatile centre. Both situations might occur in the period of menopausal transition. Concerning bone, no reliable epidemiological data are available for the combined contraceptive patches and vaginal rings.

The effect of progestin-only contraception on bone remains unclear. No data are available for the desogestrel-only pill and the etonorgestrel-implant, and no data for the classical mini-pill containing levonorgestrel. No data either are found for progestin-loaded IUDs. On the other hand, data exist for depot-medroxyprogesterone-acetate (DMPA) showing that bone mineral density (BMD) is reduced and the incidence rate ratio for fractures significantly increased in DMPA-users. Reduction of BMD seems to be reversible after stopping DMPA. However, DMPA use should be limited to 2 years.

In conclusion, in women over 45, COC with  $>30 \mu\text{g/day}$  would be the safest hormonal contraception if bone only is considered and if the patient does not present any contraindication against a 30-µg-pill.

## Basics in biostats: understanding the published literature and introduction to study design

### *Statistics can be surprisingly interesting: understanding the published literature*

Robin Bell (AU)<sup>a</sup> and Robert Langer (US)<sup>b</sup>

<sup>a</sup>Monash University, Melbourne, Australia; <sup>b</sup>University of Nevada School of Medicine, USA

*Objective:* There is a need to improve the scientific literacy of clinicians and trainee doctors. Whether you are reading the literature or contemplating your own research, understanding issues associated with study design and statistical analysis is crucial. Furthermore, rather than having clinicians feel intimidated by epidemiology and statistics, our aim in this session is to inspire clinicians about the power of these tools.

*Methods:* The speakers will provide a framework for their discussion and then use examples from the published literature.

*Results:* We will present pitfalls in study design, execution, analysis and interpretation and discuss alternative approaches.

*Conclusions:* We aim to remind clinicians of the need for critical appraisal in their reading and careful planning in their approach to their own research. However, we also aim to pique your interest in epidemiology and statistics such that you may even want to explore these fields for your own interest.

## Ovarian insufficiency before 40 – what's new?

### *Does POI increase CVD risk?*

Svetlana Vujović (RS)

Medical Faculty, University of Belgrade, Clinic of Endocrinology, Diabetes and Diseases of Metabolism, Clinical Center of Serbia, Belgrade

Gonadal steroids are essential for quality of life. In premature ovarian insufficiency (POI) (amenorrhoea, FSH  $>40 \text{ IU/L}$ , estradiol  $<50 \text{ pmol/L}$  in women younger than 40 years of age) markedly decreased gonadal steroid levels initiate cardiovascular diseases (CVD). Typical symptoms and signs are: irritability, depression, lack of concentration, insomnia, hot flushes, loss of libido, pain in muscles and bones, etc. Multifactorial and multilevel changes induced by hypoestrogenism include: 1. Lipid changes: increase of cholesterol, low density lipoproteins, decrease of hepatic excretion of apolipoproteins, etc. 2. Insulin sensitivity decrease: abdominal obesity and adipocyte proliferation, metabolic syndrome induce gaining weight of app. 5–6 kg and fluid retention. 3. Changes in blood vessels: smooth muscle cells and collagen changes in blood vessels induce changes in intima-media thickness ratio. 4. Proinflammatory status is induced by increase of proinflammatory cytokines and changes in plasminogen activator inhibitor. 5. Sympathoadrenal system changes: increased activity of sympathetic system. 6. Transient hypertension is induced by vasoconstriction, activation of renin-angiotensin-aldosterone

system, hyperaldosteronism, hypokalaemia, sodium retention, dysfunction of autonomous nervous system, endothelial dysfunction, decreased arterial elasticity and myocardial fibrosis and necrosis. Oxidative stress and prothrombotic activity are present and ventricular arrhythmias can occur. POI represents independent risk factor for CVD. Urgent, prompt estro-progestagen therapy is needed at the time of diagnosis until the natural age of the menopause, at least. Androgens are added to women with bilateral adnexectomy and hypoactive sexual desire. Therapy with gonadal steroids improves quality of life, protects from CVD and decreases mortality rate.

## Disorders of sleep

### *Sleep and aging in women*

Julie Carrier (CA)

Université de Montréal

Many sleep characteristics change acutely as early as during one's thirties and forties, while others change gradually throughout a woman's life span. Recent studies identified cerebral mechanisms underlying age-related changes in sleep and their functional consequences. For instance, studies put in evidence important changes in non-rapid-eye-movement (NREM) sleep oscillations in the middle years of life. Furthermore, challenging conditions (such as shift work, jet lag, and caffeine) more easily disrupt sleep in middle-aged and older individuals. Importantly, NREM sleep oscillations and REM sleep are linked to cerebral and cognitive integrity in aging. However, the mechanisms eliciting sleep disturbances during the menopausal transition are still poorly understood. Lately, large population-based studies assessing both objective and subjective sleep variables in women contributed to a better understanding of sleep in middle-aged women. However, heterogeneity between studies still prevents drawing robust conclusions on the factors making middle-aged women more at risk for sleep disturbances and precludes filling the major gaps in the knowledge necessary to significantly reduce sleep difficulties in women during the menopausal transition. Due to the multivariate nature of the research questions and since ecological sleep studies require much expertise and financial resources, an international multisite effort is necessary to understand the complex associations between menopausal transition and subjective and objective sleep quality in women.

### *What are the consequences of not enough sleep?*

Torbjörn Åkerstedt (SE)

Karolinska Institute

Acute experimental loss of one night's sleep will result in high levels of sleepiness, reduced performance on tasks that require sustained attention (e.g. driving) and an increased accident risk. The effects are noticeable up to 5 h of obtained sleep. Repeated partial sleep restriction will lead to similar, but gradually increasing effects if the the sleep obtained is 6 h or less. Shorter sleep will cause a steeper increase of impairment. Habitual short (5 h or less) or long (>8 h) are associated with increased mortality, but with short sleep there is also a subgroup of "efficient" sleepers that do not have an increased risk. There seems to be no gender differences in the effects discussed above, but women seem to sleep "better" than men (more deep sleep and less superficial sleep), particularly at higher age. Women also seem better at responding to sleep loss

in terms of increases of deep sleep. Women are relatively good at estimating their physiological sleep quality but with increasing age poorer subjective sleep tends to be rated as good sleep. It is not yet clear how the good physiological sleep squares with the higher level of sleep complaints in women.

## SYMPOSIA

### *Hormones and the heart: do they help or hurt?*

#### *Estrogens*

Maria Grazia Modena (IT)

Università Modena Reggio Emilia

Extensive epidemiological observations, clinical mechanistic studies, and basic laboratory research have suggested that the incidence of cardiovascular disease increases with menopause and that hormone replacement therapy (HRT), or more specifically, estrogen replacement therapy (ERT) is associated with beneficial cardiovascular effects in postmenopausal women. Estrogen has a multitude of biological effects that may account for its apparent cardiovascular protection, including favorable effects on the lipid profile, antioxidant activity, enhanced fibrinolysis, and a series of actions on the vasculature. However, because estrogen affects so many cellular processes, it is imperative to gain a better understanding of the molecular mechanisms, both genomic and non-genomic, by which estrogen induces cellular signals and modulates vascular responses. While there is no question that HRT effectively mitigates troublesome menopause symptoms, conflicting evidence about other effects of HRT has fueled controversy concerning its relative benefits and risks. Moreover, it could seem that CVD protection mediated by replacement therapy is maximum when the therapy was initiated in the absence of signs of atherosclerosis (typically in pre-menopausal) while it vanishes as atherosclerosis proceeds (postmenopausal). In addition, many questions remain regarding the effectiveness of type of hormonal compounds, doses, regimens, route and, mainly, on time of administration. There is evidence from most recent literature that early menopause and not menopause per se is a risk factor for CVD and that early ERT may have a role on delay atherosclerosis process in post menopausal women. We may conclude that is not time yet to write the word "End" on the chapter of the role of estrogens in women protection in menopause

### *Androgens and cardiovascular health in women*

Susan Davis (AU)

Monash University

Androgens, including testosterone (T), are essential precursors for estrogen biosynthesis, with the main source of estrogen production in postmenopausal women being conversion of androgens to estrogens in non-gonadal tissues. At physiological concentrations T has favourable direct effects on vasomotor tone, endothelial function and peripheral vascular resistance through direct effects on the vessel wall. T improves arterial function by enhancing endothelium-dependent (flow mediated) and endothelium-independent brachial artery vasodilation. Whether endogenous T protects against CVD (ischaemic heart disease and ischaemic

stroke) and death is uncertain. Most, but not all studies, have shown that low T increases CVD risk. These studies have significant limitations including small sample size, recruitment of convenience, clinic-based samples, case-control design and long intervals between the time of blood draw and CV events. Furthermore, the association between androgens and CVD risk cannot be interpreted in isolation from the effects of sex hormone binding globulin (SHBG). This protein binds T with high affinity, such that only 1–2% of T circulates unbound (free). Originally thought to be a simple sex hormone transport protein, SHBG has been identified as an independent risk factor for type 2-diabetes and CVD. Only one study has reported on exogenous T therapy in women with existing CVD. Lellamo and colleagues randomised 36 women with severe congestive cardiac failure to transdermal T/placebo for 6 months<sup>1</sup>. The T-treated group demonstrated significant improvements (vs placebo) on the 6-minute walk test, oxygen consumption and insulin resistance; each of these is associated with better prognosis. This study supports the need for a better understanding of the role of T in the pathogenesis of CVD in women.

## Reference

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## *Cardiac mortality risk in relation to the progestin component of hormone therapy*

Tomi Mikkola (FI)

Helsinki University Hospital

Coronary artery disease (CAD) remains the leading cause of morbidity and mortality among women in Western populations. New clinical trials and epidemiological studies suggest that postmenopausal hormone therapy (HT) reduces the incidence of CAD in recently menopausal women. The progestin component of HT, and particularly medroxyprogesterone acetate (MPA), has often been blamed for the failure of HT in prevention of CAD. We studied if the various progestins as part of estradiol-based HT were any determinants for the CAD death risk by using a large nationwide patient series, with more than 3 million HT exposure years and 9 million follow-up years.

Our data indicate that the use of estradiol-based HT was accompanied with larger reductions in cardiac death if initiated before 60 years of age. However, 60 years of age at the initiation of HT is not a threshold age, but the earlier the HT had been started, the smaller was the cardiac mortality risk. Thus, our findings support the “timing hypothesis” but not the “window hypothesis” since we did not detect a cardiac mortality risk increase when HT was initiated after 60 years of age. In our study, dydrogesterone, being a less androgenic progestogen than e.g. MPA, and thus in theory, more beneficial for the cardiovascular system, showed a non-significant tendency of being more beneficial than the other HT regimens when started in recently menopausal women. Otherwise, in combination with estradiol the different progestins appeared to possess a rather similar “timing effect” in CAD death risk. These findings imply that the younger the women are at the initiation of estradiol-based therapy, the smaller is their cardiac mortality risk. The progestin component of HT does not modify this “timing effect”.

## *Meeting the challenge of health equity for menopausal women across the globe*

### *Healthcare for aging women in India – bridging the gap*

Duru Shah (IN)

Gynaecworld

Population ageing is one of the most discussed global phenomenon in the present century with women over 60 years in India in 2011. In the next four decades in India is 67 million by 2021, 89.24 million by 2031 and 150.48 million by 2051. In India 85–87% women above 60 years are economically dependent.

India is undergoing a demographic transition with the young population being one of the largest in the world, and simultaneously due to better life expectancy, the older population is simultaneously increasing. Lack of health awareness, inadequate healthcare facilities and financial constraints are the major contributory factors for the poor health of the elderly in India. Medical insurance schemes and Government policies do exist, but the needs of ageing women are not being met. Current existing gaps include under 3% GDP spent on health which should have been 5–6% as per WHO guidelines.

The Government policies have not been actively promoted in the past due to economic reasons. But with India now becoming more self-sufficient, various programs for older women have been initiated. Several NGOs are now significantly involved in providing care and support to the elderly.

The Indian Menopause Society has created awareness programs for midlife women to sensitize women on preventive healthcare.

The International Menopause Society has worked on developing a Mobile App which women can use to assess their own risk for non-communicable diseases (NCDs) as they age. This App will go a long way to educate millions of women on their risks, will sensitize them on healthy lifestyles, will assist in collating data which does not exist in many developing countries and will help in maintaining long term data of individual women, thus helping to understand the progress of NCDs in every ethnic population

### *Attitude and know-how towards menopause and menopause management among Chinese women and medical workers*

Qi Yu (CN)

Peking Union Medical College Hospital, Peking Union Medical College

With the accelerated pace of aging, the population of menopausal women in mainland China exceeds 200 million. However, the awareness of menopause and related treatment among Chinese menopausal women and physicians is limited. The average age of natural menopause among Chinese women is  $49.2 \pm 3.3$  years. The data show that nearly 78.4% of women suffered from menopausal symptoms during the menopausal transition. Though MHT is the most effective therapy for menopause symptoms, its acceptance is very low in China: only 1% in 1990s. The Chinese Menopause Society (CMS), Chinese Society of OBGYN was founded in 2001. Since that time, CMS has devoted itself to popularize the knowledge about menopause and MHT. In 2013, the society published the “Standard Road Map of

Menopause Management” and a new version (4th version) of “The guideline of Menopause Management in Mainland China”. Based upon the road map and the guideline, we promoted the setting up of menopause clinics by the name of the Menopause Activation Project (MAP) countrywide.

To investigate the awareness of menopause and MHT and prompting the skill of clinical practice among physicians in menopause clinics, a multi-center, cross sectional, face to face survey was carried out in 2013. The interviewees include 194 clinical physicians from 100 MAP hospitals in 42 cities. Over 60% of physicians been interviewed reported that most or a majority of the patients had good compliance with MHT. Over 90% of the physicians were familiar with the guideline and the road map, and about 70% reported that they followed the guidelines and complied with recommendations. About 92% of the patients in MAP clinics preferred to use MHT for treatment of menopause-related symptoms. Another investigation in PUMCH showed that PUMCH staffs knew better about the indication and complication of MHT. The use of MHT was also better than average.

### *Meeting the needs of women at midlife in Latin America*

Peter Chedraui (EC)

Institute of Biomedicine, Facultad de Medicina, Universidad Católica de Santiago de Guayaquil

Mid-life is a vulnerable period for women in which there are changes marked by end of the reproductive stage with the menopause. Due to this there are bio-psycho and social changes that increase the prevalence of menopausal symptoms, sexual dysfunction and chronic diseases (i.e. diabetes, hypertension, osteoporosis) that significantly impair female quality of life (QoL). These facts have well been delineated in developed countries, with less being reported from non developing countries, specifically Latin America (LA; including Central and South America). Nevertheless, for more than ten years epidemiological research of mid-life problems of LA have well been described by our research network for the study of the climacteric in LA (REDLINC). Reports indicate that female mid-life of women from Latin America does not differ for that of Europe or the US; however, poverty conditions seem to enhance many of these. For instance we have reported in mid-aged women high rates of the metabolic syndrome (METS), sexual dysfunction and menopausal symptoms, specifically muscle and joint problems. We have recently carried out a second phase of the OMEGA project with the participation of various South American study sites, and found that depressive symptoms were highly prevalent and related to ethnicity. This presentation aims at presenting data from LA related to mid-life problems and presents cost-effective proposals to counteract these problems, intending to meet the specific needs of these affected women. Sociodemographic, education and economic conditions interact with women’s health.

### *Meeting the challenge of menopause in South Africa*

Nicole Jaff (ZA)

University of the Witwatersrand

Apartheid in South Africa lasted for over 40 years, segregating people by ethnicity and discriminating against people of colour, significantly affecting the healthcare system. In 1994, the African

National Congress promised changes to the system. Access to healthcare, in relation to communicable diseases has improved, but general healthcare quality continues to deteriorate for several reasons, including the burden of non-communicable diseases (NCDs), HIV infection and tuberculosis. The high prevalence of HIV infection in South Africa means this is a primary focus in public healthcare. The system is under pressure to deliver services to approximately 84% of the population and there is a severe shortage of doctors and trained personnel. In South Africa 81% of women are black, over 4 million women are 40 to 59 years old, but reproductive aging has not been a principal concern. Western data describe a high risk for NCDs in midlife women, and recent South African research has shown that the prevalence of NCDs and obesity is high in this group. Although the Department of Health has identified a need for both information on and management of the menopause transition (MT), specific guidelines are not readily available, and there is scant understanding of possible health risks associated with the MT in African women, although these risks are commonly explained in healthcare systems in high resource countries. General healthcare screening is not the norm in this population, and this cost may be beyond the scope of the system. There is an urgent need to identify NCD risks amongst these women, especially those with HIV infection. Identifying and implementing appropriate lifestyle interventions such as healthy eating, regular exercise, cessation of smokeless tobacco use and education on the MT and associated risks, may improve the risk for metabolic syndrome in this population.

### *Challenges in breast cancer*

#### *Do all progestogens increase breast cancer risk?*

Alfred Mueck (DE)

University Women’s Hospital

The WHI has been the only large double-blind placebo-controlled study testing the risk of breast cancer (BC) using HRT. No increased risk for women using estrogen (E)-only was seen, even a significant decrease in compliant women which persisted after stop of study. In contrast in the combined arm the risk increased. For total evidence also observational studies should be considered. Few studies confirmed lower or no risk using E-only. In about 20 studies using mostly MPA or NET(A) an increased risk has been observed comparable with the WHI. Only for dydrogesterone and progesterone comparing directly with other progestogens no increased risk has been seen up to 5–8 years, but longer treatment also increased risk. In contrast the mortality of patients with BC decreased in large observational studies independent from the type and regimen of HRT. Experimental research can explain those results: Various carcinoprotective effects can work, even by E itself like apoptosis and production of carcinoprotective E-metabolites. If in a population for more women the proliferation of BC cells is slow enough to destroy the cancer before its clinical detection, the statistics will show a decrease of risk. However, if fast proliferation, clinical cancer can develop. Progestogens can accelerate proliferation via special cell components which we detected in patients with BC, and we found differences testing all available progestogens. In addition also other mechanisms may work like impact on the development of carcinoprotective mechanisms. Future research may lead to the possibility to screen for patients at risk derived from those mechanisms. For clinical practice this may be more useful than more studies because the overall risk is small and we have to detect those few patients who are at risk.

## *Coping with the menopause after breast cancer: quality of life and sexual well-being*

Nicoletta Biglia (IT), Valentina Bounous (IT), Elisabetta Robba (IT), Valentina Tuninetti (IT), Marta D'Alonzo (IT) and Silvia Pecchio (IT)

SCDU Ginecologia e Ostetricia - Osp. Mauriziano - Dept. Surgical Sciences - University of Turin

*Context:* Breast cancer is increasing worldwide and the survival rate has significantly increased due to earlier diagnosis and advances in adjuvant treatments. Breast cancer survivors (BCSs) experience long-term treatment-related side effects and decreased quality of life (QoL). Many BCSs experience climacteric symptoms, which result directly from therapy with tamoxifen, aromatase inhibitors, ovarian suppression, ovariectomy or chemotherapy. The more frequent symptoms are hot flushes but also genitourinary syndrome of menopause (GSM), a new terminology referring to the wide range of vaginal and urinary symptoms related to menopause, has become a main problem for BCSs. Estrogen therapy is the most effective treatment for menopausal symptoms, however it is contraindicated for BCSs.

*Objective:* To review alternative strategies to cope with menopause in BCSs.

*Results:* Open and controlled trials demonstrated that selective serotonin reuptake inhibitors (SSRIs), as well as selective serotonin-norepinephrine reuptake inhibitors (SNRIs) are effective non-hormonal alternatives for the treatment of vasomotor symptoms. For GSM treatment, non-hormonal vaginal moisturizers or lubricants are the first choice for BCSs but only have limited and short-term efficacy. Vaginal estrogens at standard dosage might influence the risk of recurrence because they cause a significant increase of circulating estrogens. New strategies for the management of GSM include: low-dose or ultra low-dose vaginal estrogens that can be discussed with symptomatic women, oral selective estrogen receptor modulator ospemifene, after the completion of adjuvant treatments and physical treatment with vaginal laser.

*Conclusion:* QoL and sexual well-being are important for BCSs, especially for young women. Many different alternative strategies to estrogen therapy can be discussed with symptomatic menopausal BCSs.

## *Breast cancer effects on bones and joints*

Hadji Peyman (DE)

Department of Bone Oncology, Endocrinology and Reproductive Medicine, Krankenhaus Nordwest, Frankfurt, Germany

Osteoporosis is one of the most frequent diseases in postmenopausal women leading to an increased fracture risk due to the physiologic loss of the bone protective effects of estrogen. Hereby, several risk factors for fracture such as prevalent fracture, low bone mineral density (BMD), age, low BMI, family history, tendency to falls, smoking, use of SSRIs, glucocorticoid use, etc. have been identified. Additionally, the further reduction of endogenous estrogens with chemotherapy (CHT), GnRH-analogs or aromatase inhibitors (AI) continuously increases fracture risk. Breast cancer (BC) on the other hand is the most frequent cancer type in women. Recent reports indicated a continuous increased incidence while mortality, due to early diagnosis and treatment improvements, is decreasing. Dependent on specific tumor characteristics, radiation, CHT, antibody treatment as well as

endocrine treatment have been introduced into the adjuvant clinical treatment setting. Some but not all of this cancer specific treatments interfere with bone turnover leading to an accelerated bone loss referred to as cancer treatment induced bone loss (CTIBL). Whereas CHT leads to an unspecific increase of bone resorption, aromatase inhibitor (AI) reduces residual serum endogenous estrogen level and is associated with a decrease of BMD and increased fracture risk. Independent of the type of AI administered, bone loss is 2-3 fold increased compared to healthy, age matched postmenopausal controls. Therefore several guidelines have emerged to help managing CTIBL in women with BC including strategies to identify and treat those at highest risk for fractures. The talk will summarize the current knowledge on CTIBL and fracturing risk and indicate current treatment guidelines and intervention options.

## *What have we learned from longitudinal studies of women's health?*

### *Lessons from the Study of Women's Health across the Nation (SWAN)*

Nancy Avis (US)<sup>a</sup>, Sybil Crawford (US)<sup>b</sup> and Ellen Gold (US)<sup>c</sup>

<sup>a</sup>Wake Forest School of Medicine; <sup>b</sup>University of Massachusetts Medical Center; <sup>c</sup>University of California, Davis, School of Medicine

SWAN is a multi-site, multi-racial/ethnic longitudinal study characterizing the physiological, behavioral, and psychosocial changes that occur during the menopausal transition (MT) and the effect of the MT on subsequent health and age-related diseases. Data collection for 3302 women enrolled at 7 sites in the US began in 1996. Baseline eligibility criteria included: age 42–52 years, uterus and 1+ ovary, no current exogenous hormones affecting ovarian function, at least one menstrual period in the previous 3 months, not pregnant or lactating, and self-identification with a site's designated racial/ethnic groups. About half of each site's sample, recruited from the community, consisted of white women and the other half from one minority population (African-Americans, Japanese, Chinese, or Hispanic). The cohort has thus far completed a baseline visit and 14 annual follow-up visits. SWAN investigators have reported findings on a variety of topics related to the MT, including age at menopause; onset, risk factors for, and duration of vasomotor symptoms; and changes in cognition, sexual functioning, mood, sleep, quality of life, body composition, and sex hormones. Nearly the entire cohort has reached early postmenopause. This presentation will highlight some of the key findings and lessons learned from SWAN. As an example, race/ethnicity is an important predictor of multiple aspects of the menopause experience, lower risk of depressive symptoms in Chinese women, greater prevalence and longer duration of vasomotor symptoms in African American women, and highest rates of difficulty staying asleep in Caucasian women. SWAN's contributions have helped clinicians and women by increasing our understanding of the factors related to and consequences of the physiologic and symptomatic changes that occur during the MT that will aid in prevention and treatment of age-related diseases.

## Lessons from the Japan Nurses Health Study

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The Japan Nurses' Health Study (JNHS) is a prospective cohort study in investigating the effects of lifestyle and healthcare practices on women's health. It was initiated in 2001, with a seven-year entry period and a planned twenty-year follow-up period. Participants were recruited in cooperation with the Japanese Nursing Association and the Japan Society for Menopause and Women's Health. A total of 49,927 female nurses from all 47 prefectures in Japan responded to the baseline survey. Among them, 15,019 agreed to be followed-up and the cohort receives biennial follow-up questionnaires by mail.

The estimated median age at natural menopause was 52.1 years in the JNHS study population. Older generation, cigarette smoking, low body mass index, regular menstruation cycle at 18–22 years of age, nulliparity and unilateral oophorectomy were associated with earlier onset of natural menopause. We also reported that menopause in women who have a past history of infertility, especially in those who have suffered from endometriosis, is significantly earlier than that in women without such a history.

Women experience various diseases at different life stages that correspond to reproductive events. We classified diseases in women by identifying age at peak incidence and demonstrating their co-occurrence with other diseases based on the JNHS baseline data. While there were significant associations between the four early-onset diseases (endometriosis, anemia, migraine headache and uterine myoma), women with a history of these early-onset diseases had a higher risk of other diseases later in the life course. Understanding the history of early-onset diseases in women may help reduce the subsequent risk of chronic diseases in later life. Further research based on longitudinal follow-up studies is needed to clarify the associations between diseases in women's life course.

## What are we learning from InterLACE?

Gita Mishra (AU)

University of Queensland

*Context:* The timing of reproductive markers across life is associated with a range of health outcomes in women, but relatively little is known about the correlation between these markers and their variability. The International collaboration for a Life course Approach to reproductive health and Chronic disease Events (InterLACE) has obtained participant level pooled data on reproductive markers and chronic diseases (markers of cardio-metabolic conditions) from 20 cross-sectional and longitudinal observational studies in nine countries.

*Objective:* We shall present some preliminary results on the variability of reproductive markers (e.g. age of menarche, age at first birth, age at menopause) and how they correlate. We shall also outline the methods needed to address challenges posed by InterLACE, the lessons learnt, and the broader recommendations for future studies on women's health.

*Methods:* Variables were harmonised across the InterLACE studies to create a new and systematic synthesis of life course data for over 220 000 women.

*Main outcome measure:* Harmonised individual level data were derived for three domains: 1) socio-demographic and lifestyle

factors, 2) female reproductive markers, and 3) chronic disease outcomes (cardiovascular disease (CVD) and diabetes).

*Results:* The study identifies relationships between age at menarche, age at first birth, number of children, and age at menopause, including the effects of ethnicity and sociodemographic factors. It also finds associations between these markers and key chronic disease outcomes.

*Conclusions:* The scale and heterogeneity of InterLACE data provide clear evidence concerning the relationships between reproductive markers through life and subsequent risks of chronic disease, including cross-cultural comparisons, that can improve the targeting and timing of preventive health strategies for women.

## Fat matters

### Neuroendocrine basis of fat accumulation at the time of the menopause

Angelica Hirschberg (SE)

Karolinska Institutet

Weight gain is common during the menopausal transition and longitudinal studies have demonstrated an increase in total and abdominal fat and a decrease in lean body mass. These changes have been observed as early as 3–4 years prior to the onset of menopause and to remain relatively stable for at least 1–2 years after menopause. It could be difficult to separate age-related changes in body composition from hormonal changes at menopause. However, menopause per se has been associated with reductions in energy expenditure and oxidation of fat that can predispose to weight gain. The reduction in energy expenditure is probably a consequence of loss in lean body mass due to a decrease in physical activity, while the alterations in fat distribution appear to reflect modified metabolism in adipose tissue. Thus, estrogen promotes female fat distribution by stimulation of the activity of lipoprotein lipase in femoral fat tissue, whereas lipolysis is stimulated in abdominal fat tissue. Conversely, estrogen deficiency and menopause are associated with enhanced accumulation of abdominal fat. Furthermore, loss of progesterone and increased levels of testosterone may induce accumulation of abdominal fat and insulin resistance. Menopause-related weight gain and increased abdominal fat accumulation have major cardiovascular and metabolic health risks including coronary heart disease and type 2 diabetes mellitus. Combined hormone replacement therapy (HRT) and estrogen alone seem to have beneficial metabolic effects if the treatment is initiated shortly after onset of menopause. In contrast to the general view of women, HRT does not increase body fat or body weight but instead counteracts the accumulation of abdominal fat. However, testosterone supplementation could have potential adverse metabolic effects which should be taken into account.

### Metabolic and cardiovascular implications of fat accumulation at the time of the menopause

Tommaso Simoncini (IT)

University of Pisa

Abdominal fat accumulation is one of the hallmarks of the menopause transition. Redistribution of fat accumulation towards the

visceral compartment is largely dependent on neuroendocrine and endocrine changes, and it implies profound metabolic consequences. Visceral fat is metabolically active and releases a series of pro-inflammatory intermediates that impact general metabolism and cardiovascular function. In addition, the endocrine interference of the increased amounts of visceral fat are of relevance for the menopausal transition and its clinical correlates. This presentation will cover the pathophysiology and the metabolic and cardiovascular consequences of fat deposition linked to menopause.

### *Dietary and lifestyle interventions to counteract fat accumulation at the menopausal transition*

Irene Lambrinoudaki (GR)

National and Kapodestrian University of Athens

Menopause is associated with multiple metabolic changes, part of which are attributed to the decline of ovarian estrogens. Menopause inflicts a redistribution of fat in the abdomen, resulting in central obesity, which along with dyslipidemia lead to an increase in insulin resistance. Aging on the other hand decreases energy expenditure, due to sarcopenia and reduced physical activity. Women therefore tend to gain weight during midlife. Measures to prevent the lipid accumulation associated with menopause include most importantly the incorporation of physical activity in the daily routine. Physical exercise should consist of at least 30 minutes per day moderate exercise, or at least 75 minutes per week vigorous exercise. Exercise counteracts insulin resistance and increases muscle mass, helping thus in the restoration of basal metabolic rate. The diet should consist of nutrients rich in fiber, such as fruits and vegetables and should be low in refined carbohydrates, saturated fats and salt. Frequent small meals of low glycemic load prevent the postprandial increase in insulin and the resulting storage of meal glucose and fat in adipose tissue.

### *Endometriosis update*

#### *The immunological aspect and epigenetics of endometriosis*

Areepan Sophonsritsuk (TH)

Ramathibodi Hospital, Mahidol University

Despite the fact the endometriosis has been well known for a long time, a unifying theory regarding the etiology of endometriosis remains inconclusive. Hormone, genetics and inflammatory components seem to play key role in endometriosis. A possible immunological role of pathogenesis of endometriosis is demonstrated from the defect of specific cell mediated cytotoxicity activity, i.e. macrophages, NK cells, regulatory T cell, and so on. Data for role of macrophages and NK cells in endometriosis are the most abundant among all the immune cells. The primary defense cells, macrophages, are significantly changed in patients with endometriosis both in peritoneal fluid and ectopic endometrium. Although the number of macrophages is increased, their function is suppressed. The reduction of cytotoxicity of peripheral blood NK cells have shown in vitro. Peritoneal fluid collected from women with endometriosis reduced the NK cells function in vitro. Study regarding regulatory T cells and endometriosis is scarce. The immunosuppressive effects are not correlated with

the phases of the menstrual cycle. Although estrogen enhances the pro-inflammatory and anti-apoptotic effects in endometrial cells and endometriosis, GnRHa and OCP decrease the pro-inflammatory effect by reducing the number of macrophages in endometriotic cyst wall tissues.

Progesterone resistance which promotes local E2 accumulation enhances the proliferation of endometriosis. PR-B promoter hypermethylation, an epigenetic phenomenon, is concomitant with reduced PR-B expression. The up-regulation of aromatase gene in endometriosis caused by aberrant DNA demethylation in a nonpromoter CpG island results in the enhancement activity of aromatase and an increase in local E2 in endometriotic lesion. Differential expression of several microRNAs is found in endometriosis.

### *Surgical approach to endometriosis in peri- and postmenopausal women*

P. Santulli, L. Marcellin, V. Gayet, P. Marzouk, M.C. Lamau, B. Borghese and C. Chapron

Université Paris Descartes, Sorbonne Paris Cité, Faculté de Médecine, Assistance Publique – Hôpitaux de Paris (AP-HP), Groupe Hospitalier Universitaire (GHU) Ouest, Centre Hospitalier Universitaire (CHU) Cochin, Department of Gynecology Obstetrics II and Reproductive Medicine (Professor Chapron), Paris, France

Endometriosis, which is defined as the presence of endometrial-like tissue outside of the uterine cavity, is a public health issue that bears an important economic burden. There are three histological types of endometriosis: peritoneal superficial (SUP), ovarian endometrioma (OMA) and deep infiltrating endometriosis (DIE). DIE is actually considered the most severe form of endometriosis, arbitrarily defined as a peritoneal invasion over 5 mm or by the involvement of the muscular layer of the target organs (intestine, bladder, uterus, ureter). In addition adenomyosis, defined by the presence of islands of ectopic endometrial tissue within the myometrium, is frequently associated to endometriosis. Thus, endometriosis should not be considered a disease of a specific organ but represents rather a multifocal and heterogeneous disease requiring a multidisciplinary integrated approach.

The management of endometriosis includes specific questioning, clinical examination, and imaging process to decide the best therapeutic option: medical treatment, surgery and sometimes assisted reproductive technologies, even if this last option is less common among perimenopausal women.

Endometriosis multifocality justifies a complete abdomino-pelvic work-up, because if surgery is decided, the anatomical location of endometriotic lesions governs the surgical approach. Therefore pre-operative imaging work-up is essential and transvaginal ultrasonography must definitely be considered as the first-line imaging process.

Surgery is efficient, not only for managing pelvic pain and treatment of endometriosis-related infertility, but also for improving quality of life. Endometriosis has a high potential risk for recurrence which many reports have attributed to incomplete surgical procedures. In literature, incompleteness of initial surgery is a parameter that has been described to be significantly correlated with an increased rate of reoperation. Taken together, these findings suggest that it is necessary to perform a complete surgical exeresis when operating on patients to treat endometriosis-related pelvic pain, irrespective of patient age. Nevertheless, the benefits of surgery should not obscure the fact that interventions can be associated with adverse outcomes.

## *Medical treatment of endometriosis at the menopausal transition and beyond*

Ludwig Kiesel (DE)

University Hospital Muenster

Endometriosis is an endocrine dependent disease that generally occurs in women during the fertile phase of their life. It is characterized by the presence of endometrial tissue outside of the uterus. This disease mostly affects women before they have undergone the menopausal transition. While the estimated prevalence of the disease is up to 10%, the exact numbers for this specific age group is unknown. In the literature, several publications suggest that up to 5% of cases with endometriosis occur after menopause. This article summarizes the current state of knowledge on postmenopausal endometriosis and its therapy.

Since the disease is oestrogen dependent, there is still a debate about using hormone therapy after menopause in women with previous history of endometriosis. The risks and benefits of hormone therapy (either only oestrogens, or a combination of oestrogen and progesterone) in patients with the history of endometriosis is still unclear. Some studies reported a low risk of recurrence of symptoms in women using only oestrogen therapy. Until now the primary treatment of endometriosis after menopause has been surgery which often includes total abdominal hysterectomy and bilateral oophorectomy in addition to the removal of the endometrial implants. Individual case reports have shown that patients with endometriosis who have undergone bilateral oophorectomy may benefit from the use of aromatase inhibitors as the primary oestrogen source in these patients is extraovarian, where this medication primarily acts to inhibit oestrogen synthesis. According to these recent data aromatase inhibitors may have a future role in the treatment of women with severe active postmenopausal endometriosis.

## *Osteoporosis: from the womb to the grave*

### *Epigenetic mechanisms in the developmental origins of osteoporosis, and implications for life course prevention*

Cyrus Cooper (GB)

University of Southampton

Osteoporosis is a skeletal disease characterised by low bone mass and susceptibility to fracture. Preventive strategies against osteoporotic fracture can be targeted throughout the life course. Although there is evidence to suggest that peak bone mass is inherited, current genetic markers are able to explain only a small proportion of the variation in individual bone mass or fracture risk. Evidence has begun to accrue that fracture risk might be modified by environmental influences during intrauterine or early postnatal life: 1) Epidemiological studies which confirm that subjects who are born light and whose growth falters in the first year of postnatal life, have significantly lower bone size and mineral content, at age 60 to 75 years; 2) Cohort studies demonstrating that subsequent lower trajectories of childhood growth are associated with an increased risk of hip fracture among such men and women; 3) Detailed physiological studies of candidate endocrine systems which might be programmed have shown that birthweight and growth in infancy alter the functional settings of the GH/IGF-1, and vitamin D/PTH axes; (4) Studies characterising the nutrition, body build and lifestyle of pregnant

women which relate these to the bone mass of their newborn offspring, have identified a number of important determinants of reduced fetal mineral accrual: these include maternal smoking, excessive weight bearing physical activity in late pregnancy, and low maternal fat stores. More recently, maternal vitamin D insufficiency during mid and late gestation has been associated with bone mineral content and areal BMD in the offspring at age 9 years. As a consequence, large randomised controlled trials of vitamin D supplementation in pregnancy have been instituted and the results of these will inform public health interventions aiming to reduce the frequency of maternal vitamin D deficiency.

## *Postmenopausal osteoporosis in Asia: unmet needs?*

Joon Kiong Lee (MY)

Osteoporosis Awareness Society of Kuala Lumpur & Selangor

The improvement in the health care system and prosperity over the past few decades in Asia has resulted in better quality of life and increase in life expectancy of Asian population. Between the years 2000 and 2050, it is predicted to have a 7.6 folds increase in the number of elderly population. By the year 2050, it is predicted that more than 50% of the hip fractures worldwide will occur in Asia. Lack of epidemiological data on the prevalence of osteoporosis and osteoporosis related fractures in Asia has resulted in underestimation of the actual burden of the disease.

Osteoporosis is still a neglected disease and therefore is greatly underdiagnosed and undertreated in many Asian countries. Fracture Liaison Service (FLS) is still uncommon in many Asian countries. Effort to prevent second and subsequent fracture has not been recognized as an important step among many medical practitioners. Inadequate calcium and vitamin D intake is common throughout Asia. This involves individuals from all age groups. Vitamin D insufficiency and deficiency have been reported in children and adolescents before reaching their peak bone mass. However, this has not been recognized by most health care providers and public.

The availability and accessibility of diagnostic tools such as DXA scans are still limited in many countries in Asia. The public does not get the opportunity to have their osteoporosis diagnosed early and receive treatment early. Risk assessment tool such as FRAX is not used widely by clinicians in their daily clinical practice too.

Treatments with different pharmacological agents for osteoporosis might not be available and accessible in many countries in Asia due to limited health care budget in some countries as well as the reimbursement policy in some countries.

## *A clinical approach to early menopausal osteopenia and osteoporosis*

Florence Tremollieres (FR)

Hôpital Paule de Viguier, CHU Toulouse

Post-menopausal osteoporosis is a chronic disease related to prolonged estrogen deficiency. The natural history of osteoporosis and, in particular, the rapid increase in fracture recurrence after a first major fracture should justify an early detection of women at higher risk at the beginning of menopause. Therefore, the prevention strategy of osteoporosis has to begin with screening and

Careful assessment for risk factors for fracture and DXA bone mass measurement. The choice of the 1st treatment is important especially in early postmenopausal women (within the first decade of menopause) with a moderate to high risk of fracture. In the absence of contraindication, menopause hormone therapy (MHT) should remain the preferred option whenever possible. Moreover, MHT has the capacity to improve quality of life in most postmenopausal women, more than other more specific osteoporosis treatments. The use of MHT has declined considerably after the publication of the WHI results due to safety concerns. However, later analyses of the WHI as well as new data from randomized trials in early postmenopausal women have tempered the negative messages emerging from the first publications. MHT thus still constitutes a first line choice for prevention of bone loss and fracture in the early postmenopausal period. Raloxifene can be an interesting alternative, due to its mechanisms of action and multiplicity of targets with, in particular, its preventive effect on the risk of estrogen receptor-positive breast cancer. It is only when there are contraindications to these two molecules that other osteoporotic treatments can be discussed. They should nevertheless be considered only in women whose 10-year fracture risk is significantly increased.

## Focus on sexual health

### *New pharmacological therapy for FSD: focus on centrally acting agents*

Annamaria GiralDI (DK)

Sexological Clinic, Psychiatric Center Copenhagen, Copenhagen University, Denmark

The female sexual response is traditionally described in the phases of desire, arousal and orgasm. Sexual desire is influenced by several bio-psycho-social factors interacting with each other. Key regions within the brain that regulate sexual desire include the prefrontal cortex, locus coeruleus, medial preoptic area, paraventricular nucleus, and the reward and attention processing centers of the ventral tegmental area and the nucleus accumbens. On the central hormonal and neurotransmitter level desire is influenced by an interaction between stimulatory modulators as dopamine, testosterone, melanocortin and oxytocin and inhibitory factors as serotonin and opioids.

The most prevalent sexual problem in women is low sexual desire with a prevalence of distressful low desire in 7–10% of women. Studies have shown that distress in low desire may diminish women's quality of life.

With the launch of Viagra® for treatment of erectile dysfunction a search for drugs for treatment of sexual problems in women was intensified, and as a culmination on this, FDA in 2015 approved Flibanserin (Addyi®) for the treatment of acquired Hypoactive Sexual Desire Disorder (HSDD) in premenopausal women after many years of studies, controversies and debates of how to treat women's sexual problems. Before that a testosterone patch (Intrinsa®) for HSDD in surgically menopausal women had been the only approved compound.

Flibanserin, dosed at 100 mg at bedtime, is a non-hormonal, centrally acting postsynaptic 5-HT<sub>1A</sub> receptor agonist and a 5-HT<sub>2A</sub> receptor antagonist (a multifunctional serotonin agonist and antagonist) that results in a decrease in serotonin activity and an increase in dopamine and norepinephrine activity. Clinical studies of the effect of Flibanserin have shown a statistically significant increase in desire compared to placebo, though the effect is relatively modest.

Other centrally acting compounds are being investigated for treatment of HSDD; Bupropion, a norepinephrine-dopamine reuptake inhibitor, Buspirone, a serotonin 5-HT<sub>1A</sub> partial agonist,

Bremelanotide, a melanocortin agonist and the combination compounds Lybrido® (a combination of testosterone and sildenafil) and Lybridos® (a combination of testosterone and buspirone).

## *Sexuality in the aged woman*

Woet Gianotten (NL)

De Trappenberg Centre for Physical Rehabilitation

Sexuality in the aged woman can be approached from various sides:

- The taboo that exists in part of society, in the professionals, in the offspring, and also in part of the aged women themselves. The taboo has many colors with denial, disgust, and misunderstanding, but also with humor and tenderness.
- The influence of aging on sexuality and intimacy. Although there are some physiologic and endocrine changes, the aging body keeps the capacity for sexual responding and meaningful sexual expression.
- The influence of life style, disease, and medical interventions. Aging can be accompanied by physical deterioration and impairment, that can disturb sexual function and sexual pleasure.
- The influence of male aging and relationship changes. Some couples lose erection, but continue physical intimacy. Others cannot cope with that and lose all intimacy. Many heterosexual women become single and alone for many years. A smaller group reaches 'virtual widowhood' when their partner is caught by dementia.
- The influence of changes in our cultures. Gradually the differences between generations seem bigger than between the ages.
- The meaning of sex. We gradually learn about the benefits of sexual expression. Next to quality of life and a medium to ameliorate the relationship, sexual expression promotes physical health and longevity.
- The significance of dealing with this topic of sexuality and intimacy with our aged patients. When done well, it can not only result in better care (and even cure), but it can also improve the relationship between patient and health care professional.

All these elements will be addressed in the presentation, aiming at the message: 'Don't pathologize sexuality of the aged women!'.

## *Beyond the DSM V: update in the classification and treatment of female sexual disorders*

Sharon Parish (US)

Weill Cornell Medical College

DSM-5 definitions of sexual dysfunctions do not identify all of the sexual problems experienced by women and are not necessarily applicable for management of female sexual disorders. Nomenclature should be based on evidence from well-conducted research trials, case reports and expert opinion. The committee on incidence and prevalence on sexual dysfunctions from the 4th International Consultation on Sexual Medicine (ICSM) in June 2015 endorsed the widely agreed upon clinical principles

regarding sexual desire and arousal in women. The committee report stated that Hypoactive Sexual Desire Disorder (HSDD) should be maintained as an entity separate from Female Sexual Arousal Disorder (FSAD). Incidence, prevalence and risk factor data clearly show that delineating these 2 functions is supported by published evidence. To examine the need for diagnostic criteria developed for clinicians and researchers and to develop definitions, the ISSWSH convened an international panel of experts in desire, arousal and orgasm disorders in women to develop a multi-disciplinary, evidence-based nomenclature. Key opinion leaders were invited based on their contributions to the field of female sexuality. The ISSWSH definitions include hypoactive sexual desire disorder, female genital arousal disorder, female orgasmic disorder, pleasure dissociative orgasm disorder, female orgasmic illness syndrome, and persistent genital arousal disorder. Currently, the Beta draft of ICD-11 is available online, which specifies that there will be a new category focused on human sexuality included in the ICD-11. This category will be called "Conditions Related to Sexual Health"; published literature describing its rationale and coding structure will be discussed. Currently available pharmacotherapy and drugs in development for HSDD will be summarized in the context of current definitions of this disorder.

## Caring for women with Turner syndrome

### *Improving well-being and sexual function in women with Turner syndrome*

Camil Castelo-Branco (ES)  
University of Barcelona

Turner syndrome and idiopathic congenital hypogonadism including Kallmann syndrome are conditions associated to a large number of widely known comorbidities that need a medical support forever. One of the characteristics shared by both conditions is the lack of sexual development that influences the sexuality functioning and quality of life of the affected women. Few studies have been conducted to assess these topics, but they need to be considered in the treatment to all women with hypogonadism. This review on the major medical issues and psychological aspects also focuses in the present knowledge about sexual function and quality of life of women with Turner syndrome and idiopathic congenital hypogonadism, which aims to help in the comprehensive management of these patients.

### *Optimizing hormone therapy in Turner syndrome*

Wendy Wolfman (CA)  
Mt. Sinai Hospital, University of Toronto

Patients with Turner's syndrome have many of the same issues as other women with premature ovarian insufficiency such as primary and or secondary amenorrhoea, estrogen deficiency and its ramifications on multiple organ systems, as well as infertility. In addition they may have other significant health risk factors related to associated cardiac, renal anomalies, autoimmune problems and malignancies which could impact the prescription of hormone therapies. These patients are typically diagnosed in infancy or young childhood or more recently in prenatal life via

genetic screens. The initiation, choice and dosages of estrogen and progestin hormone therapies should be judicious in consideration of maximizing growth potential and ultimate breast character and development. These patients will require long term usage of hormones after the initiation of pubertal development. The young Turner's patients require higher dosages of estrogen and progestins than are prescribed for women of typical menopausal age. The risks and potential benefits and the sparse literature on this subject will be reviewed. It is recommended that these patients be managed in multi-disciplinary clinics with expertise to manage the myriad of issues that these patients may have. Our experience in a multi-disciplinary adult Turner's clinic at the University of Toronto combining the care of an endocrinologist and gynaecologist will be discussed.

### *CVD and Turner syndrome women: what are the risks and when and how to screen*

Claus Gravholt (DK)  
Department of Endocrinology and Department of Molecular Medicine, Aarhus University Hospital

Treatment with growth hormone (GH) during childhood and adolescence allows a considerable gain in adult height. SHOX deficiency explains some of the phenotypic characteristics in Turner syndrome, principally short stature. Puberty has to be induced in most cases, and female sex hormone replacement therapy should continue during adult years. These issues are normally dealt with by the paediatrician, but once a TS female enters adulthood it is less clear who should be the primary care giver. Morbidity and mortality is increased, especially due to the risk of dissection of the aorta and other cardiovascular diseases, as well as the risk of type 2 diabetes, hypertension, osteoporosis, thyroid disease and other diseases.

The proper dose of hormone replacement therapy (HRT) with female sex steroids has not been established, and, likewise, benefits and/or drawbacks from HRT have not been thoroughly evaluated. In most countries it seems that the transition period from paediatric to adult care is especially vulnerable and the proper framework for transition has not been established. Likewise, no framework is in place for continuous follow-up during adult years in many countries. Today, most treatment recommendations are based on expert opinion and are unfortunately not evidence based, although more areas, such as GH treatment for increasing height, are well founded.

During the transition period many young females opt out of longitudinal follow-up, probably because they feel well and cannot clearly see the need for continued medical surveillance. However, osteoporosis, diabetes, both type 1 and 2, hypothyroidism, obesity and a host of other endocrinological diseases and conditions are seen more frequently in Turner syndrome in the long term. Prevention, intervention and proper treatment are only just being recognized. Hypertension is frequent and can be a forerunner of cardiovascular disease. The description of adult life with Turner syndrome has been broadened and medical, social and psychological aspects are being added at a compelling pace. Proper care during adulthood should be studied and a framework for care should be in place, since most morbidity potentially is amenable to intervention. In summary, Turner syndrome is a condition associated with a number of diseases and conditions which need the attention of a multi-disciplinary team during adulthood.

## Screening for gynecological cancers

### Screening for ovarian cancer

Usha Menon (GB)

University College London

Ovarian cancer is the 5th most common cause of cancer death among women in the UK, with ten-year survival rates of 35%. The continued high case fatality ratio has underpinned efforts to develop a screening strategy that could impact on mortality. In the UK large ovarian cancer screening trials have been completed both in the general (United Kingdom Collaborative Trial of Ovarian Cancer Screening – UKCTOCS) and high-risk (UK Familial Ovarian Cancer Screening Study – UKFOCSS) population. Initial results from UKCTOCS have shown an overall significant stage shift in invasive epithelial ovarian/tubal/peritoneal cancer in the multimodal screening group compared to control in an intention to screen analysis. This was associated with a delayed but not yet statistically significant mortality reduction. Disease specific mortality rates in the control arm were continuing to rise while they appeared to have plateaued in the screen arms at censorship for the mortality analysis on 31st December 2014. Further follow-up is now underway to confirm the mortality reduction and determine its full extent. Meanwhile new insights into carcinogenesis with a better understanding of the target lesion, improved design of biomarker discovery studies, a focus on detecting low volume disease using cancer specific markers, novel biospecimens such as endocervical samples, targeted imaging and time series algorithms for interpreting marker profile suggest that a new era in ovarian cancer screening is underway.

### Screening for cervical cancer in low- to middle-income countries

Fanghui Zhao (CN)

National Cancer Center & Cancer Hospital, Chinese Academy of Medical Sciences

Approximately four fifths of the global burden of new cases (N = 530,000) and cervical cancer deaths (N = 275,000) are experienced in low- and medium-resourced countries due to lack of effective cervical cancer screening and prevention programmes. Although repeated Pap smear screening has largely been responsible for the 50–80% reduction in cervical cancer cases and deaths in the developed countries, it is not feasible to introduce large scale Pap smear screening in many developing countries due to resource constraints.

Recent research has shown that screening tests such as VIA and HPV testing can accurately detect precancerous lesions and can lead to reduced death rates from cervical cancer, implying these can be effective alternative tests to Pap smear. HPV testing seems to be a more promising approach as compared to Pap smear or VIA due to its objectivity and its higher accuracy in the early detection of biologically significant precancerous changes more likely to progress to cancer if untreated. Although the majority of currently available HPV testing methods may not be widely feasible in developing countries, a more rapid and affordable HPV test, suitable for use in developing countries has been successfully developed and ready for the implementation. More low-cost Point of Care tests for cervical cancer screening are in development. Strategies such as screening women aged 30–59 years or 35–49 years at least once in a life time, in order to cover a large proportion of eligible women, have been found to be effective in reducing cervical cancer cases and deaths in experimental,

population-based studies. Political commitment and sincere investments in health services are essential to translate the encouraging research findings into effective public health policies and interventions in developing countries.

## Stroke in women

### Gender differences in stroke management

Karin Schenck-Gustafsson (SE)

Department of Medicine, Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden

Stroke is the third leading cause of death and the most common cause of functional impairment. In younger ages males suffer more strokes than females while the proportions change in older ages. Mean age for men is 72 years and for women 78 years in Sweden. There are specific risks associated with child bearing and menopause and prevalence, presentation, and treatment of risk factors for stroke vary between men and women as do the subtypes of stroke. In our studies stroke women have more speech problems and decrease in mental status compared with men. Women have a general poorer outcome than men after stroke. There are still sex differences in the preventive treatment after TIA and ischemic stroke. In older women there is an undertreatment with anticoagulant therapy as well as with lipid-lowering drugs compared with men. Since a couple of years new treatments of ischemic stroke have emerged, that is thrombolysis which should be performed within 4.5 hrs and thrombectomy within 6 hrs after debut of symptoms. Actual figures from the Swedish Stroke registry reveal that 13.5% of men and 12.5% of women get treatment with thrombolysis and the optimal figure should be about 25%. In ischemic stroke 0.5% of the patients are treated with thrombectomy, 52% of the male and 48% of the female patients according to the Swedish registry.

### Hormone therapy: dose, formulation and risk of ischemic stroke

Christel Renoux (CA)

McGill University

The use of oral hormone replacement therapy is associated with an increased risk of stroke, mainly driven by an increased risk of ischemic stroke. In randomised controlled trials, the use of conjugated equine estrogens alone or in combination with medroxyprogesterone acetate was associated with a 30% increased risk of stroke compared with placebo. Recent large observational studies assessing exposure to oral hormone therapy compared with no use and meta-analyses found similar estimates. Inconsistencies with results of some earlier observational studies suggesting no increased risk or a protective effect of oral hormone therapy are in relation with methodological issues that will be discussed during the presentation. The risk of ischemic stroke may differ among different routes of administration and recent observational studies suggest that low dose transdermal hormone therapy does not increase the risk of stroke. Interestingly, similar findings have been shown regarding the risk of venous thrombosis which is not increased with the transdermal route. Dose may be of importance as the risk of stroke may still be increased with high dose of transdermal hormone therapy whereas oral hormone replacement therapy increases the risk regardless of dose.

## Hormones and the brain

### *Is it depression or menopause?*

Claudio Soares (CA)

Queen's University School of Medicine

Depression is a complex, multi-faceted phenomenon, particularly during midlife years. Its occurrence poses a diagnostic and therapeutic challenge to clinicians, since this condition is often affected by age, co-morbid conditions (e.g. cardiovascular events, metabolic issues) and menopause-related symptoms (vasomotor, pain, sleep changes). Other contributing and/or moderating factors include ethnicity, lifestyle behaviors (e.g. exercise, smoking) and stressful life events.

Many have supported the notion of reproductive-related 'windows of vulnerability' for depression across a woman's life cycle; based on this theory, some (but not all) women would be particularly sensitive to develop mood changes while experiencing significant disruptions in their hormonal milieu. The hypothesis of a 'menopause-associated depression', however, has been more controversial, in part due to some methodological difficulties: studies to date have not consistently defined menopausal staging or clearly distinguished/characterized the presence and severity of depressive symptoms. Moreover, anxiety and sleep problems were not always identified or taken into consideration, particularly in intervention studies.

There is little doubt that estrogen plays an important role in mood regulation due to its overall effects on synthesis, metabolism, and receptor density/activity of neurotransmitters such as serotonin and norepinephrine. There is also evidence supporting antidepressant effects of estrogen, particularly transdermal estradiol for perimenopausal women, reinforcing the notion of a 'window of opportunity' for the benefits of estrogen therapy and mood regulation.

New studies focusing on the neurobiology of depression during midlife years will provide us with a unique opportunity to better understand, diagnose and properly manage depression in this sub-population.

### *Depression and cognition in the menopausal transition*

Pauline Maki (US)

University of Illinois at Chicago

In clinical practice and research studies, midlife women report a worsening of mood and memory as they transition through the menopause. In addition to subclinical depressive symptoms, the risk of major depressive disorder (MDD) increases as women transition through the menopause. Cognitive performance also decreases during the menopausal transition, particularly on measures of verbal memory. Early removal of the ovaries is a risk factor for both depression and cognitive impairment. The co-emergence of depression and cognitive difficulties during the transition suggests a possible interdependence and/or common etiology. Memory and mood complaints are significantly correlated, suggesting a possible interdependence. However, multiple lines of evidence demonstrate that they are dissociable. First, many women report memory difficulties despite having minimal to no depressive symptoms. Second, in a large randomized, pla-

cebo-controlled clinical trial, hormone therapy improved mood without affecting cognition. Third, although memory performance and mood decrease during the menopausal transition, the stage-related decrease in memory persists after controlling for mood. Hormonal changes during the transition have been examined in relation to mood and cognition. Evidence suggests a possible role for testosterone, estradiol, and FSH in mood-related changes though these associations are not necessarily reliable across cohort studies. Hormone levels do not reliably relate to cognitive changes during the transition. Understanding the natural history, etiology, and treatments for cognitive and mood changes is important not only for improving quality of life during the menopausal transition but also for improving long-term health. Both cognitive complaints and depression at midlife are associated with an increased risk of Alzheimer's disease later in life.

### *Predictors and time course of depression across the menopause transition*

Martha Hickey (AU)

The University of Melbourne

This presentation will present the current evidence on the relationship between (1) depressive symptoms and (2) depressive illness over the menopause transition. New evidence on trajectories of depressive symptoms and risk factors for clinically significant depression will be presented. The potential mechanisms underlying this relationship will be discussed as well as practical clinical guidance for detecting and managing depression over the menopause transition.

## SPECIAL SYMPOSIUM

### The hot flush

#### *Understanding the etiology of the hot flush*

Naomi Rance (US)

University of Arizona College of Medicine

Hot flushes are characterized by the activation of the physiological effectors that dissipate heat, including skin vasodilation, sweating, and cold-seeking behavior. We have hypothesized that flushes are due to altered function of KNDy neurons, a group of neurons in the infundibular (arcuate) nucleus of the hypothalamus that express kisspeptin, neurokinin B (NKB), dynorphin and estrogen receptor alpha. In postmenopausal women, KNDy neurons exhibit hypertrophy and increased NKB and kisspeptin gene expression. Studies in experimental animals indicate that these changes are due to estrogen withdrawal. Because KNDy neurons are conserved among mammalian species, we began a series of studies in the rat to determine if these neurons modulate tail skin vasodilatation, a major heat dissipation effector. Track-tracing studies showed that KNDy neurons project to preoptic thermoregulatory areas that express the NKB receptor (NK3R). Interestingly, focal infusion of an NK3R agonist into the median preoptic nucleus markedly reduced body temperature, showing that NKB signaling can activate the heat-dissipation pathway. To further understand the role of KNDy neurons in thermoregulation, we developed a method to selectively ablate them using a

saporin-conjugate. Remarkably, tail skin temperature was consistently lower in KNDy-ablated rats and the effects of estrogen on thermoregulation were partially blocked. These data showed that KNDy neurons promote cutaneous vasodilation and participate in estrogen modulation of body temperature in the rat. Because cutaneous vasodilation is a cardinal sign of a hot flush, these data support the hypothesis that KNDy neurons play a role in the generation of flushes. This hypothesis is also supported by a recent study showing that NKB administration induces hot flushes in women (Jayasena et al, Sci. Rep. 2015).

## CVD risk and flushing

Rebecca Thurston (US)

University of Pittsburgh

*Context:* Vasomotor symptoms (VMS; hot flushes, night sweats) are reported by 70% of women during the menopause transition. VMS are known to have important impact on quality of life, yet are generally considered to have few implications for physical health. However, emerging data link VMS to markers of cardiovascular disease (CVD) risk.

*Objective:* This talk will review evidence on VMS and CVD risk from published work and ongoing studies. Particular attention will be paid to the MsHeart Study, one of the only studies specifically designed to investigate relations between VMS and CVD risk, and the Study of Women's Health Across the Nation (SWAN), one of the largest prospective cohort studies of the menopause transition.

*Methods:* MsHeart enrolled 304 nonsmoking late peri- and postmenopausal women ages 40–60. Women underwent physiologic VMS monitoring, vascular ultrasounds, and blood sampling. SWAN enrolled 3302 pre- and early perimenopausal women ages 42–52 who completed annual assessments for over 14 years; a subset also completed vascular measures.

*Results:* Findings largely show more frequent VMS associated with indicators of poorer vascular health (e.g. carotid intima media thickness, brachial artery flow mediated dilation), controlling for CVD risk factors. Findings also show VMS associated with acute decreases in cardiac vagal control (MsHeart), and VMS with a poorer CVD risk factor and poorer clotting profile (SWAN). Estradiol does not appear to account for links between VMS and CVD risk markers. Yet positive findings are not universal in the literature; a woman's CVD risk factor burden or age may be important considerations.

*Conclusions:* Emerging data largely link VMS to markers of CVD risk, particularly among women with some degree of CVD risk factor burden. How best to conceptualize VMS–CVD relations and the clinical implications of this work will be discussed.

## MEET THE EXPERTS

### Postmenopausal bleeding: when to investigate and how

Steven Goldstein (US)

New York Medical Center, New York, US

Postmenopausal bleeding is “endometrial cancer until proven otherwise”. In various studies the incidence of cancer in patients with postmenopausal bleeding ranged from 1–14%, although

most studies place it between 3–7%. The majority of bleeding, staining or spotting occurs as the result of atrophic changes of vagina or endometrium, but clearly cancer, hyperplasia and even frank proliferation should be diagnosed and treated. In the past, dilation and curettage was the mainstay of diagnosis. This gave way to in-office suction pump-generated biopsies. Most recently, disposable biopsy instruments with their own internal piston to generate suction have become the standard of care. Rarely has such a technique received such widespread acceptance with such limited validation. Transvaginal ultrasonography, when technically feasible, is a noninvasive way to image the endometrial cavity. Saline-infusion sonohysterography is a subset of transvaginal ultrasonography reserved for patients in whom an adequate endometrial echo is not seen or when an endometrial echo is seen but not sufficiently thin. Appropriate understanding and use of transvaginal ultrasonography and addition of sonohysterography when necessary can allow a clinical algorithm that can triage patients with abnormal uterine bleeding to (1) no anatomic pathology best treated expectantly; (2) a global endometrial process, in which case random blind endometrial sampling is appropriate; or (3) a focal endometrial abnormality in which case endometrial sampling should be done with the visualization offered by hysteroscopy. It is also important to understand that the incidence of thick endometrial echo found incidentally in postmenopausal women with no bleeding is extremely high (10–17%), has been shown to be associated with a very low risk of endometrial cancer (<1 in 250) and should not automatically trigger invasive endometrial sampling.

### Management of postmenopausal bleeding in women on MHT

Serge Rozenberg (BE)

Department of Obstetrics and Gynaecology, CHU ST Pierre, Université Libre de Bruxelles, Vrije Universiteit Brussel

During this “Meet the Expert” session, based on several clinical cases, we will discuss the management of post-menopausal bleeding for women using several MHT regimens. The following questions will be raised: How prevalent is the bleeding? When should it become a serious concern? When and how do we need to investigate the bleeding? How can the bleeding be avoided or minimised? Answers to these questions will be sought using interactions with the attending public while confronting evidence based data.

### Non-hormonal therapy: efficacy and use

Margaret Rees (GB)

University of Oxford

Women who have contraindications to estrogens or who do not wish to take them may find non-hormonal management for menopausal symptoms helpful. The options span lifestyle modifications, diet and food supplements, non-hormonal medications (e.g. SSRIs, SNRIs and gabapentin) and use of behavioral and complementary and alternative medicines. Of the SSRIs, paroxetine seems to have the best evidence base of efficacy and is approved by Food and Drug Administration (FDA) for the treatment of menopausal hot flushes. SNRIs (venlafaxine, desvenlafaxine) have been used to treat menopausal symptoms, mainly in

women in whom MHT is contraindicated. Clonidine is approved for the treatment of menopausal flushes in some countries, as it seems that it can reduce the occurrence of hot flushes after 3 months of use. With regard to stellate ganglion blockade a randomized sham-controlled trial found no significant differences between the treatment group and the sham-group regarding vasomotor symptoms frequency. There is insufficient or conflicting evidence from randomized controlled trials to suggest that exercise, supplements or a diet rich in phytoestrogens are effective for vasomotor menopausal symptoms. Cognitive-behavioral, behavioral, and mindfulness-based (CBBMB) therapies have been used to deal with menopausal symptoms. Alternative medicine interventions have been tried, but the available evidence is still limited.

### *When can HT be used in those at increased risk of breast cancer?*

Anne Gompel (FR)

Université René Descartes, Paris 5, France

Menopausal hormone therapy (MHT) is associated with a mild increase in the risk of breast cancer. The current opinion is that this increase is due to a promoter effect of MHT on preexisting lesions. Indeed, increase in the risk is time dependent and stop progressively after cessation of the treatment. It is likely that women at high risk for breast cancer are the ones where the treatment might increase further the risk of breast cancer. The first step should be to evaluate the level of this risk. Women with a family history of breast cancer – especially if cancers were premenopausal, women who experienced thoracic radiotherapy, or who have a history of biopsy with atypical hyperplasia are at the highest risk. High breast density in the category of Birads 4 is also considered as a high risk factor. In these women MHT cannot be a first line and non-hormonal treatment should be privileged. However, in case of failure of non-hormonal therapies, then MHT can be discussed according to the severity of climacteric symptoms and the will of the patient. Categories of intermediate risk include women with Birads 3 breast density, post-menopausal family history of breast cancer, obesity, sedentarity, reproductive risk factors, excessive alcohol intake. Several studies nevertheless reported that, in obese women, MHT does not further increase their risk. Several studies using a model for predicting absolute risk of breast cancer and its modulation by life style strategies suggest that women with modifiable risk factors would benefit most from risk-reduction strategies based on altering modifiable factors such as losing weight, reduce alcohol, exercise. We will present how to evaluate the risk of breast cancer and the recent scientific evidence for using estrogen, combined therapy and alternatives according to the level of the risk of breast cancer and strategies to decrease the risk when possible.

### *Using cognitive behaviour therapy to alleviate menopausal symptoms*

Myra Hunter (GB)

King's College London

Cognitive behaviour therapy (CBT) is an effective treatment for anxiety and depression and sleep disorders for men and women

across the age range. CBT is also an effective intervention for women with problematic hot flushes and night sweats and, in three recent trials, CBT has been found to help women to reduce the impact of these symptoms, as well as produce benefits to quality of life. In this session the CBT interventions will be described using four cases examples. Many women seek help during the menopause transition when they experience a combination of vasomotor symptoms, together with stress, anxiety, low mood or sleep problems. CBT can offer strategies that once learnt can be applied to a range of problems; some CBT strategies will be demonstrated during the session. Self-help and face to face versions of the CBT for menopausal symptoms are available.

### *Essential assessments for women pre MHT: the endocrinologist's view*

Mark Brincat (MT)

University of Malta, Msida MSD, Malta

Adult women's health care is an important topical issue. Women going to their transitional phase can utilise the opportunity of having a general health care check which at the same time directs the practitioner as to the direction where his advice needs to be given.

Advice needs to centre around lifestyle habits, general medical screening, specific screening for pre-existent conditions including chronic conditions and general oncological screening particularly in the care of women at different ages (breast, ovaries, uterus and cervix). Consideration has to be given to women with cardiovascular disease, which far outstrips breast cancer as a leading cause of morbidity and mortality.

Women going through the transition phase can be grouped according to their age range; from 35–45, 46–55, 56–65 and over 66 years. These age cohorts are especially interesting in the wake of the reanalysis of WHI, where, when broken down into cohorts, the pathology and outcome variables varied in important manners.

Thus the efforts of any HRT in the 46–55 years cohort was different to that in the over 65 year old when it came to the particular outcome variable of cardiovascular disease, and incidence of breast cancer as an example.

A careful work up of individuals will render specific advice and possible medical interventions to the individual as necessary, much more accurate, thus reinforcing the current concepts as indicated from such documents as the IMS recommendations which emphasises both the individualisation of therapy and utilising the various 'windows of opportunity' for management that present themselves.

### *Optimal use of SERMS after menopause*

James Pickar (US)

Columbia University

Selective Estrogen Receptor Modulators (SERMs) are a group of estrogen receptor agonist/antagonists with tissue selective effects. They have been used to treat a variety of conditions and one (bazedoxifene) also been combined with estrogens in what has been referred to as a Tissue Selective Estrogen Complex (TSEC). The first SERM, clomiphene citrate, was approved for use

in the U.S. in 1967, the most recent, Ospemifene and the TSEC conjugated estrogens/bazedoxifene in 2013.

Following menopause, SERMs are now commonly used to treat a number of menopause associated conditions including osteoporosis, vasomotor symptoms and symptoms of vulvovaginal atrophy.

Some of the wide variety of indications obtained by members of this family include the treatment of ovulatory dysfunction in women desiring pregnancy (clomiphene citrate), various indications related to breast cancer (tamoxifen citrate, toremifene citrate, raloxifene hydrochloride, fulvestrant), indications related to osteoporosis (raloxifene hydrochloride, bazedoxifene, conjugated estrogens/bazedoxifene), the treatment of dyspareunia due to menopause (ospemifene) and the treatment of vasomotor symptoms associated with menopause (conjugated estrogens/bazedoxifene). In India, ormeloxifene has been available for contraception and dysfunctional uterine bleeding.

Following a brief presentation of background information, clinical case examples will be used to explore the optimal use of SERMs after menopause.

### *What is the best way of preventing fractures in women under 65 with and without osteoporosis?*

Anna Fenton (NZ)

Christchurch Women's Hospital

The primary aim of managing low bone density or osteoporosis is to prevent fractures. Most fractures occur in men and women with low bone density rather than in those with Dual energy Xray Absorptiometry (DXA) defined osteoporosis. This session will focus on fracture risk assessment using clinical risk factor assessment and vertebral imaging, understanding who to treat and what the management options are. Using a case-based approach this interactive session will discuss the role of lifestyle options such as exercise, diet and complementary therapies. The risks and benefits of calcium and vitamin D supplements, the re-emerging role of menopause hormone therapy and the role of other pharmacological therapies will be highlighted.

### *Less than 40 with amenorrhea – assessment, diagnosis and management*

Nick Panay (GB)

Imperial College London

Amenorrhoea is a problem experienced by many women during their reproductive lives. Early diagnosis will facilitate appropriate management and will minimize morbidity and even mortality. For normal menstruation to occur the following are necessary: hypothalamic function, pituitary function, ovarian function, endometrial function, patent cervix and vagina. Absence of bleeding may therefore be caused by malfunction or disease at any of these levels. Amenorrhoea may be primary, where periods have never started, or secondary where periods have stopped for six months or more. Irregular periods are a particularly common problem as women enter their late thirties and early forties. In trying to determine the etiology of absent periods the following should be considered: (1) central nervous system dysfunction; (2) gonadal dysfunction; (3) genital tract disorders; (4) endocrine disorders; (5) drug therapy. Whilst

amenorrhoea may not be pathological, for example in pregnancy, many predisposing conditions carry potential risks. The hypo-estrogenic states of hypothalamic amenorrhoea and premature ovarian insufficiency are associated with quality of life, fertility issues and increased risks of osteoporosis, ischaemic heart disease and cognitive problems. Endometrial hyperplasia and endometrial carcinoma occur more frequently in women with anovulatory cycles and polycystic ovarian syndrome due to unopposed estrogenic effects on the endometrium associated with chronic anovulation. Prompt investigation and diagnosis are therefore of paramount importance to facilitate early management. Patient assessment, investigation and diagnostic strategies will be discussed in detail to facilitate healthcare professionals in optimising their management of women with amenorrhoea.

### *Osteopenia and osteoporosis: when and how to intervene*

John Stevenson (GB)

National Heart & Lung Institute

The main objective of therapy for osteopenia and osteoporosis is fracture prevention. Fracture risk relates particularly to age and to bone density. The highest fracture risk is seen in patients with osteoporosis, and the lower the bone density the greater the risk. However, the majority of fractures occur in women with osteopenia because of their greater numbers. Anyone sustaining a typical osteoporotic fracture should be considered for treatment intervention irrespective of their bone density. In premenopausal women with low bone density but without fracture, intervention may not be necessary, whereas in postmenopausal women it should be considered. Hormone replacement therapy (HRT) should remain the first-line therapy for primary prevention of osteoporosis, and is an effective and safe therapy providing it is used appropriately. Bisphosphonates are a widely used treatment for postmenopausal osteoporosis. However, long term safety issues have become apparent. An increased incidence of atrial fibrillation has been found in some clinical trials; osteonecrosis of the jaw has been seen particularly following dental extractions, and inflammatory eye disease has also been reported. These adverse effects, fortunately rare, are found mainly, or exclusively, with intravenous bisphosphonates. There are increasing numbers of reports of fragility fractures of the femur with long-term bisphosphonate use and with denosumab. Bisphosphonates have an extremely prolonged skeletal retention time, and since unexpected adverse effects could yet arise in the future they should be avoided where possible in women aged below 60 years. Newer agents which affect the Wnt-LRP signal to osteoblasts or block the osteoclast-produced cathepsin K protease are under development, but again there are safety issues and efficacy is not established for all treatments.

### *Does this patient have dementia? How can I tell?*

Victor Henderson (US)

Stanford University

Forgetfulness and other cognitive complaints are common in midlife, but dementia is rare. Subjective cognitive complaints are not confined to midlife and occur in men as well as women.

Estradiol levels during midlife are not related to memory. It is important to realize that memory, processing speed, and organizational skills decline to a modest degree with normal aging. A perceptive woman who notices these age-related changes may understandably become worried about incipient dementia. If the history and examination do not raise new concerns, the clinician can assure the patient that cognitive symptoms are common, are sometimes associated with the menopause transition, are usually self-limited, and are not known to lead to dementia later in life. To help rule out a neurological disorder, a clinician must first decide whether cognitive complaints reflect objective decline beyond that of normal aging. Once an underlying neurological disorder is reasonably excluded, stress, depression, sleep disorders, and medication side-effects, and other contributors should be considered. Results from large randomized clinical trials now demonstrate that menopausal hormone therapy used in midlife does not benefit or harm memory or global cognition over a several year period of use.

### *Contraception in the perimenopause*

Delfin A. Tan (PH)

St. Luke's Medical Center, Quezon City

Although fertility declines with advancing age as the woman approaches the menopause, some risk of pregnancy persists, and effective contraception needs to be offered to avoid an unintended pregnancy. No method of contraception is contraindicated by age alone. However, clinical problems frequently arising at this period such as menstrual cycle abnormalities, vasomotor instability, the need for osteoporosis and cardiovascular disease prevention, as well as the increased risk of gynecological cancer, should be taken into consideration before the initiation of a specific method of contraception. The choice of contraceptive method during perimenopause is therefore critical as each method holds special benefits and risks that should be carefully balanced, after a thorough consultation and according to each woman's contraceptive and health needs. The objective of this session is to present four clinical cases of perimenopausal women requiring contraception and to draw the audience into a discussion of which method is best for each individual woman.

### *New treatment options: risks and benefits*

JoAnn Pinkerton (US)

University of Virginia Health System

Hormone therapy (HT) treats symptomatic menopausal women at risk for bone loss but the progestogen component has been associated with irregular bleeding, breast tenderness and increased breast density. The novel tissue selective estrogen complex (TSEC) combines conjugated estrogens (CE) with the estrogen agonist/antagonist (SERM) Bazedoxifene (BZA). The SMART studies demonstrated that CE/BZA 0.45/BZA 20 mg improved VMS, VVA, prevented loss of bone, and had a neutral effect on the breast, with similar effects on breast tenderness, breast density, and breast cancer incidence as those seen with placebo; protected against estrogen-induced endometrial hyperplasia and cancer, with similar amenorrhea rates to placebo. The lack of significant breast tenderness or vaginal bleeding with CE/BZA is a major benefit of CE/BZA for women with a uterus.

VMS: In PM women with mod-severe VMS, HF frequency reduced by 74% vs 51% for placebo.

Bone: In SMART-1, lumbar spine BMD increased from baseline at 12 and 24 months (1.05% and 1/6%), compared to a loss of 1.81% with placebo.

VVA: In SMART-1 and -3, vaginal superficial and intermediate cells increased vs placebo after 12 wks, with less dyspareunia.

Breast pain and tenderness: In SMART-5, similar effect on breast pain, tenderness and breast density to placebo with less effect than seen with CE 0.45 mg/MPA 1.5 mg. Rates of breast cancer similar to placebo for up to 2 years.

Endometrial hyperplasia: increase in endometrial hyperplasia observed vs placebo (<1%) at 1 and 2 years. Rates of endometrial cancer not increased for up to 2 years.

CVD: CVD, cerebrovascular events, cancers (endometrial, breast and ovarian) and mortality similar to placebo. 2-fold increased risk of VTE expected, no additive effects

Consider TSEC CE/BZA for symptomatic postmenopausal women with a uterus to relieve hot flashes and prevent bone loss.

### *Cardiovascular disease: when can HT safely be used?*

Marco Gambacciani (IT)

Pisa University Hospital

Safety of any given therapy depends on a variety of factors including medical errors such as overdose, misuse and abuse. Climacteric complaints are the main indication for hormone replacement therapy (HRT) in the clinical practice. Observational studies consistently demonstrate a protective effect of HRT on cardiovascular disease (CVD) in postmenopausal women (PMW). All these studies were conducted in early, young, symptomatic PMW. Vasomotor symptoms correlate with lower level of plasma antioxidant activity, an increased cardiovascular reactivity to stressful situations, elevated cholesterol, higher sympathetic nerve activity, impaired flow-mediated dilation, hypertension and an higher risk of aortic calcification. Therefore, all the available findings indicate that hot flashes can be seen as a marker for underlying vascular changes among midlife, in otherwise healthy, PMW. Thus, young, healthy symptomatic PMW differ from those without vasomotor symptoms with regard to cardiovascular risk factors. Therefore, responses to HRT can change in terms of cardiovascular outcomes according to the baseline vasomotor complaints. This evidence supports the "timing hypothesis", which theorizes that cardiovascular benefit may be derived when HRT is used close to the menopause onset. This point may explain at least in part the negative/null effects of HRT on cardiovascular disease observed in the trials where HRT was given to largely asymptomatic, elderly women. In addition, HRT discontinuation in healthy PMW is bound to a significant increase in CVD. Since women aged 65 years and older may continue to need systemic HRT for the management of a variety of symptoms, routine discontinuation of systemic HRT at any predefined age should be avoided. As with younger women, use of HRT should be individualized based on each woman's risk-benefit ratio and clinical presentation

## SYMPOSIA BY SCIENTIFIC SOCIETIES/ CAMS

### EMAS Symposium: Lifestyle and culture in the promotion of healthy aging

#### *The Mediterranean lifestyle and longevity*

Faustino Perez-Lopez (ES)

University of Zaragoza and Lozano-Blesa University Hospital, Zaragoza, Spain

The Mediterranean lifestyle is a term coined by Axel Keys to include simple food and daily physical activity that was supposedly the way of life among the common people living close to the Mediterranean sea. Diet includes basic nutrients such as olive oil, grain products, fish, nuts, fruit and vegetables. Adherence to this diet has been associated with higher longevity and reduced risk of developing chronic diseases, including cancer, the metabolic syndrome, type 2 diabetes, depression and cardiovascular and neurodegenerative diseases. The possible beneficial anti-aging benefits may be related to olive oil, omega-3 and -6 polyunsaturated acids, flavonoids and polyphenols. Physical activity may reduce the risk of insulin resistance, excessive weight gain, regulation of adipose tissue and pancreatic function. The identification of selective food components may allow the development of specific anti-aging approaches.

#### *Personalized prevention and treatment strategies for a healthy pelvic floor aging*

Tommaso Simoncini (IT)

University of Pisa

Female pelvic floor is a complex functional unit involved in multiple functions that extend beyond the sole support of pelvic organs. Pelvic floor dysfunction globally affects micturition, defecation and sexual activity. Evolutionary modifications such as adaptation to upright standing, walking and the need to deliver fetuses with larger head diameters made the fascial and muscle support of the pelvic floor vulnerable, therefore predisposing women to pelvic organ prolapse and incontinence. Different than in males, the female pelvic floor undergoes a number of adaptive changes related to life and endocrine events. Most of the clinical manifestations of these changes become apparent after menopause and throughout ageing in women. This presentation will highlight the key aspects of the pathophysiology and the clinics of the modifications of the pelvic floor in women through midlife and beyond with a focus to the modern integrated treatment options.

### NAMS symposium: New from NAMS: important updates on women's health at midlife and beyond

#### *Vasomotor symptoms, cognition and brain function*

Pauline Maki (US)

University of Illinois at Chicago

Memory complaints are more frequent among perimenopausal and postmenopausal women compared to premenopausal women, even when controlling for age and other relevant factors. Women's performance on standardized neuropsychological tests of memory decreases as they transition through the menopause, but appears to rebound during the postmenopausal stage. Diary and questionnaire-based measures of vasomotor symptoms (VMS; hot flashes and night sweats) are associated with memory complaints but not with performance on memory tests. An emerging body of research, however, shows a link between memory performance and physiologic VMS measured with ambulatory skin conductance monitors. Among women with moderate-to-severe VMS, physiologic VMS, but not reported VMS, are associated with worse memory performance. The possibility that treating physiologic VMS may improve memory performance was supported by findings from a randomized, sham-controlled pilot trial of stellate ganglion blockade (SGB), a non-hormonal anesthesia intervention for VMS. In that study, the magnitude of improvement in VMS correlated significantly with the magnitude of improvement in memory performance. Neuroimaging studies suggest a link between physiologic VMS and brain health. Physiologic VMS were correlated with white matter hyperintensities, structural brain abnormalities that are associated with an increased risk of dementia. Physiologic VMS are also associated with alterations in the function of the hippocampus during the resting state and in the function of the hippocampus and prefrontal cortex during performance of verbal memory tasks. These studies suggest an association between physiologic VMS, memory and brain function/structure, but larger studies are needed to examine the robustness of these associations.

### ISGE symposium: Menopause hormone therapy: problems and solutions

#### *Menopausal hormone therapy (MHT): optimal risk minimization*

Martin Birkhäuser

Professor Emeritus of Gynaecological Endocrinology and Reproductive Medicine, University of Berne, Switzerland

Today, it has been generally accepted that, for healthy women, the benefits of MHT are greater than the risks if MHT is started within the "window of opportunity". This means MHT should be started within 10 years after menopause or before the age of 60 years. However, in addition to this basic rule, the risk of MHT can be further minimized by respecting some simple principals: First of all, a full history has to be taken. An evaluation by the Menopause Rating Scale II (or an other similar questionnaire) might be helpful to decide on the indication of MHT. Then, all candidates for MHT should be screened for overweight, diabetes

(fasting blood glucose, if needed HbA1C), cardiovascular risk (blood pressure, lipids), urogenital and sexual health (need for local hormonal therapy only? need for non-hormonal measures?), cancer (gynaecological examination with PAP smear, examination of the breast with mammography), bone densitometry/FRAX®, thrombophilia (if indicated only). Depending on the family or personal history, other tests might be indicated. In younger women with suspicion of early menopause, other reasons for secondary amenorrhea have to be excluded (hypo-/hyperthyroidism, hyperprolactinemia, pregnancy, psychogenic amenorrhea, etc.).

To take the risk of stroke as an example, it has been shown by the Women's Health Initiative for MHT and by the RUTH study for raloxifene that the risk of stroke is not increased if all women presenting at least one of the risk factors listed above (including history) are not treated by oral MHT or a SERM.

Finally, it has to be remembered that (1) transdermal MHT is linked to significantly lower risks than oral MHT, except for cancers; (2) low-dose MHT has lower risks than the classical per oral 2 mg oestradiol/day (= 0.625 mg conjugated estrogens) or 50 µg transdermal oestradiol/day; (3) micronized progesterone and some progestins, e.g. dydrogesterone, might involve lower risks than other progestins.

### Optimising cardiovascular safety of HRT

John Stevenson (GB)

National Heart & Lung Institute

Observational studies have consistently shown a benefit of hormone replacement therapy (HRT) on coronary heart disease (CHD) prevention, although the biggest beneficial impact has been seen in those women who initiated HRT close to the menopause. However, randomised clinical trials of HRT in women with established heart disease have not shown any significant cardiovascular benefit. The Women's Health Initiative (WHI) showed no overall effect of estrogen/progestogen on CHD outcomes, but the estrogen-alone arm showed an eventual significant reduction in CHD events if initiated below age 60 years. Thus, the age at initiation of HRT seems to be important for cardiovascular benefit and risk, with the biggest benefit being seen in women starting treatment below 60 years of age and within 10 years of onset of menopause as confirmed by large meta-analyses of randomised clinical trials of HRT. The Danish Osteoporosis Prevention Study was a prospective clinical trial of 1000 women in the early postmenopause who were randomised to either HRT or no treatment, studied for 10 years and followed up for a further 6 years. HRT produced a significant reduction in a composite end-point of myocardial infarction, death or heart failure. The dose of estrogen at initiation may be critically important; inappropriately high doses of estrogen can increase coagulation activation and promote adverse vascular remodelling, and the standard dose used in WHI, whilst suitable for women aged under 60 years, was inappropriately high for the older women. Different progestogens have different metabolic and cardiovascular effects, and medroxyprogesterone acetate (MPA) used in WHI has some detrimental effects. Other progestogens such as micronized oral progesterone or dydrogesterone may be more beneficial in this respect. HRT appears effective and safe for the primary prevention of CHD in women.

## Asia Pacific Menopause Federation symposium

### *The perspectives of Asian women on breast cancer*

Ko-En Huang (TW)

Kaohsiung Chang Gung Memorial Hospital

**Objectives:** This study was designed to evaluate the epidemiology and perspectives on breast cancer of Asian women.

**Methods:** A literature review was done on the epidemiology of breast cancer of Asian women. A multinational survey was done by face-to-face interview of 1,000 postmenopausal women ages 45 to 60 years in China (300), Hong Kong (100), Malaysia (300), Taiwan (150) and Thailand (150). Data were collected and analyzed.

**Results:** The SWAN study showed that blood levels of estrogen of oriental women are lower than that of Caucasians. The age specific incidence of breast cancer showed bell shape distribution with peak age at 45–55 years in Asians compared to at over 70 years in Westerns. Of those women surveyed, 27% said there was breast discomfort with sore and tender; 70% had breast self-examination, but only 47% had mammography; 43% worried when having screening and 58% worried about the results when they had a recall examination; 50% of women worried about getting breast cancer, but 91% thought they did not have higher than average risk of getting breast cancer; 50% of women thought hereditary and 24% thought HT is the main risk factor; the fear of breast cancer prevent the use of HT in 55% of women surveyed.

**Conclusions:** The majority of women in Asia do not experience breast discomfort. Asian women do conduct self-examination of their breasts but not many went for a mammogram. In Asia, the breast cancer incidence increases more in young women with the peak age in late 40th. Most of the Asian women consider HT a high breast cancer risk, which prevents them from HT. The majority of women said they were not advised by their doctors for HT and feel more confident in having HT with doctors' advice. Breast cancer screening should be started at younger age group, such as at 40 or 45 years of age.

### *Metabolic syndrome in Asia Pacific countries*

Sunila Khandelwal (IN)

Fortis Escorts Hospital

The epidemic of "Metabolic Syndrome"(MetS) is increasing worldwide, reported higher in Asian than Caucasian women, resulting in an enormous health, social and economic burden to the Asia Pacific Region. Comparative studies indicate that higher percentage body fat in Asians at given BMIs and metabolic responses to obesity may be greater in South and East Asians than their western counterparts at given BMIs. Increasing consumption of an energy-dense diet, decreasing physical activity, and elevated psycho-social stress by economic development and urbanization are associated with not only obesity, but also impaired glucose regulation, high blood pressure and dyslipidemia, resulting in an increased risk of MetS. Asian Indians have a stronger genetic predisposition to diabetes than other ethnic groups. Lower disease awareness and health-seeking behaviour, delayed diagnosis due to atypical presentation, language barriers, religious and sociocultural factors, all result in higher morbidity and mortality in these

women. The age-adjusted prevalence India reported was 26.9% by the original NCEP/ATP III criteria, 32.7% by the modified NCEP/ATP III criteria, and 38.2% by the IDF criteria.

Screening at menopause is an ideal opportunity for the physician to look for factors that may in future lead to a full blown metabolic syndrome. There is an urgent need to develop effective long term community-based preventative health plan by encouraging combination of exercise, dietary modifications, behavioral therapy and pharmacological interventions with appropriate use of MHT.

New ethnic-specific guidelines and prevention strategies will be discussed in this presentation. Aim is to highlight the prevalence of MetS, identify reasons and the key metabolic issues based on recent researches with focus on aggressive early therapy for achieving targets in women of Asia Pacific countries.

### *Hormone replacement therapy and the risk of cardiovascular disease in Japanese postmenopausal women*

Akihiko Wakatsuki (JP)

Aichi Medical University

**Objective:** Although oral conjugated equine estrogen (CEE) favorably affects lipids by reducing plasma LDL cholesterol and increasing HDL cholesterol, it increases plasma triglyceride. We previously demonstrated that CEE-induced increases in plasma triglyceride decrease the size of LDL particle, which may act counter to estrogen's antioxidant effect that opposes oxidation of LDL particles. In this study, we investigated differential effects of CEE, oral 17 $\beta$ E2, and transdermal 17 $\beta$ E2 on plasma arterial (ATE) and venous thromboembolic (VTE) risk markers in Japanese postmenopausal women.

**Methods:** Japanese postmenopausal women were treated with 0.625 mg CEE daily, with 2 mg oral 17 $\beta$ E2 daily, and with 0.72 mg 17 $\beta$ E2 patch every other day for 3 months. Plasma concentrations of D-dimer for a VTE risk marker, and lipids, metallic ions, derivatives of reactive oxygen metabolites (d-ROMs), and biological antioxidant potential for ATE risk markers were measured.

**Results:** CEE, but not oral 17 $\beta$ E2, increased the plasma concentrations of triglyceride, copper (Cu), d-ROMs, D-dimer, and the ratio of small dense LDL/total LDL cholesterol, a marker for plasma distribution of small dense LDL. Transdermal 17 $\beta$ E2 decreased d-ROMs concentrations, but did not significantly change other parameters. Estrogen-induced changes in triglyceride correlated positively with changes in the ratio of small dense LDL/total LDL cholesterol ( $R=0.65$ ,  $P<0.0001$ ). Changes in Cu correlated positively with changes in d-ROMs ( $R=0.86$ ,  $P<0.0001$ ).

**Conclusions:** CEE, but not oral and transdermal 17 $\beta$ E2, may adversely affect ATE risk by elevating plasma triglyceride and Cu, which may increase plasma distribution of small dense LDL and oxidative stress, respectively. CEE may also increase the risk of VTE by increasing D-dimer.

### **British Menopause Society symposium**

#### *NICE guideline, implications and impact*

Mary Ann Lumsden (GB)

University of Glasgow

The Guideline "Menopause: Diagnosis and Management" was published by the National Institute of Health and Care Excellence

[NICE] in the UK in November 2015, the aim being to improve the knowledge level of both health care professionals and their patients regarding the menopause and to standardise care across the UK. Recommendations were developed following the systematic review of the current evidence-base. Each review question posed (17 in all) was subject to systematic review and meta-analysis and appropriate recommendations written by a multidisciplinary group of doctors, nurses and a technical team from NICE including systematic reviewers, a health economist and a statistician among others.

Recommendations were made on:

- Individualised care.
- Diagnosis of perimenopause and menopause.
- Information and advice.
- Managing short-term menopausal symptoms (a full range of treatments).
- Long-term benefits and risks of hormone replacement therapy (HRT).
- Diagnosing and managing premature ovarian insufficiency (POI).

The aim of the guidelines is to give the woman and her doctor as much information and explanation as possible in order to achieve the best individualised care. This should enable her to make an evidence-based choice. There are sections on a 'normal' menopause, specific recommendations for women with POI, and women with vasomotor or other menopausal symptoms for whom standard HRT is contraindicated (e.g. those with breast cancer).

Since publication there has been considerable publicity with the development of Quality Standards by NICE against which care can be audited, and which can be used to commission services in the community. 'Infographics' have been developed by the BMS, which are very helpful in communicating risk and benefit in the clinical situation and are appealing to both the patients and the health care professionals looking after them.

### **BEST ABSTRACTS FOR THE ROBERT GREENBLATT AWARD: CLINICAL**

#### *Sexual dysfunction and related distress in the late postmenopause: results from an Australian study*

Berihun Zeleke (AU)<sup>a</sup>, Robin Bell (AU)<sup>a</sup>, Baki Billah (AU)<sup>b</sup> and Susan Davis (AU)<sup>a</sup>

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**Objectives:** The understanding of sexual wellbeing amongst older women is limited, and normative data are lacking. This study was undertaken to determine the prevalence of low sexual desire and its association with personal distress, and in turn the presence of hypoactive sexual desire disorder (HSDD), amongst sexually active and inactive older Australian women.

**Methods:** 1548 Australian women, aged 65 to 79 years, living independently in the community were recruited to this cross-sectional study. A questionnaire, completed between April and August 2014, assessed socio-demographic and health factors. Sexual function and sexual distress were assessed by the Female Sexual Function Index (FSFI), and the Female Sexual Distress Scale-Revised (FSDS-R), respectively. HSDD was defined as the presence of both low sexual desire (FSFI desire domain score of  $\leq 5$ ) and sexual distress (FSDS-R score  $\geq 11$ ).

**Results:** The mean  $\pm$  SD age of the 1321 women who provided sexual function data was  $71 \pm 3.4$  years. 56.3% were partnered and 42.9% reported being sexually active in the last month (48.0% of those partnered and 24.3% of those un-partnered). 1183 women (89.6%; 95% CI 16.2–20.3%) had low sexual desire and 18.2% (95% CI 16.2–20.3%) had sexual distress, resulting in a 15.9% (95% CI 14.0–18.0%) prevalence of HSDD. HSDD was significantly more common among partnered than non-partnered women (23.7% vs 5.9%;  $p < 0.001$ ) and among sexually active than sexually inactive women (31.5% vs 17.2%;  $p < 0.001$ ). Furthermore, 32% of partnered sexually active women had HSDD, as did 22% of un-partnered sexually active women.

**Conclusions:** HSDD is common amongst sexually active older Australian women. It should not be assumed that older un-partnered women are not sexually active or do not have HSDD.

### **Hormone replacement therapy (HRT) and cognitive function in relation to the timing of menopause: a prospective cohort study of 164,997 women from the UK Biobank**

Stamatina Iliodromiti (GB)

University of Glasgow

**Context:** The impact of HRT use on cognitive function is unclear. Studies suggest a possible “window of opportunity”, others show no overall benefit and some demonstrate an adverse effect in older women.

**Objective:** To investigate the impact of HRT use in measures of cognitive function in relation to the timing of menopause.

**Methods:** A cohort study that recruited over half a million of UK participants from 2006 to 2010. Data collected at their baseline visit were used in this analysis. Regression modelling with adjustment for age, socioeconomic status, cardiovascular disease, diabetes, hypertension, smoking and obesity was conducted.

**Patients:** 273,488 women aged 40–70 years were recruited. 164,997 were menopausal at recruitment, of whom 77,574 reported the use of HRT (current or past). 6,272 women underwent menopause under the age of 40 years, 51,226 women underwent menopause between 40 to 50 years and 107,499 women underwent menopause over the age of 50 years.

**Intervention:** Use of HRT.

**Main outcome measures:** Fluid intelligence score ( $n = 55,262$ ), reaction time ( $n = 163,786$ ) and pair of incorrect matches ( $n = 152,972$ ).

**Results:** In women that menopause occurred over the age of 50 years, fluid intelligence was lower in HRT users compared with non HRT users (mean difference  $-0.05$  (95% CI:  $-0.09$  to  $-0.002$ ),  $p = 0.04$ ). This finding remained significant only in women aging 50 to 60 years following further stratification. Reaction time was

lower in HRT users irrespective of timing of menopause (average by 1%,  $p < 0.001$ ). Discordance in correct matches was greater in HRT users (by an average of 1%,  $p = 0.001$ ) in women that menopause occurred over 40 years but not in those with an early menopause.

**Conclusions:** HRT use does not have an adverse impact on cognitive function of women undergoing early menopause and improves the reaction time in all women irrespective of timing of menopause.

### **Pilot study: Investigating the cardiovascular effects of transdermal testosterone in postmenopausal women using hormone replacement therapy**

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**Objectives:** Concerns have been raised regarding potential adverse cardiovascular (CV) effects of postmenopausal (PM) testosterone (T) therapy. Studies to date have frequently used high dose parenteral or oral therapy and there are limited data on the CV effects of transdermal T. This pilot study aimed to investigate the CV effects of transdermal T by assessing risk factors and surrogate markers for CV disease including arterial stiffness, endothelial function, lipid metabolism and insulin resistance.

**Methods:** Open label pilot study using 300  $\mu$ g transdermal T patch (Intrinsa®) for 12 weeks. Participants were 21 healthy PM women, age 45–70, reporting low libido and on a stable HRT regimen. Primary outcome measures were (1) Arterial stiffness (Alx), assessed using pulse wave analysis (PWA, SphygmoCor), (2) Endothelial function (digital reactive hyperaemia index (RHI)), using peripheral artery tonometry (Endopat) and (3) Insulin resistance using the homeostasis model. Anthropometry and lipids were also assessed.

**Results:** 12 weeks of T was associated with a reduction in hip circumference ( $-0.74$  cm,  $p < 0.05$ ), but no other changes in anthropometrics or blood pressure. Total cholesterol was unchanged, but there were decreases in high-density lipoprotein cholesterol ( $-0.25$  mmol/L,  $p < 0.05$ ) and lipoprotein(a) ( $-3.11$  mg/L,  $p < 0.05$ ). Fasting insulin, fasting glucose and insulin resistance were unchanged. There was no change to Alx (1.07,  $p = 0.43$ ), or RHI (0.06,  $p = 0.61$ ) but there was a significant increase in salbutamol-mediated vasodilatation ( $p < 0.05$ ), assessed by PWA.

**Conclusion:** This study found no adverse effect from transdermal T on surrogate markers for CV disease, with a potential benefit to endothelial function and small changes in lipid profile (both adverse and beneficial). Further randomised studies are needed to establish the long term implications of these changes.

## BEST ABSTRACTS FOR THE ROBERT GREENBLATT AWARD: BASIC

### *Do nulliparity and menopause modulate the expression levels of main pro-angiogenic factors: VEGF, VEGFR2, Akt and ERK2, in the mouse ovary?*

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University of L'Aquila, MeSVA Department

**Objective:** Nulliparity and menopause are considered risk factors for ovarian cancer. Nulliparity represents a condition capable of affecting the expression levels of the pro-angiogenic factors and modulating the degree of phosphorylation of signals involved in endothelial cell proliferation. This experimental animal study involved a total of 40 CD1 female mice, young (4-months-old) and old (15-months-old), both parous and nulliparous, where the expression levels of VEGF, VEGFR2, ERK2, Akt and PTEN proteins were determined.

**Methods:** Mice, called Mothers (M), were mated and sacrificed after the first pregnancy and lactation (Young, Y, n = 10) or at 15 month (Old, O, n = 10) of age, when they're in menopause. The same protocol was adopted for the group of nulliparous mice, called Virgins (V), sacrificed without mating either young (YV, n = 10) or old (OV, n = 10). Ovaries were collected and stored for Western blot analysis. The expression levels of VEGF, VEGFR2, ERK2, Akt and PTEN proteins were determined into the 4 groups. **Results:** VEGF content was always higher in V than in M, but no age-dependent increase of VEGF was recorded in V because of the high levels already present in the YV. VEGFR2 content was higher in V than in M, and was accumulated in OV. Akt and ERK2 were phosphorylated more efficiently in V than in M. PTEN was under phosphorylated in OV.

**Conclusion:** The finding that in the ovaries of nulliparous (V) mice the expression levels of pro-angiogenic proteins are enhanced in comparison to parous (M) mice, contributes to explain epidemiological data by providing the first molecular explanation of the protective role of pregnancy on female health; the over-expression of specific pro-angiogenic proteins and their over-activity can contribute to explain the reason why the incidence of ovarian cancer in nulliparous women is higher than in parous ones.

### *Screening for osteoporosis in amenorrheic and postmenopausal women*

Antonina Smetnik (RU), Vera Smetnik (RU), Gennady Sukhikh (RU), Andrey Donnikov (RU) and Svetlana Yureneva (RU)

FSBI "Research Center for Obstetrics, Gynecology and Perinatology" Ministry of Healthcare of the Russian Federation

**Context:** Menopause and secondary amenorrhea is usually associated with bone loss.

**Objective:** To work out non-instrumental screening for low bone mineral density (BMD) in amenorrheic and postmenopausal women.

**Methods:** Patients. 54 women with secondary hypothalamic amenorrhea (HA), 55 with premature ovarian insufficiency (POI)

and 191 postmenopausal women (without metabolic syndrome and prior HRT) were enrolled in cross-sectional study. Interventions. We evaluated BMI, BMD (by DXA), levels of reproductive hormones, markers of bone and lipid metabolism. SNPs of genes regulating differentiation and function of bone cells and adipocytes (COL1A1, CYP19A1, ESR1, ESR2, LEP, LEPR, LRP5, TNFRSF11B, RANKL, SOST, VDR, PPARG, FTO, INS) were assessed by PCR. Main Outcome Measures. Correlation analysis and logistic regression analysis were performed.

**Results:** 48.2% of women with HA and 23.6% with POI had low BMD. There were positive correlations between BMI and BMD in all groups. We worked out a screening for low BMD in women with amenorrhea:  $y = 2.67 + 0.22^*$  (duration of amenorrhea, years)  $- 0.29^*$ (BMI)  $+ 0.74^*$  (atherogenic index). AUC 0.79 (95% CI 0.68–0.89),  $p < 0.001$ . Probability (P)  $> 50\%$  ( $y > 0$ ) -high-risk group (Sp = 85%, PPV = 70%);  $P < 27\%$  ( $y < -1,0$ ) -low-risk group (Se = 87%, NPV = 88%). The probability of postmenopausal osteoporosis:  $y = 6.65 - 0.07^*$  (body mass, kg)  $- 0,97^*$  (LEPR, rs8179183)  $+ 0,56^*$ (RANKL, rs9594759). AUC 0.75 (95% CI 0.68–0.82),  $p = 3^*10^{-9}$ .  $y > 0$  -high-risk group (Sp = 73%, PPV = 85%);  $y < -1,0$  -low-risk group (Se = 97%, NPV = 83%). We found a significant influence of LEPR (rs8179183) on BMD in underweight women with HA and postmenopausal women with obesity ( $p < 0.05$ ).

**Conclusions:** Significant associations of bone and fat were found in women with estrogen deficit of different age - with the key role of leptin receptor, connecting reproductive system, fat and bone, that led to new screening approaches.

### *Effect of Rosmarinic acid on sexual behavior and hormones levels in diabetic rats*

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Women's Reproductive Health Research Center of Tabriz University of Medical Sciences, Iran

**Objective:** Rosmarinic acid from the plants quenched superoxide radicals from xanthine oxidase and inhibited cyclooxygenase I and II enzymes. Antioxidants have essential effect on diabetes. Enhanced oxidative stress and changes in antioxidant capacity are considered to play an important role in the pathogenesis of chronic diabetes mellitus.

**Methods:** Wistar male and female rats (n = 40) were allocated into three groups, control group (n = 10) and Rosmarinic acid (Ro) group that received 5 mg/rat (gavage) (n = 10), and Diabetic group that received 55 mg/kg (IP) streptozotocin (STZ) (n = 20) which was subdivided to two groups of 10; STZ group and treatment group. Treatment group received 55 mg/kg (IP) STZ plus 5 mg/ratRo, daily for 4 weeks, respectively; however, the control group just received an equal volume of distilled water daily (gavage). Diabetes was induced by a single (IP) injection of streptozotocin (55 mg/kg). Animals were kept in standard condition. In 28 days after inducing diabetic 5 cc blood were collected for testosterone levels from whole groups' analysis.

**Results:** Level of sexual behavior and testosterone significantly increased in groups that received Ro, in comparison to whole groups ( $P < 0.05$ ).

**Conclusion:** Since in our study 5 mg/rat of Ro have significantly preventive effect on diabetic disorder in libido, so it seems that using it can be effective for treatment in diabetic rat.

## RESEARCH BURSARY AWARD

### *Menopausal symptoms; prevalence and impact on the health and wellbeing of older women*

Berihun Zeleke (AU), Robin Bell (AU), Baki Billah (AU) and Susan Davis (AU)

Monash University

**Objectives:** Normative data for the persistence of postmenopausal symptoms including vasomotor symptoms (VMS; hot flushes and night sweats), urogenital atrophy and pelvic floor disorders in older women are lacking. This study was undertaken to determine the prevalence of vasomotor (VMS), vulvovaginal atrophy (VVA) symptoms, and pelvic floor disorders in community-dwelling older Australian women.

**Methods:** 1548 women, aged 65–79 years, were recruited to this national cross-sectional study between April and August 2014. Participants provided demographic data and completed the Menopause Quality Of Life questionnaire and validated questionnaires for assessing pelvic floor disorders.

**Results:** Among 1426 women not using systemic hormones, 32.8% had VMS, with 10.3% having moderate-to-severe VMS. Obesity (OR = 1.44; 95% CI, 1.07–1.93), being a carer for another person (OR, 2.54, 95% CI, 1.33–4.84), and bilateral oophorectomy (OR, 2.41, 95% CI, 1.25–4.61) were positively associated with any VMS. 20.3% of women (32.5% of partnered and 7% of un-partnered women) reported having VVA symptoms in the last month. 47.2% of women had at least one pelvic floor disorder (36.2% urinary incontinence, 19.8% faecal incontinence, and 6.8% pelvic organ prolapse). Obesity (OR = 1.77; 95% CI, 1.36–2.31), and parity (OR = 1.93; 95% CI, 1.30–2.88) were positively associated with having at least one pelvic floor disorder.

**Conclusions:** VMS, VVA symptoms, and pelvic floor disorders are common in older Australian women. Physicians caring for older women should consider that older women may have ongoing estrogen deficiency symptoms and women with symptoms of one pelvic floor disorder are likely to have a concurrent pelvic floor problem. The degree of distress caused by VVA symptoms amongst older women needs further exploration.

## ORAL COMMUNICATIONS

### *OC2: Predicting and assessing cardiovascular disease risk*

#### *Evaluation of metabolic health parameters at menopause transition*

Meeta Meeta (IN), Deepa Agarwal (IN), Sameena Shehvar (IN), Tanvir Singh (IN) and Akanshi Madan (IN)

Tanvir Hospital, India

**Objective:** To examine the changes in body composition (BC) and lipid profile at menopause transition in a South Indian Cohort  
**Methods:** Institutional Ethics Committee approval, written consent from participants obtained. Hospital based prospective cross sectional study in 754 urban women in the age of 35–80 years (yrs). Analysis of body composition was by dual-energy x-ray absorptiometry (DXA, Lunar Prodigy Advance) with a precision of 1.5%, 1% and 0.5% for adipose tissue, lean muscle mass and bone mass respectively. The variables measured were the total fat mass (TFM), the visceral adipose tissue (VAT), adipose tissue in the android (AA) and gynecoid (GA) area. Fasting levels of lipid

profile measured by enzymatic method. Statistical analysis was carried out using SPSS version 18.1.

**Results:** TFM significantly increased ( $p < 0.01$ ) from premenopause to postmenopause being highest at 47–48 yrs with a mean age of 47 yrs as indicated from the scatter plot. With increasing age between 46–49 yrs a linear correlation was observed with TFM ( $r = 0.02$ ). Android obesity relatively increased ( $p < 0.01$ ) in postmenopausal women (50–60 yrs) compared with premenopausal women. Gynecoid obesity also relatively increased ( $p < 0.05$ ) in postmenopausal women, decline was noted after 60 yrs. The VAT significantly increased ( $p < 0.001$ ), the highest being at 50–60 yrs. In women, during the time from the premenopause to postmenopause (50–60 yrs), the changes in lipid profile were larger than those between early perimenopause.

**Conclusion:** The significant change in BC seen in our study between the age of 45–50 yrs correlates with the early age of menopause (46.5 yrs) of Indian women. Changes in the fat indices by DXA are seen at an earlier age (45–50 yrs) than the changes in the lipid profile, indicating that BC by DXA in at risk population may be used as a screening tool for metabolic health risk assessment.

### *Differences between men and women in cardiovascular aging*

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<sup>a</sup>Fukui-ken Saiseikai Hospital; <sup>b</sup>Fukui-ken Saiseikai Check-up Center

**Objective:** This retrospective study aimed to evaluate the differences between the sexes in atherosclerotic changes of coronary and peripheral arteries preceding cardiovascular disease (CVD).

**Methods:** During 7 years starting from October 2008, we identified a total of 494 Japanese participants (399 men and 95 women) without known CVD and hormonal treatment. They underwent both coronary computed tomographic angiography (CCTA) and vascular function tests such as ankle-brachial index (ABI) and cardio-ankle vascular index (CAVI). Coronary stenosis and calcification were measured and evaluated by radiologists and expert cardiologists. These findings were summarized according to the degree of lesion and number of involved vessels, then categorized into 4 types such as “no abnormality”, “no trouble”, “observation”, and “need further examination”. Screening of peripheral atherosclerosis was defined as positive when the level of either ABI or CAVI was out of the standard.

**Results:** Participants were classified into 8 groups according to the age, namely A: less than 40, B: 40–44, C: 45–49, D: 50–54, E: 55–59, F: 60–64, G: 65–69, H: 70 or more. By CCTA analyses there were no men who needed observation or further examination in group A, and no such women in group A through D. The same categorized men were increasing in proportion gradually from group B (8.3%) to H (53.3%), while the rate of those women was increasing in group E (11.8%) to H (60.0%). Peripheral indicators showed no positive participants in group A and B, and no such women in group C. The positive ratio jumped up from group F to G then H both in men (20.5%–39.0%–60.0%) and women (16.7%–40.0%–60.0%).

**Conclusion:** Coronary artery stenosis and calcification seemed to start earlier in men by 10 years than in women although peripheral atherosclerosis progression seemed to have no significant difference between the sexes.

### *Pregnancy-induced hypertension as a risk factor in the occurrence of hot flashes among perimenopausal women: results of a prospective cohort study from the Japan Nurses' Health Study (JNHS)*

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**Objective:** To examine the association between demographic characteristics and health behaviors among Japanese women who currently experience perimenopausal hot flashes.

**Methods:** We used baseline data from the Japan Nurses' Health Study (JNHS) 2001–2007 and data from a 4-year follow-up survey of the women enrolled in the JNHS. A cohort of 4,560 women aged 45–54 years was analyzed in this study. A self-administered questionnaire provided information on demographic characteristics, health behaviors, and history of hot flashes. Multivariable logistic regression was conducted to examine the association between potential risk factors and hot flash outcomes.

**Results:** At the four-year follow-up, of the 4,560 women in the study, 2,672 (58.6%) were premenopausal, 1,411 (30.9%) were postmenopausal, 465 (10.2%) were perimenopausal (undetermined), and 1,228 (26.9%) reported current hot flashes. In the multivariable analysis (adjusted), women with a history of pregnancy-induced hypertension (PIH) (adjusted OR, 1.34; 95% CI, 1.06–1.68), women with alcohol consumption 5–7 days/week (adjusted OR, 1.29; 95% CI, 1.06–1.58), and women with BMI 25–29 (adjusted OR, 1.35; 95% CI, 1.09–1.68) were significantly associated with current hot flashes. A total of 3,801 women in the sample (83.4%) have given birth. In the multivariable-adjusted model including hypertension in women who have given birth, those with a history of PIH were significantly associated with hot flashes (adjusted OR, 1.35; 95% CI, 1.07–1.70) compared with those with no history of PIH.

**Conclusions:** More than one in four (26.9%) women aged 45–54 years from the JNHS follow-up survey reported current hot flashes. Women who experienced pregnancy-induced hypertension (PIH) have an increased risk of current hot flashes, even after taking age and hypertension into account.

### *Ovarian infertility is associated with cardiovascular disease risk factors in later life: A Japanese cross-sectional study*

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**Context:** Recently, emphasis on women's health aspects of polycystic ovary syndrome (PCOS) has been changing from early age reproductive disorders to long-term metabolic and cardiovascular health

**Objective:** This study aimed to clarify the association between ovarian infertility and cardiovascular disease risk factors in later life in Japanese women.

**Methods:** The Japan Nurses' Health Study (JNHS) is a cohort study of Japanese women's health. Data from the JNHS baseline survey (n=49,927) between 2001 and 2007 were used in a cross-sectional, retrospective analysis. A total of 44,601 women were classified into three categories: ovarian infertility group (n=1,167), other infertility group (n=4,619), and no infertility group (n=38,815). Logistic regression analysis compared with the no infertility group was performed.

**Main outcome measures:** Age-adjusted odds ratios (ORs) and multivariable-adjusted ORs for hypertension, hypercholesterolemia, and diabetes mellitus (DM).

**Results:** The prevalence of obese women (BMI  $\geq 25$ ) who were <45 years old in the ovarian infertility group was significantly higher compared with that in the other groups. Women in the ovarian infertility group were at risk for hypertension at  $\geq 45$  years old (age-adjusted OR: 1.65, 95% confidence interval (CI): 1.23–2.21); for hypercholesterolemia (serum total cholesterol level  $> 240$  mg/dl) at  $< 45$  and  $\geq 45$  years old (age-adjusted OR: 1.42, 95% CI: 1.06–1.88 at  $< 45$  years; age-adjusted OR: 1.39, 95% CI: 1.06–1.81 at  $\geq 45$  years); and for DM at  $< 45$  years old (age-adjusted OR: 2.92, 95% CI: 1.57–5.46).

**Conclusions:** Japanese women with ovarian infertility (most women have PCOS) are at high risk of hypertension from 45 years of age, hypercholesterolemia at all ages, and DM before 45 years old. Therefore, ovarian infertility is a matter of great importance for women's healthcare across their lifespan.

### *Serum estrogen as predictor of cardiac risk in peri- and postmenopausal women*

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<sup>a</sup>King George Medical University; <sup>b</sup>Manipal Institute of Medical Sciences

**Objectives:** To investigate whether serum estradiol (SeE2) and lipid variables in peri (PeriMW) and (PMW) predict CVD risk.

**Methods:** This cross sectional study of 100 asymptomatic women (50 PeriMW, 50 PMW) attending the outpatient clinic, Dept OBGYN, KGMU, Lucknow, India, April 2011–April 2012. All subjects age, duration of menopause, had a fasting lipid profile and SeE2, as BMI, WHR and blood pressure measured.

**Results:** Subjects mean age, duration of menopause, middle class and urban-dwelling. PMW were overweight compared to the PeriMW (p=0.023) but WHR did not differ between groups. Hypertension was more frequent in PMW vs PeriMW (p<=0.001); SeE2 levels were significantly lower in PMW (p<0.001). Dyslipidemia was more prevalent in the PMW. The prevalence of at least one CVD risk factor in PeriMW was 42% vs 78% in PMW (p=0.012), and more than two CVD risk factors in PeriMW 36% vs PMW, 62% (p=0.02). In the PeriMW serum cholesterol, LDL-chol and triglycerides (TG) were significantly inversely associated with SeE2 levels (p<0.001). In PMW higher serum cholesterol and TG directly associated with SeE2 levels (p<0.05) and HDL-chol and SeE2 levels were directly associated (p<0.05). Bivariate

analysis revealed significant and inverse correlations between SeE2 and both systolic and diastolic BP and most lipid variables, except for HDL-cholesterol which was positively correlated with seE2. On multivariate analysis the association between biochemical parameters age, WHR and duration of menopause was found significant for LDL-cholesterol, cholesterol:HDL-cholesterol and SeE2. SeE2 < 40 pg/ml was 78.7% sensitive and 74.2% specific for predicting a serum HDL-cholesterol < 51 g/dL.

**Conclusion:** Age, duration of menopause, WHR, serum HDL-cholesterol and cholesterol:HDL were significantly associated with SeE2 levels on multivariate analysis. SeE2 and dyslipidemia may be predictors of CVD risk in PeriMW and PMW.

### Sex-related emerging cardiovascular risk factors and evaluation of the individual cardiovascular risk score

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**Objective:** Cardiovascular disease (CVD), the main cause of death worldwide, has a higher prevalence in women and recent evidence show that beside the traditional CVD risk factors (CVDRF) new potentially independent gender-specific CVDRF, such as obstetric, reproductive endocrine and rheumatic disorders, could accelerate the development of CVD. Since appropriate strategies for the improvement of high-risk women early identification must be created, we calculated the individual CVD risk scores (ICVDS) in a population of climacteric patients and we analysed them according to the pre-existing traditional and new CVDRF.

**Methods:** We assessed the individual ICVDS of 390 women without previous pathologic cardiovascular events, aged 41–69 years, who referred to the Menopause and Osteoporosis Centre of the University of Ferrara. The ICVDS were estimated using National Institute of Health Core.exe software, on the base of patient's age, latter blood cholesterol and blood pressure values, smoking habits and anti-hypertensive therapy usage.

**Results:** Mean age of the sample was 54 years and mean ICVDS, 1.6%. Postmenopausal women had mean ICVDS of 1.8% while premenopausal subjects, of 1.1% ( $p < 0.0001$ ). ICVDS were significantly related to Body Mass Index ( $r = 0.340$ ,  $p = 0.001$ ), abdominal circumference ( $r = 0.331$ ,  $p = 0.001$ ) and blood glucose ( $r = 0.275$ ,  $p = 0.001$ ) values. The average ICVDS of rheumatic patients was significantly higher than that of healthy women (2.5% vs 1.5%,  $p = 0.004$ ), while patients who suffered from gestational diabetes mellitus or by pre-eclampsia had a mean ICVDS which was slightly, even if not significantly, higher than that of people without obstetric CVDRF (2.0% vs 1.6%,  $p = 0.140$ ).

**Conclusions:** Climacteric patients affected by obstetric and rheumatic CVDRF showed higher ICVDS than otherwise healthy patients, and values were statistically significant in the second subgroup.

## OC3: Menopause, beyond hot flushes

### Vasomotor symptoms are associated with impaired wellbeing and self-assessed work ability

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**Objectives:** We investigated the association between vasomotor symptoms (VMS) and each of psychological general wellbeing and work ability.

**Methods:** This was a cross-sectional study of 2020 community dwelling Australian women, aged 40–65 years, recruited July 2013–March 2014. Participants completed the Menopause Specific Quality of Life Questionnaire, the Psychological General Well-Being (PGWB) Index and the Work Ability Index (WAI).

**Results:** 1524 women were included in the analysis of PGWB (excluding 492 women using psychotropic medications and 4 women who did not complete the PGWB questionnaire). Moderate-severely bothersome VMS had a strong significant negative association with PGWB [regression coefficient ( $\beta$ ) = -8.17, 95% confidence interval (CI) -10.90 to -5.45]. Socio-demographic factors associated with lower wellbeing included being un-partnered ( $\beta$  = -2.80, 95% CI -4.74 to -0.86), obese ( $\beta$  = -5.46, 95% CI -7.24 to -3.68) and a smoker ( $\beta$  = -3.47, 95% CI -6.10 to -0.84). Older age ( $\beta$  = 0.29, 95% CI 0.06 to 0.42) and participation in paid and/or volunteer work ( $\beta$  = 2.72, 95% CI 0.61 to 4.82) were positively associated with wellbeing. 1263 of the 1274 women in paid employment completed the WAI. Work ability was poor-moderate for 18.53%. After adjustment for socio-demographic factors, having any VMS was associated with a greater likelihood of poor-moderate work ability [odds ratio (OR) = 2.45, 95% CI 1.69–3.54]. Poorer work ability was significantly and independently associated with being un-partnered, obese or overweight, smoking, being a carer and having insecure housing finance, but not age.

**Conclusions:** VMS are associated with impaired personal wellbeing and self-assessed work ability. Recognising and de-stigmatizing the psychological and physical consequences of the menopause may improve wellbeing and work performance of this significant workforce demographic.

### Menopause-specific health literacy in Japanese women

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**Background:** Menopause symptoms can be troublesome and interfere with quality of life. There are many treatment options available like hormone replacement therapy and kampo medicine. However, only one quarter of women with severe menopausal symptoms are being treated for them in Japan.

**Objectives:** This study proposed a method for assessing 'menopause-specific health literacy' on the basis of the Theory of Planned Behavior.

**Methods:** A cross-sectional web-based survey was conducted in September 2015 among Japanese women aged 30–59 years. Of 1236 participants in the survey, 1196 eligible participants who were not under treatment for menopausal symptoms were included. Participants were presented with a vignette describing a typical case of menopausal symptoms and were then asked a series of questions to assess their recognition of the disorder and intention, attitude, subjective norm, perceived behavioral control, and available information related to seeking medical care.

**Results:** The majority (87%) of participants correctly labelled the vignette as menopausal symptoms and 60% expressed a positive intention to seek medical care for the problem. Multiple logistic regression analysis showed that attitude, subjective norm, and perceived behavioral control were significant predictors of the intention to seek medical care. A structural equation model depicting the relationship among the variables based on the Theory of Planned Behavior revealed acceptable fit indices (GFI = 0.948, AGFI = 0.905, CFI = 0.884, RMSEA = 0.093). Subjective norm had the greatest direct effect on the intention to seek medical care.

**Conclusions:** The concept of menopause-specific health literacy is useful for dealing with the issue of untreated menopausal symptoms. Universal interventions designed to change subjective norm are likely to influence treatment seeking behavior of women with menopausal symptoms.

### *Personality traits and work-related stress are associated with women's health and wellbeing during transition to menopause*

Aila Collins (SE)

Karolinska Institute

**Objective:** The objective was to examine whether personality traits and personal resources are associated with symptom reporting. Another aim was to assess whether characteristics of the psychosocial work environment are associated with levels of stress in terms of elevated morning cortisol and unfavorable lipid profiles.

**Methods:** A representative sample of 150 menopausal women was drawn from a population-based sample of 950 women aged 49 to 53 years who had completed a health survey. The women participated in a longitudinal follow up study entailing baseline and two follow up sessions. The relative contribution of menopausal symptom reporting was assessed. Variables included menopausal status, life style, personality traits such as stress tolerance and neuroticism, and Sense of Coherence. Measures of work-related stress, in terms of job strain and social support from co-workers as measured by the Job Content Questionnaire, were related to levels of morning cortisol and serum lipids and to self-rated health.

**Results:** The results showed that personality traits, particularly stress sensitivity and anxiety proneness, play an important part in symptom reporting. Work demands, job strain and lack of social support from coworkers were significantly related to adverse health outcomes, particularly to increased morning cortisol and unfavorable lipid profiles.

**Conclusions:** Our results support the notion that psychosocial factors such as personality traits, personal resources as well as work-related stress are significant modulators of women's health and wellbeing during the transitional years.

### *The association of individual and workplace factors with menopause-related work absence*

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**Objective:** To examine prevalence and predictors of menopause-related work absence in a large sample of UK working women.

**Methods:** 896 peri- and postmenopausal working women, aged 45–55 years, completed an electronic survey across 10 UK-based organizations. Participants answered socio-demographic (age, ethnicity, dependents), general distress (General Health Questionnaire), physical activity, hot flush frequency, symptom bother (psychological, sleep, somatic, cognitive, vasomotor), work environment, perceived job performance, and job satisfaction questions.

**Results:** Women were on average 50 years (SD = 3.19), experiencing hot flushes for an average of 3.45 years; averaging 6 per day, and 4 during a work shift. The majority (n = 784, 88%) had not taken any absence from work because of the menopause, while 112 (12%) had. Results from univariate logistic regression analyses showed that work absence due to menopause was associated with self-reported impaired job performance (attributed to menopause), finding work difficult to manage because of menopause, lower job satisfaction, lower levels of physical activity, non-white ethnicity, higher psychological distress (GHQ), higher perceived symptom bother (particularly psychological and somatic symptoms, but not hot flush frequency), having a young and/or male line manager, being more able to negotiate work hours/practices, having insufficient rest areas, working in a shared office, and dissatisfaction with toilet cleanliness. Further multivariate analyses are in progress.

**Conclusions:** Menopause-related work absence is associated with socio-demographic, health, psychological, organizational and work environment factors. These results suggest areas for intervention to improve the experience of menopause at work, and will be used to develop a theoretical model of menopause-related work absence that can be tested in future research.

### *An International Menopause Society study of Climate, Altitude, Temperature (IMS-CAT) and vasomotor symptoms in Bangkok and Chiang Mai, Thailand*

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<sup>a</sup>Chiang Mai University; <sup>b</sup>Chulalongkorn University; <sup>c</sup>Heart of England NHS Foundation Trust; <sup>d</sup>King's College London

**Objective:** To examine relationships between location, sociodemographics, lifestyle, beliefs, and experience of hot flushes and night sweats (HFNS) amongst mid-aged women living in two cities in Thailand.

**Methods:** Peri- and postmenopausal women, aged 45–55 years, from Bangkok (sea level) and Chiang Mai (341m, mountainous) were recruited. Data collected between June and October 2015 (rainy season, temperatures 26–28 °C). Participants completed questionnaires (sociodemographics, HFNS (prevalence, frequency and problem-rating), body mass index, diet, exercise, alcohol use, and beliefs about menopause (Menopause Representations Questionnaire)).

**Results:** 632 women, aged 50.88 (3.06) years, provided data; 320 Bangkok and 312 Chiang Mai. Prevalence of HFNS was 65%, with average frequency of 8.7 (10.8) per week and problem rating of 4.3/10. Women residing in Chiang Mai had significantly more problematic HFNS, but prevalence and frequency were similar in both sites. Poor general health and negative beliefs (coping/control) were predictors of HFNS frequency, while Chiang Mai location, less education, less exercise, younger age and negative beliefs (coping/control and negative impact) about menopause were associated with more problematic HFNS. Location and beliefs remained significant controlling for education, age and exercise. Treatments used included HRT (6.5%), SSRI (2.2%), complementary (5.5%), vitamin (21.5) and herbal (20.7%) remedies. **Conclusions:** HFNS reports are prevalent with moderate frequency and problem-ratings in these urban centers in Thailand. Health, lifestyle, education and beliefs were associated with problematic HFNS but location was also a predictor; further analyses are in progress. The results will be included in a wider comparison of the impact of climate and altitude with data from India, UAE and Latin American countries, as part of the IMS-CAT Study.

### Predictors for sleep disturbances in menopausal transition

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**Objective:** We aimed to evaluate risk factors for menopausal sleep disturbance that could be identified already before menopause.

**Methods:** A total of 81 women, all being premenopausal and aged 46 years at baseline, participated in this follow-up study. At five-year follow-up, 27 of the women were premenopausal, 40 postmenopausal and 14 were postmenopausal using hormone therapy (HT). To study sleep, we used the validated Basic Nordic Sleep Questionnaire, which evaluates subjective sleep quality during the three preceding months. Additional questionnaires were used to evaluate risk factors for sleep impairment.

**Results:** Sleep quality differed only marginally between premenopausal and postmenopausal women at follow-up. Depressive symptoms at baseline increased the risk for nocturnal awakenings ( $P=0.025$ ), morning tiredness ( $P=0.007$ ), daytime tiredness ( $P=0.007$ ) and propensity of falling asleep at work or during leisure time ( $P=0.036$ ) at follow-up. Personal crises at baseline increased the risk for longer sleep latency ( $P=0.035$ ) and propensity of falling asleep when not active ( $P=0.014$ ) at follow-up. Baseline use of medication with central nervous system (CNS) effects increased the risk for worse general sleep quality ( $P=0.044$ ) at follow-up. Perceived impaired general health at baseline increased the risk for difficulty falling asleep ( $P=0.043$ ) at follow-up. Frequent night sweats at baseline increased the risk for difficulty falling asleep ( $P=0.003$ ) at follow-up.

**Conclusions:** Various premenopausal health-related factors seem to predict poor sleep in menopausal transition. Instead, menopause per se appears to have only a minor effect. Thus, it would be essential to identify high-risk women, which may allow timely interventions to possibly prevent development of sleep disturbances at menopause.

## OC4: Novel approaches to alleviate menopausal symptoms

### Efficacy and safety of Lenzetto in postmenopausal women: results from the EST-01 Phase 3 trial

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**Objectives:** To assess the efficacy and safety in a Phase 3 clinical trial (NCT01389102) of Lenzetto<sup>®</sup>, an estradiol metered-dose transdermal spray approved in the US and in Europe to treat postmenopausal vasomotor symptoms.

**Methods:** EST-01 was a US randomized, double-blind, placebo (pbo)-controlled trial in healthy postmenopausal women ( $n=458$ ) aged  $\geq 35$  yrs with  $\geq 8$  moderate-to-severe hot flushes/day. Women applied 1 ( $n=77$ ), 2 ( $n=76$ ), or 3 sprays ( $n=76$ ) of Lenzetto or matching pbo (1 spray,  $n=77$ ; 2 sprays,  $n=76$ ; 3 sprays,  $n=76$ ) to the same forearm once daily (in the morning). Coprimary efficacy endpoints were mean change from baseline in frequency and severity of moderate-to-severe hot flushes at Weeks 4 and 12. Safety assessment included adverse events (AEs) evaluation. AEs were also analyzed by age ( $\leq 49$  vs 50–59 yrs), menopausal status (natural vs surgical), body mass index (BMI) and timing.

**Results:** Significant decreases in hot flush frequency were achieved with all three Lenzetto groups vs. pbo ( $p < 0.01$ ) after both 4 and 12 weeks of treatment. The severity score of hot flushes was significantly lower in the 2- and 3-spray dose groups vs pbo ( $p < 0.05$ ) after both 4 and 12 weeks of treatment. A significant decrease in severity score was observed in the 1-spray dose group vs pbo at Week 12 ( $p < 0.001$ ), with a trend for decreased severity vs pbo at Week 4 ( $p = 0.057$ ). Analysis of AEs with frequency differences of  $\geq 5\%$  in subgroups of women revealed no safety issues. Most AEs were experienced in the first month of treatment and their frequency did not increase with increasing Lenzetto treatment exposure or duration.

**Conclusion:** EST-01 demonstrated that Lenzetto provided a clinically meaningful reduction in frequency and severity of hot flushes. Lenzetto was well-tolerated and had a positive safety profile regardless of age, menopausal status or BMI.

### The effect of tomato juice (*Lycopersicon commune*) on estradiol level, fibroblast proliferation and vaginal wall thickness of experimental menopause in rat

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**Objective:** To evaluate the effect of tomato juice (*Lycopersicon commune*) on estradiol level, fibroblast proliferation and vaginal wall thickness of experimental menopause in rat.

**Methods:** This study was a laboratory experimental research designed by a post-test only control group design. This study used 24 ovariectomized rats, divided into 4 groups: control and treated (T) groups giving tomato juice with dose of 110 mg/kg

bw/day (T1), 220 mg/kg bw/day (T2) and 330 mg/kg bw/day (T3). All groups were treated for 28 days. Estradiol level, fibroblast proliferation and vaginal wall thickness were evaluated and analysis using Anova test.

**Result:** There was a significant difference of estradiol level between control (40.739.08); T1 (92.821.85); T2 (117.759.17) and T3 (167.3313.49) ( $p < 0.05$ ). The highest fibroblast proliferation are found in group with dose of 220 mg/kg bw/day and 330 mg/kg bw/day compare with the control ( $p < 0.05$ ). There was no significant difference of vaginal wall thickness between control (657.17 25.78); T1 (620.50106.87); T2 (689.50144.95) and T3 (820.673144.31) ( $p = 0.05$ ), but tendency of vaginal wall thickness was found in dose of dose 220 mg/kg bw/day and 330 mg/kg bw/day.

**Conclusion:** In experimental menopause in rat, Tomato Juice may increase estradiol level. In dose of 220 mg/kg bw/day and 330 mg/kg bw/day it may increase fibroblast proliferation and tendency of vaginal wall thickness. Further study is needed.

### *A non-hormonal treatment, efficient and safe on climacteric symptoms during premenopause and menopause, improve women's quality of life*

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**Background:** In western countries, women live longer and longer, spending 1/3 of their life in estrogenic deficiency. 70% of them show climacteric symptoms. Since the WHI (Women's Health Initiative) study, hormonal prescriptions have dropped tremendously, leaving patients in a decreased quality of life level.

**Method:** We report a clinical study conducted by 90 gynecologists on 324 patients based on the use of a non-hormonal treatment (Sérélys®, Relizen, Femal®, Femalen®) for 3 month, looking at the evolution of their main climacteric symptoms: hot flashes, sweating, fatigue, irritability, quality of sleep, quality of life (Visual Analytical scales and questions). Tolerance was evaluated by each investigator. Patients took 2 tablets/day during 90 days. Assessment of the patients/symptoms was made at D1 and D89.

**Results:** For the 324 patients, respectively 85.5% and 91% of the women had an improvement of their hot flashes in frequency and intensity. On the 100 mm VAS, a mean decrease of  $41.7 \pm 23.6$  ( $p < 0.0001$ ) for frequency and  $45.8 \pm 23.0$  ( $p < 0.0001$ ) for intensity of hot flashes has been registered. Over 60% of the women had a significant improvement ( $p < 0.0001$ ) in irritability (from  $41.8 \pm 31.5$  to  $16.5 \pm 20.0$ ) and fatigue (from  $45.5 \pm 31.2$  to  $19.8 \pm 22.4$ ). Monitored parameters have been significantly improved leading to an improved quality of life of about 70% on average for 71.9% of the patients. Tolerance was excellent.

**Conclusions:** Sérélys® (Relizen, Femal®, Femalen®) exhibit a good efficacy and safety on climacteric symptoms. Serelys® (Relizen, Femal®, Femalen®) is a non-hormonal alternative therapy to HRT leading to a significant improvement of quality of life, for women both in pre-menopause and in menopause period.

### *Update of randomized controlled clinical trials confirm no evidence of hepatotoxicity for Cimicifuga racemosa*

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Schaper & Brümmer GmbH & Co. KG

**Objective:** Cimicifuga racemosa (CR) is a popular medicinal plant for the treatment of menopausal vasomotor symptoms. Discussions regarding CR's hepatic safety were raised after publication of case reports. However, our meta-analysis of randomized controlled clinical trials (RCT) including 1117 patients (*Menopause* 2011;18:366–75) found no evidence for hepatotoxicity. The aim of this safety update was to analyze data from new clinical trials with special reference to the liver.

**Methods:** In accordance with good pharmacovigilance practices, we weekly monitor literature in reference databases (e.g. MEDLINE, EMBASE, BIOSIS). For the purpose of this analysis, we included only RCT that investigated the safety of CR on the liver and were published after 2011. No restriction was made regarding the CR-extract, the primary parameter for efficacy, the duration of treatment or the language of publication.

**Results:** The search identified 904 patients in 11 studies. Eight trials involving 761 participants met our inclusion criteria (6 placebo controlled and 2 RCT with reference treatment). Five RCT, including 443 patients, investigated the isopropanolic CR extract (iCR). Patients were treated with the standard dose (about 40 mg drug/d) and the treatment duration ranged from 8 to 24 weeks. In 6 RCT, liver function tests (LFT)-values were measured before and at end of treatment. No increase of LFT-values was observed and no patient reported any adverse effect on the liver. In the remaining 3 studies (2 with iCR) that were excluded from the analysis, with 143 patients, no effect on LFT-values was found.

**Conclusions:** This update of randomized, double-blind, and controlled clinical trials confirms our meta-analysis that Cimicifuga racemosa and especially iCR has no evidence of hepatotoxicity.

### *Evaluating the content and development of decision aid tools for the management of menopause: a scoping review*

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University of Alberta

**Objective:** Decision making during menopause can be complex given the variability in women's risk-benefit perceptions of menopausal treatments. Decision aid tools (DATs) help women participate in the decision-making about options. Our objective is to identify and evaluate the content and development of DATs for managing natural or surgical menopause.

**Methods:** We systematically searched electronic databases, including MEDLINE and EMBASE from inception to October 2015 for published articles. Inclusion criteria included articles on DATs for managing menopause. Search terms were derived from two concepts: menopause and DATs. Two reviewers independently screened titles and abstracts for eligibility, and extracted data on manuscript, target population and DAT characteristics. Data extracted also included information on DAT content and

development for evaluation based on International Patient Decision Aid Standards' (IPDAS) quality elements. The unpublished literature search and extraction is currently underway.

**Results:** Our search yielded 15,478 records. Of these, 19 met inclusion criteria and 15 DATs identified. Majority of DATs were paper-based (74%) and all were for use in natural menopause. Most focused on hormone therapy only (65%) while one DAT provided all options. Twelve DATs were developed after the Women's Health Initiative and 7 after the IPDAS publication. None of the DATs targeted surgically menopausal women. None of the DATs' content provided information about options in sufficient detail for decision-making. None of the studies met all of the content and development quality criteria established by IPDAS.

**Conclusion:** This review highlights limitations in available DATs for managing menopause. No DATs were identified for surgical menopause. There is a need for a comprehensive, evidence-based DAT with direct applicability to surgical menopause.

### *Iranian postmenopausal women's experiences of treatment for symptomatic vulvovaginal atrophy: a qualitative study*

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**Objectives:** To explore the experiences of Iranian postmenopausal women who seek medical help for their symptomatic vulvovaginal atrophy (VVA).

**Methods:** Five focus groups (FG) were conducted in three different clinics in Iran from January to February 2016. Participants had to be postmenopausal; had symptoms of VVA for which they came to gynecology clinics; and had confirmed physical signs of VVA upon examination. Facilitated discussion topics included: knowledge of and views towards menopause, VVA awareness and knowledge, VVA symptoms, impact of VVA, treatments offered and barriers to treatment.

**Results:** 25 women, mean age of 54.8 years (range: 49–60 years), participated in the FGs. Twenty women said they currently had >1 VVA symptom at presentation to the clinic. All said they had previously been to other doctors for treatment of their symptoms. The reasons given for seeking medical help included intolerable pain interfering with their daily activities, exercise and sexual function; negative impact of symptoms on their quality of life and marital relationship. Some women were psychologically hurt by their husband's inappropriate reactions and behaviors towards their symptoms and were deeply humiliated. Lubricants only provided partial relief during intercourse, and no relief for ongoing VVA symptoms. Despite its efficacy and safety, none of the participants reported ongoing treatment of their VVA with local low dose estrogen. Women further commented that although local estrogen products were costly, they would like to use them if they were prescribed.

**Conclusions:** Considering the negative impact of VVA symptoms on women's lives, health professionals in Iran should be prescribing approved and effective therapies for symptomatic women.

## **OC5: Understanding, preventing and treating VVA**

### *The REJOICE Trial: A phase 3 randomized controlled trial evaluating the safety and efficacy of a novel vaginal estradiol softgel capsule for symptomatic vulvar and vaginal atrophy (VVA)*

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**Objective:** Efficacy and safety of TX-004HR (4 µg, 10 µg, 25 µg) for menopausal vulvar and vaginal atrophy (VVA) was compared with placebo. TX-004HR is an investigational, applicator-free, low-dose, vaginal softgel capsule containing solubilized 17β-estradiol (E2).

**Methods:** The REJOICE Trial was a randomized, double-blind, placebo-controlled, phase 3 study in which postmenopausal women (40–75 years) with VVA and a most bothersome symptom (MBS) of moderate-to-severe dyspareunia received TX-004HR 4 µg, 10 µg, 25 µg, or placebo for 12 wks. Changes from baseline in vaginal superficial cells, parabasal cells, and pH, and severity of dyspareunia were tested at wks 2, 6, 8, and 12 (4 co-primary endpoints [wk 12]). Safety was assessed by examinations and adverse events (AEs).

**Results:** All TX-004HR doses significantly decreased the percentage of parabasal cells and vaginal pH, increased the percentage of superficial cells, and reduced the severity of dyspareunia at wk 12 (all  $P < 0.00001$ , except dyspareunia at 4 µg  $P = 0.0149$ ). The significant effect was observed by wk 2 and sustained through wk 12. Vaginal dryness significantly improved with all doses at all time points (except 4 µg at wk 2). Vulvar and/or vaginal itching/irritation significantly improved at wks 8 (10 µg) and 12 (10 µg and 25 µg). TX-004HR had high acceptability and was well tolerated. No treatment-related serious AEs were reported, and no clinically significant differences were observed in any AEs between TX-004HR and placebo.

**Conclusions:** All TX-004HR doses were effective for symptoms of VVA and safe with high acceptability. Onset of efficacy was seen at 2 wks and continued through wk 12. With negligible to very low systemic absorption of E2 seen in PK studies, this applicator-free novel product is a promising new option for women with postmenopausal symptomatic VVA.

### **TX-004HR vaginal estradiol effectively treats vulvar and vaginal atrophy (VVA) with negligible to low systemic absorption of estradiol**

David Archer (US)<sup>a</sup>, Ginger Constantine (US)<sup>b</sup>, James Simon (US)<sup>c</sup>, Harvey Kushner (US)<sup>d</sup>, Philip Mayer (US)<sup>e</sup>, James Pickar (US)<sup>f</sup>, Brian Bernick (US)<sup>g</sup>, Shelli Graham (US)<sup>g</sup> and Sebastian Mirkin (US)<sup>g</sup>

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<sup>g</sup>TherapeuticsMD, Boca Raton, FL, USA

**Objective:** To determine the systemic absorption of TX-004HR, an investigational, applicator-free, low-dose vaginal softgel capsule containing solubilized 17 $\beta$ -estradiol (E2) in postmenopausal women with VVA and moderate-to-severe dyspareunia, as measured by pharmacokinetics (PK).

**Methods:** This was a PK substudy in a 12-wk, multicenter, double-blind, randomized, placebo-controlled, phase 3 trial evaluating the efficacy and safety of TX-004HR (4  $\mu$ g, 10  $\mu$ g, and 25  $\mu$ g) compared with placebo for postmenopausal moderate-to-severe dyspareunia. Treatments were 1/day for 2 wks then 2/wk for 10 wks. Serum was sampled pre-dose and at 2, 4, 6, 10, and 24 h post-dose on days 1 and 14, and one sample 4 days after the last dose (~day 84) for E2, estrone (E1), and estrone conjugates (E1Cs). Unadjusted results are reported for AUC, Cmax, and Cavg.

**Results:** The substudy randomized 72 women (mean 59 y). E2 AUC and Cavg were similar with 4- and 10- $\mu$ g TX-004HR vs placebo ( $P > 0.05$  for all), but were significantly higher with 25  $\mu$ g at days 1 and 14 ( $P < 0.05$  for all). Mean E2 Cmax was not significantly different with 4  $\mu$ g on day 1 (6.5 pg/mL) or day 14 (4.8 pg/mL) vs placebo (6.6 pg/mL day 1; 5.5 pg/mL day 14); differences in Cmax were low but significant from placebo with 10  $\mu$ g on day 1 (10.9 vs 6.6 pg/mL), and with 25  $\mu$ g on day 1 (29.8 vs 6.6 pg/mL) and day 14 (15.7 vs 5.5 pg/mL). AUC, Cavg, and Cmax for metabolites E1 and E1Cs did not differ vs placebo. In the MITT population, efficacy was demonstrated for all co-primary endpoints and vaginal dryness.

**Conclusions:** Vaginal TX-004HR resulted in negligible to very low systemic absorption of E2. Clinically significant improvement in dyspareunia was associated with improved vaginal maturation indices, vaginal pH, and vaginal dryness and irritation in the main study. Data support the local benefits of vaginal E2 without increasing systemic exposure.

### **A European observational study on vulvo-vaginal atrophy prevalence and its impact on QoL and sexual life: The EVEs (European Vulvo-vaginal Epidemiological Study) preliminary data results**

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**Context:** Vulvovaginal atrophy (VVA) is a chronic and progressive condition caused mainly by decreased estrogen levels. Symptoms include dryness, irritation, soreness, and dyspareunia. Sexual pain secondary to VVA is an important contributor to female sexual dysfunction. In addition to the impact on sexual activity, VVA may interfere with urinary function and even influencing daily living activities. Such effects have been shown to cause significant emotional distress and reduced quality of life in postmenopausal women. **Objective:** Therefore, we designed the EVEs (European Vulvo-vaginal Epidemiological Study) study to identify the prevalence of VVA in a population of postmenopausal women attending specialized menopause clinics. Associated factors, impact on QoL and sexual life will be also evaluated.

**Methods & patients:** This is a cross-sectional study, observational and multinational (Italy and Spain). Approximately 2500 postmenopausal women (age range 45–75 years) attending 66 specialized centers have been screened for VVA symptoms. The primary endpoint is the prevalence of VVA, confirmed by an objective Ob/Gyn clinical assessment with the use of Vaginal and a Vulva Health Index. Secondary endpoints are the prevalence of postmenopausal women reporting VVA symptoms, analysis of the clinical profile of the VVA population and impact of VVA on physical status, quality of life and sexual life. The study included a semi-structured questionnaire on VVA, menopause and sexuality and the use of validated questionnaires on vaginal health (DIVA), QoL (EQ-5D) and sexual function (FSFI and FSDS).

**Results:** The study will be the first to include both subjective and objective VVA's measures for the evaluation of the pathology. Data analysis is in progress and results will be available and presented at the IMS World Congress on Menopause 2016 in Prague.

### **VVA in Italian postmenopausal women: adherence to local treatment**

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**Context:** Postmenopausal decline in oestrogen levels induces VVA in a high percentage of women. Despite many treatments available and severity of symptoms of VVA negatively affecting quality of life, women often drop out the therapy.

**Objective:** To investigate adherence of Italian women at regimens to local treatment and the reasons of abandon of cure.

**Materials and methods:** 300 healthy postmenopausal outpatients (mean age  $\pm$  SD: 63  $\pm$  5 years) affected by VVA were enrolled. They filled a questionnaire related to impaired sexual desire and satisfaction, dyspareunia, vaginal burning, irritation and dryness and urinary discomfort. The questionnaire investigated, in a retrospective way, if the women had treated the VVA symptoms with a local vaginal therapy (moisturizers, suppositories or tablets both hormonal and non), the adherence at these regimens and the reasons of potential drop out.

**Results:** 245 patients (81.7%) declared the use of local treatment to improve VVA symptoms prescribed from the beginning of discomfort. Adherence to treatment was 84.9%, 50.3%, and 15.7% after 3, 6 and 12 months, respectively. The main drop out reasons were: negative consequences on sex life, decrease of arousal that restrains the woman from self-administration of treatment, pasty sensation, treatment posology problems (several times per week or not- practical self administration).

**Conclusions:** Symptomatic VVA treatment is required and its management could be improved to obtain a higher adherence and satisfactory results. The VVA treatment and counseling should be personalized and comfortable. An improvement of sexual sphere would lead to increase compliance with therapies. Use of therapeutic options like estradiol vaginal ring characterized by lower frequency of self-administration might decrease dropouts and improve adherence to local vaginal therapies for the relief of VVA symptoms.

### Long-term effects of Vaginal Erbium Laser on the Genitourinary Syndrome of Menopause

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**Aim:** To evaluate the effectiveness and acceptability of Vaginal Erbium Laser (VEL) as a new, second generation, non-ablative photothermal therapy for the treatment of postmenopausal women (PMW) suffering from genitourinary syndrome of menopause (GSM)

**Methods:** GSM was evaluated either with subjective (visual analog scale, VAS) and objective (Vaginal Health Index Score, VHIS) measures. In PMW suffering from stress urinary incontinence (SUI), the International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form (ICIQ-UI SF) was administered before and after VEL treatments. Patients were treated with 3 laser applications, every 30 days, with screening visit prior the first laser treatment (Baseline) and follow up visits after 4, 12 weeks, and 6, 12, 18 and 24 months from the last laser application.

**Results:** VEL treatment induced a significant decrease of VAS of both vaginal dryness and dyspareunia ( $p < 0.01$ ), with a significant ( $p < 0.01$ ) increase of VHIS. In the 48 patients suffering from mild-moderate SUI the VEL treatment induced a significant ( $p < 0.01$ ) decrease in the ICIQ-SF scores. The effects were rapid and long lasting, up to the 12 months of the observation period. VEL was well tolerated with less than 3% of patients discontinuing treatment due to adverse events.

**Conclusion:** This study demonstrates that VEL induces a significant improvement of GSM, including vaginal dryness, dyspareunia and mild-moderate SUI. Thus, VEL is reasonable, efficacious and safe as a new, second generation, non-ablative photothermal therapy for the treatment of GSM. Further controlled studies are required to explore the use of VEL in comparison with different therapeutic options, to offer a procedure in alternative or in association to proven therapies, as a new safe and effective option to treat GSM symptoms in menopausal practice.

### The diagnosis of atrophic vaginitis by vaginal pH in postmenopausal women and evaluation of treatment response of vaginal estrogen vs. isoflavones

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**Aims and objectives:** Establish cut off values of vaginal pH for diagnosis of atrophic vaginitis (AV) and to correlate 5.estrogen (seE2) levels, vaginal pH and vaginal maturation value in women with AV. Compare and evaluate clinical response at 4 and 12 weeks in cases after treatment with estrogen vs isoflavones.

**Materials and methods:** Double blind randomized control study done at Dept of ObGyn KGMU and RMLIMSLko. A total of 277 subjects of which 177 cases (Group I) and 100 controls (Group II). History examination, vaginal pH, VMI and SeE2 levels estimated. Diagnosed cases of AV were randomized in two groups of 64 subjects in estrogen arm group I and 66 subjects in isoflavone in group II. Treatment response evaluated at 4 and 12 weeks.

**Results:** In two groups I & II mean age  $55.52 \pm 7.86$ ,  $54.56 \pm 6.17$  years; duration of menopause  $7.00 \pm 5.90$ ;  $4.60 \pm 4.61$  years,  $p < 0.016$ ; mean vaginal pH  $6.59 \pm 0.48$ ;  $4.60 \pm 0.38$ ,  $p < 0.001$ ; mean of VMV  $34.7 \pm 16.2$  and  $83.8 \pm 9.4$ ,  $p < 0.001$ ; mean of se.E2  $11.2 \pm 5.4$  and  $32.2 \pm 15.5$ ,  $p < 0.003$  respectively. The primary objective of the study was to establish cut off value of vaginal pH in the diagnosis of AV. The vaginal pH  $\geq 6$  has got sensitivity and specificity of 81.50% and 65% respectively. The treatment response in two group cases at four weeks in clinical signs symptoms, change in VMV and pH seen individually was  $p < 0.001$ ; difference in response at 12 weeks in both the groups were  $p > 0.05$ .

**Conclusion:** Hence, we conclude that vaginal pH  $\geq 6$  in symptomatic women is highly sensitive for diagnosis of AV in PMW with a sensitivity of 81.5%, specificity 65%. Treatment with E2 and isoflavones show significant response in both groups on urogenital symptoms, vaginal pH and on VMV as an individual.

### OC6: An update on clinical trials of hormonal therapies

#### Menopausal hormone treatment is associated with lower coronary artery calcium scores: a population-based study

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**Introduction:** Coronary artery calcification (CAC) score is a marker of coronary plaque burden and is associated with risk of adverse cardiovascular outcomes. The current use of menopausal hormone therapy (MHT) could be associated with coronary plaque deposition.

**Objectives:** To assess whether MHT is associated with coronary artery calcium (CAC) scores in women during pre-, peri- and post-menopausal periods.

**Design and methods:** In this cross-sectional study nested in a longitudinal population-based study, anthropometric and metabolic data from 295 South Brazil women were analysed. Habitual physical activity was assessed by pedometer. CAC was assessed by a multi-detector computed tomography system. Average Agatston score was used to stratify participants as CAC  $> 0$  and CAC = 0. A Poisson regression model with random effects was used to assess the relation between CAC and cardiovascular risk factors. Data were considered to be significant at  $P < 0.05$ .

**Results:** Women with CAC  $> 0$  (34.7%) were older ( $58.7 \pm 5.4$  versus  $56.3 \pm 5.2$  years,  $P < 0.001$ ), had higher prevalence of central adiposity (71 versus 59%,  $P = 0.04$ ) and hypertension (71 versus 52%,  $P = 0.002$ ) compared to the CAC = 0 group. Smoking, physical activity, educational level, menopausal status, BMI, diabetes and alcohol intake did not differ between the groups. MHT was

more prevalent in the group with CAC =0 (19.7 versus 9.8%,  $P=0.029$ ). The following prevalence ratios were recorded for CAC >0 after adjustment for age, educational level, smoking, alcohol intake, and physical activity: MHT: 0.545 (95% CI: 0.309–0.962,  $P=0.036$ ); hypertension: 1.752 (95% CI: 1.207–2.541,  $P=0.003$ ); waist-to-hip ratio 1.364 (95% CI: 0.951–1.955,  $P=0.092$ ).

**Conclusion:** In this population-based sample of pre-, menopause transition and postmenopausal women, MHT was associated with CAC =0. Hypertension was associated with risk for CAC >0, independently of age.

### **Safety and comfort of long-term continuous combined transdermal estrogen and intrauterine levonorgestrel administration for postmenopausal hormone substitution – a review**

Dirk Wildemeersch (BE)

APCOR Research

**Objective:** To review the endometrial safety and patient acceptability of long-term use of continuous transdermal estrogen substitution combined with intrauterine release of levonorgestrel (LNG) in postmenopausal women.

**Design:** One-hundred and fifty-three women who utilized the regimen for 2 IUD cycles were followed-up for a period of 10 years. Histology of the endometrium was evaluated at the end of this period to assess endometrial safety and the acceptability of the method was assessed based on the replacement rate of the LNG-IUS and continuation of ET.

**Results:** The regimen, administered over a 10 year period was very well tolerated and the IUD was retained well and no expulsions occurred. The dominant endometrial histologic picture was that of inactive endometrium characterized by glandular atrophy and stroma decidualization (Kurman classification 5b). No cases of endometrial hyperplasia were found.

**Conclusion:** The low systemic absorption of LNG could be desirable thus allowing for maximization of the beneficial effects of ET on organ tissues (e.g. cardiovascular tissues and breast). Repeat LNG-IUS is associated with high patient satisfaction. If started before the age of 60, this regimen could be advised for lifelong prevention of cardiovascular disease and other prevention measures. The LNG-IUS was shown to effectively oppose the secondary effects of systemic estrogen on the endometrium tissue resulting in strong suppression during the entire period of EPT.

### **Role of SERMs in the management of abnormal uterine bleeding in perimenopausal women**

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**Introduction:** Abnormal uterine bleeding (AUB) is the most common complaint in the perimenopausal women. The complaints of menorrhagia have a substantial impact on the gynaecological services and in most of the cases, no organic pathology is identified. Nonsteroidal anti-inflammatory drugs and tranexamic acid offer a first line therapy which has to be taken during menses, with reductions of 25–35% and 50% respectively in the menstrual blood loss (MBL). The GnRH analogues and LNG-IUS form

effective but costly treatment options and oral contraceptives are unpopular because of its side effects. Ormoxifene, selective estrogen receptor modulators form best alternative in the management of abnormal uterine bleeding without the structural lesions.

**Objective:** To evaluate the efficacy of Ormoxifene in the management of abnormal uterine bleeding in perimenopausal women.

**Material and methods:** After ruling out pregnancy and structural causes of abnormal uterine bleeding, 50 patients with dysfunctional uterine bleeding were selected according to inclusion criteria and treated with Ormoxifene in the dose of 60 mg tablet twice a week for 3 months followed by once a week for another 3 months and evaluated for haemoglobin level and endometrial thickness before and after 3 months of treatment with Ormoxifene.

**Observation & results:** Out of 60 patients, 6 were lost to follow up. There was a statistically significant increase in the Hb g/dl ( $p<0.001$ ) and a statistically significant decrease in the endometrial thickness ( $p<0.001$ ) after the treatment with Ormoxifene with significant decrease in the uterine bleeding to the extent of 45 to 50%. MBL was measured objectively by Pictorial Blood Assessment chart score (PBAC) and subjectively by a Visual analog Scale (VAS).

**Conclusion:** Ormoxifene is the promising drug effective in the treatment of dysfunctional uterine bleeding.

### **Vaginal bleeding/spotting with conjugated estrogens/bazedoxifene (CE/BZA), conjugated estrogens/medroxyprogesterone acetate (CE/MPA), and placebo (PBO)**

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**Objective:** In the 1y phase 3 SMART-5 trial of CE/BZA (NCT00808132), cumulative amenorrhea rates were similar to PBO and higher than with CE/MPA. This post hoc analysis reports quarterly bleeding/spotting with these therapies and the % of cases attributable to spotting only.

**Methods:** Generally healthy postmenopausal women seeking treatment for menopausal symptoms received daily CE 0.45 mg/BZA 20 mg, CE 0.625 mg/BZA 20 mg, BZA 20 mg (excluded), CE 0.45 mg/MPA 1.5 mg, or PBO and recorded vaginal bleeding/spotting in daily diaries.

**Results:** Data were contributed for four 3-month quarters (Q1–Q4) by 1596, 1503, 1418, and 1346 women. Incidence of bleeding/spotting in Q1–Q4 with CE0.45/BZA20 (6.6%, 4.1%, 2.8%, 3.5%) and CE0.625/BZA20 (9.6%, 5.6%, 4.5%, 5.1%) was similar to PBO (7.9%, 6.3%, 5.5%, 6.6%) but significantly (all  $P<0.001$ ) less than CE/MPA (36.1%, 30.6%, 21.4%, 20.8%). Odds ratio for bleeding/spotting with CE0.45/BZA20 vs CE/MPA was 0.1 in each Q (95% CI, Q1–Q3: 0.1–0.2; Q4: 0.1–0.3). Most bleeding/spotting cases were spotting only (CE0.45/BZA20: 92–100%; CE0.625/BZA20: 88–100%; CE/MPA: 94–100%; PBO: 91–100%). Mean days of bleeding/spotting with CE0.45/BZA20 (0.59, 0.33, 0.27, 0.47) and CE0.625/BZA20 (0.80, 0.45, 0.50, 0.51) were similar to PBO (0.68, 0.56, 0.52, 0.69) but significantly ( $P<0.01$ ) less than CE/MPA (4.63, 3.88, 2.58, 3.78). Mean bleeding/spotting days in women who had bleeding/spotting were similar for CE0.45/BZA20 (9.0, 8.2, 9.7, 13.5), CE0.625/BZA20 (8.3, 8.1, 11.1, 10.0) and PBO (8.6, 8.9, 9.4, 10.4), and numerically but not significantly greater for CE/MPA (12.8, 12.7, 12.1, 18.1).

**Conclusions:** Each quarter, <10% of women taking CE/BZA or PBO had bleeding/spotting vs 21%–36%/Q with CE/MPA. Mean number of days with bleeding/spotting was significantly less with CE/BZA than CE/MPA. Spotting accounted for most bleeding/spotting cases in all groups.

### *Evaluation of ovarian reserve based on hormonal parameters, ovarian volume, and antral follicle count in women with type 2 diabetes mellitus*

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**Context:** Recent years have witnessed an increase in the incidence of type 2 diabetes mellitus (T2DM) in younger individuals, mainly attributed to changes in lifestyle. This has been paralleled by a rise in a number of females of reproductive age with a diagnosis of diabetes.

**Objective:** To evaluate ovarian reserve of women with T2DM.

**Methods:** Participants were subjected to transvaginal ultrasonographic examination on the 3 day of menstrual cycle to determine ovarian volume and total antral follicle count (AFC).

**Patients:** 89 women with T2DM and 73 healthy controls.

**Interventions:** Participants were enrolled and divided into 3 age groups: group 1 (20–29 yr), 7 diabetics and 18 healthy controls; group 2 (30–39 yr): 35 diabetics and 35 healthy controls; and group 3 (40–49 yr): 47 diabetics and 20 healthy controls.

**Outcome measures:** A significant difference in mean FSH level (international units per liter) was observed between women with T2DM and healthy controls in all age groups (group 1,  $7.8 \pm 0.9$  vs.  $5.0 \pm 1.0$ ; group 2,  $8.2 \pm 1.1$  vs.  $7.2 \pm 1.8$ ; group 3,  $9.5 \pm 3.2$  vs.  $6.4 \pm 2.4$ ;  $P < 0.001$  for all). Similarly, mean AFC was significantly lower in patients with T2DM than in healthy controls in all age groups (group 1,  $21.1 \pm 4.8$  vs.  $25.0 \pm 9.1$ ; group 2,  $10.4 \pm 5.2$  vs.  $23.0 \pm 9.5$ ; group 3,  $6.0 \pm 3.5$  vs.  $21.7 \pm 2.1$ ;  $P < 0.001$  for all). A statistically significant difference in total ovarian volume was only observed in group 1 ( $9.7 \pm 3.0$  in T2DM patients vs.  $6.8 \pm 2.7$  in healthy controls;  $P = 0.002$ ).

**Results:** AFC was found to be negatively correlated with FSH ( $r = -0.406$ ,  $P < 0.001$ ), age ( $r = -0.618$ ,  $P < 0.001$ ), glycolized hemoglobin ( $r = -0.505$ ,  $P < 0.001$ ), and fasting blood glucose ( $r = -0.687$ ,  $P < 0.001$ ).

**Conclusions:** The first to evaluate ovarian reserve in T2DM patients, we managed to demonstrate lower ovarian reserves in women with diabetes compared with healthy controls.

## OC7: Basic research in menopausal medicine

### *Estradiol reduces brain oxidative stress in an animal model of sleep apnea*

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**Objectives:** The prevalence of sleep-disordered breathing (SDB) increases after menopause in women. Exposure to intermittent hypoxia (IH - a model of SDB) leads to cardio-respiratory disorders and increased oxidative stress. Estradiol (E2) is a potent antioxidant hormone, but its roles against oxidative stress induced by IH are unknown. We tested the hypothesis that E2 protects against cardio-respiratory disorders and oxidative stress induced by IH in adult female rats.

**Methods:** Sprague-Dawley female rats (230–250 g) were ovariectomized (OVX) and implanted with osmotic pumps delivering vehicle or E2 (0.5 mg/kg/day). After 14 days of recovery, the rats were exposed to IH (21%–10% O<sub>2</sub> 8 hours/days; 6 cycles/hour) or room air (RA) for 7 days. We measured mean arterial pressure (MAP - tail cuff), the frequency of apneas during sleep (whole body plethysmography), the activity of a pro-oxidant enzyme (NADPH Oxidase; NOX), an antioxidant enzyme (mitochondrial and total superoxide dismutase; SOD), and lipid peroxidation (TBARS - a marker of oxidative damages) in the cerebral cortex (Ccox), brainstem (BS), and adrenal glands (Ad).

**Results:** IH increased MAP and the frequency of apnea during sleep. E2 treatment prevented these effects. IH increased NOX activity in Ccox (+188%), BS (+123%), and Ad (+24%), increased lipid peroxidation in Ccox (+476%), BS (+65%), and Ad (+64%), and decreased mitochondrial (-55%) and total SOD activity (-52%) in Ccox only. E2 treatment prevented these effects.

**Conclusions:** E2 prevents against IH-induced cardio-respiratory disorders likely by reducing NOX activity and/or increasing SOD activity in BS and Ad. These observations are important to understand the link between menopause and occurrence of SDB in women, and highlight a potential advantage of estradiol therapy for SDB.

### *Impact of estetrol on the modulation of plasminogen activation pathway in endothelial cells*

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MCGEL, University of Pisa

**Context:** Estetrol (E4) is a natural human estrogen present at high concentration during pregnancy. Due to its high oral bioavailability and long plasma half-life, E4 is particularly suitable for therapeutic applications. Clinical evidence suggests that E4 is associated with a neutral impact of coagulation due to minimal liver effects, as well as to potential endothelial protective actions.

**Objective:** The aim of this study was to study the effects of E4 on the expression of t-PA, u-PA and PAI-1 in cultured human umbilical vein endothelial cells (HUVEC).

**Methods:** Endothelial cells cultures: Cells were isolated from freshly obtained human umbilical cords by collagenase digestion of the interior of the umbilical vein. After treatments, cells were lysed and PAI-1, u-PA, t-PA, c-Fos, c-Jun, and GAPDH were analyzed by western-blot. Cell migration wound healing assay was performed and monitored 24 and 48 h. Gene silencing was performed using synthetic siRNAs targeting to PAI-1, uPA and tPA.

**Results:** E4 induced in doses response manner the expression of t-PA, u-PA and PAI-1 in HUVEC. However E4 has a less effective compared to E2 stimulation. When E4 was combined with E2, E4 antagonized the effects induced by pregnancy-like E2 concentrations but did not impede the effects cause by postmenopausal-like E2 levels. E4 induced cell migration. Down-regulation of PAI-1, u-PA and t-PA blunt E4 and E2 migration effect.

**Conclusions:** PAI-1, u-PA and t-PA are required for E4-induced endothelial cell migration. E4 induced PAI-1, u-PA and t-PA through up-regulation of c-Fos and c-Jun. These findings

corroborate the concept of the diversity of E4 vs. E2 related to the ability to control endothelial cells. The effects identified in this study may be related to the safer profile on vein thrombotic events that has been reported for E4.

### *Estradiol prevents endothelial dysfunction in an animal model of sleep apnea*

Alexandra Ribon (CA)<sup>a</sup>, Sofien Laouafa (CA)<sup>a</sup>, Vincent Pialoux (FR)<sup>b</sup>, Joseph Vincent (CA)<sup>c</sup> and Aida Bairam (CA)<sup>c</sup>

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**Objectives:** The prevalence of sleep-disordered breathing (SDB) and arterial hypertension increase after menopause in women, suggesting a protective role of ovarian hormones. In male rats, exposure to intermittent hypoxia (IH - a model of SDB) also leads to hypertension and endothelial dysfunction. We tested the hypothesis that IH also induces arterial hypertension and endothelial dysfunction in adult female rats, and that estradiol (E2) prevents these effects.

**Methods:** Sprague-Dawley female rats (230–250 g) were ovariectomized (OVX) and implanted with osmotic pumps delivering vehicle or E2 (0.5 mg/kg/day). After 14 days of recovery, the rats were exposed to IH (21%–10% O<sub>2</sub> 8 hours/days; 6 cycles/hour) or room air for 7 days. We measured mean arterial pressure (MAP - tail cuff), then we used isolated aortic rings to measure vascular reactivity in-vitro. We recorded the contractile response to phenylephrine (Phe), the endothelium-dependent vasodilation (vasodilatory response to acetylcholine in pre-contracted rings), and the endothelium-independent vasodilation (response to sodium nitroprusside).

**Results:** IH increases MAP and E2 treatment prevents this effect. IH does not alter the contractile response to Phe, but reduces the endothelium dependent vasodilation ( $P=0.04$ ). E2 supplementation in IH increases the contractile response to Phe ( $p < 0.001$  vs. Ovx-Veh-IH), and restores the endothelium dependent vasodilation ( $p=0.01$  vs. Ovx-Veh-IH). The endothelium-independent vasodilation is similar in all groups.

**Conclusions:** Seven days of IH alters endothelial functions in adult OVX female rats, and these effects are attenuated by E2 supplementation. These results suggest that depletion of E2 in post-menopausal women suffering from SDB contributes to the development of vascular and endothelium dysfunction leading to arterial hypertension.

### *Quantification of 27-hydroxycholesterol in mature women and its relation with body weight and symptoms at menopause*

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**Context:** Symptoms at menopause strongly impact women's quality of life. Estrogen (E2) decrease is the main factor responsible. Oxysterols, such as 27-hydroxycholesterol (27-OHC), had been

described as an agonist of estrogen receptors and has a similar functions like E2. 27-Hydroxycholesterol is also an activator of LXR  $\alpha$  and LXR  $\beta$ . It is a metabolite of cholesterol, produced by the enzyme CYP27A1. 27-OHC displays inflammatory properties favoring endothelial dysfunction and atherosclerosis.

**Objective:** We aimed to quantification 27-OHC levels during menopause and to determinate its relationship with the appearance of physical and emotional symptoms in these women.

**Methods:** We collected scales of sleep disruption, intensity and frequency of hot flashes, psychological stress, and other symptoms. Plasma 27-OHC levels and serum hormones concentrations were measured by GC-MS.

**Patients:** Women aged 45-65 at peri- (n=28) and early post-menopause (n=62).

**Results:** We found that perimenopausal women had significantly higher 27-OHC concentrations in comparison to postmenopausal women ( $p > 0.027$ ). By multivariate regression analysis we found in the whole group that 27-OHC levels inversely correlated with age ( $r=-0.29$ ,  $p < 0.012$ ) and time since last menses ( $r=-0.36$ ,  $p < 0.05$ ), but positively with triglycerides ( $r=0.43$ ,  $p < 0.025$ ), and depressive mood ( $r=0.45$ ,  $p < 0.02$ ).

**Conclusions:** These findings suggest that 27-OHC decrease with cessation of ovarian function. In addition, 27-OHC levels were related with alterations in cholesterol metabolism and symptoms.

### *Irisin inhibits the differentiation of osteoclast precursor cells*

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**Objective:** Irisin, a novel exercise-induced myokine, has been reported to play a significant role on bone metabolism. It can increase cortical bone mass and promote osteoblast differentiation. However, there is no report about the relationship between irisin and osteoclast up to now. The purpose of this study was to observe the effects of irisin on osteoclast precursor cells, in order to understand the effects of irisin on bone metabolism comprehensively.

**Methods:** Bone marrow monocytes (BMMs) was isolated from 8-week Kunming mice and cultured in Corning Osteo Assay surface 96-well plates in presence of RANKL (50 ng/ml) and m-CSF (25 ng/ml) with or without irisin (40 nM) for 5 days. The differentiation of BMMs was analyzed by tartrate-resistant acid phosphatase (TRAP) stain and bone resorption capacity. The mRNA expression level of osteoclastogenesis related genes was evaluated by quantitative PCR and the protein level of Cathepsin K was analyzed by western blot. All the experiments mentioned above was carried out on RAW264.7 cells at the same time.

**Result:** Irisin inhibits BMMs osteoclast differentiation remarkably: 312,288,276 TRAP positive multinuclear cells (>3 nuclei) were counted in BMMs without irisin treated, but none could be seen in BMMs when irisin was added. Consistently, resorption pit only formed in the group without irisin. Both q-pcr and WB showed that the osteoclastogenesis related gene expression was down regulated by irisin: NFATc1,  $0.75 \pm 0.08$  vs  $1 \pm 0.07$  ( $P < 0.01$ ); TRAP,  $0.79 \pm 0.11$  vs  $1 \pm 0.06$  ( $P < 0.01$ ); Cathepsin K,  $0.69 \pm 0.09$  vs  $1 \pm 0.10$  ( $P < 0.01$ ).

**Conclusion:** Irisin could inhibit the differentiation of osteoclast precursor cells in vitro. This project was supported by Scientific Research Projects of The National Natural Science Fund (41473097) and Scientific Research Projects of Scientific and Technology Department of Sichuan Province (no. 2012JCPT009).

## Special membrane-bound steroid receptors of breast cells may predict a poor prognosis of breast cancer patients

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**Objectives:** Progesterone receptor membrane component 1 (PGRMC1) has been shown to be higher expressed in breast cancer compared to normal tissue. It may therefore play a critical role in its progression. Despite this, little information is available if expression of PGRMC1 is associated with worse prognosis for breast cancer patients. This study aimed to investigate the clinicopathological significance of PGRMC1 expression in breast cancer.

**Design & methods:** Expression of PGRMC1 was analyzed by immunohistochemical staining of tissues from 69 breast cancer patients, and correlated with various clinic-pathological characteristics such as larger tumor size, lymph node metastasis and clinical outcome.

**Results:** Overexpression of PGRMC1 correlated with larger tumor size and lymph node metastasis. The Kaplan-Meier survival curves revealed that PGRMC1 overexpression is associated with poor disease free and overall survival, both in breast cancer patients with ER (estrogen receptor) positive and negative tumors.

**Conclusions:** PGRMC1 overexpression is significantly associated with aggressive phenotypes and poor prognosis of breast cancer. These findings support the possible role of PGRMC1 as a prognostic biomarker in ER-positive and negative breast cancer.

## OC8: Sexual function; pelvic floor dysfunction

### Prevalence of, and risk factors for, pelvic floor disorders in women at midlife in Bangladesh: a population-based study

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**Objective:** We investigated, using validated questionnaires, the weighted prevalence of symptomatic pelvic floor disorders (PFDs) and their risk factors in a nationally representative sample of Bangladeshi women randomly recruited from the community.

**Methods:** 1590 women, aged 30–59 years, were recruited from 7 districts of 7 divisions in Bangladesh, by a multistage cluster sampling technique, between September 2013 and March 2014. The weighted prevalence of, and the factors associated with, PFDs were investigated using simple and multivariable weighted logistic regression.

**Results:** The weighted prevalence of urinary incontinence (UI) was 23.7% [95% confidence interval (CI) 21.3%–26.0%], faecal incontinence (FI) 5.3% (3.7%–5.8%), pelvic organ prolapse (POP) 16.2% (14.2%–18.2%) and at least one PFD 35.3% (32.6%–37.9%). Compared with women aged 30–39 years, having at least one

PFD was more likely for women aged 40–49 years [adjusted odds ratio (AOR) 1.46, 95% CI 1.02–2.08;  $p=0.040$ ] and 50–59 years (AOR 2.39, 95% CI 1.59–3.58;  $p<0.0001$ ). Having at least one PFD was significantly associated with having >2 children compared with fewer children (AOR 1.61, 95% CI 1.14–2.27;  $p=0.007$ ), being in the middle (AOR 3.05, 95% CI 1.72–5.41;  $p<0.0001$ ), second lowest (AOR 2.49, 95% CI 1.39–4.47;  $p=0.002$ ) or lowest (AOR 3.13, 95% CI 1.68–5.86;  $p<0.0001$ ) wealth quintile compared with the highest wealth quintile, and self-reporting diabetes mellitus (AOR 2.55, 95% CI 1.54–4.23;  $p<0.0001$ ).

**Conclusions:** Symptomatic PFDs affect a substantial proportion of women at midlife in Bangladesh. Associated factors include age, higher parity, lower wealth status and diabetes. There is a need for increased attention to diagnosis, treatment, and ultimately prevention of PFDs in Bangladesh and other developing countries, as these chronic conditions are distressing, and can be disabling.

### Improvement in postmenopausal sexual dysfunction with TX-004HR as measured by FSFI

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**Objective:** To assess the effect of TX-004HR, an investigational, applicator-free, vaginal softgel capsule containing solubilized 17- $\beta$  estradiol (E2), on female sexual dysfunction using the Female Sexual Function Index (FSFI). The REJOICE trial demonstrated that TX-004HR provides efficacy with early onset of action and negligible to very low systemic estrogen levels while treating moderate-to-severe postmenopausal dyspareunia.

**Methods:** The REJOICE trial was a phase 3, randomized, double-blind, placebo-controlled, multicenter trial evaluated the efficacy and safety of TX-004HR (4  $\mu$ g, 10  $\mu$ g, or 25  $\mu$ g) compared with placebo for 12 weeks in postmenopausal women (40–75 years) with VVA and a most bothersome symptom (MBS) of moderate-to-severe dyspareunia. Changes from baseline to week 12 in total FSFI score and its six individual domains (arousal, desire, orgasm, lubrication, satisfaction, and pain) were evaluated. Sensitivity analyses are being conducted.

**Results:** Changes from baseline at week 12 in the total FSFI score, as well as the changes in its aforementioned domains, will be presented at the meeting.

**Conclusions:** TX-004HR was safe and effective for the treatment of symptomatic VVA and resulted in negligible to very low systemic absorption of E2 in women with VVA and moderate-to-severe dyspareunia. TX-004HR improved FSFI in a dose-dependent manner, with the 25- $\mu$ g dose having the greatest improvement and the 4- $\mu$ g dose not impacting FSFI. TX-004HR 10- $\mu$ g and 25- $\mu$ g doses provide a promising new treatment option for women with postmenopausal VVA and sexual dysfunction.

## Evaluation of sexual function of postmenopausal diabetic Brazilian women

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**Objective:** The aim of this study is analyze the impact of diabetes in the sexual function of postmenopausal Brazilian women for the first time.

**Methods:** A total of 184 postmenopausal women that meet inclusion criteria were selected. Inclusion criteria for the initial selection of patients were: menopause, type 2 diabetes, stable heterosexual partner relationship for a least 1 year, active sexual life for the past 6 months, have controlled concomitant chronic diseases, no recent acute illness, no psychiatric diseases. They were divided into two groups, one with type 2 diabetes and other without diabetes. Control group with 84 no diabetic women mean age 55 years were compared to 100 diabetics mean age 59 years. Each participant was given the nine-item Female Sexual Function Index (FSFI) questionnaire to complete. The domains included: desire, arousal, lubrication, orgasm, satisfaction and pain. A cut-off FSFI score of less 26,5 was set for sexual dysfunction and results were analyzed.

**Results:** The prevalence of sexual dysfunction was significantly higher in the type 2DM group (85%) than in the control group (69%) ( $P < 0,001$ ). The mean total score was lower in the type 2DM group (13,48 (1,2–37,6)) versus the control group (18,14 (2–36)) statistically significant ( $P < 0,004$ ). With regard to specific questionnaire items a significant difference was found for decreased arousal ( $P < 0,004$ ), desire ( $P < 0,000$ ), lubrication ( $P < 0,015$ ), orgasm ( $P = 0,019$ ), satisfaction ( $P < 0,002$ ) and pain ( $P < 0,002$ ) for diabetic group. The sexual dysfunction was associated with time of diabetes in the diabetic group; age ( $p < 0,001$ ) and time of menopause ( $p < 0,001$ ) for both groups. **Conclusions:** In Brazil, diabetes increases the prevalence of sexual dysfunction and impact on decrease of arousal, desire, lubrication, orgasm, satisfaction and pain among postmenopausal women

## The prevalence of sexual dysfunction among Turkish postmenopausal women and to define the association between sexual dysfunction and depression

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<sup>a</sup>Marmara University Medical Faculty; <sup>b</sup>Baku Medical Center

**Objective:** The aim is to determine the prevalence of sexual dysfunction among Turkish postmenopausal women and to define the association between sexual dysfunction and depression.

**Methods:** A prospective survey.

**Patients:** Two hundred postmenopausal women between the ages of 50–70 years and two hundred premenopausal women between the ages of 30–49 years who applied to Menopause and Gynecology Clinics at Marmara University affiliated Pendik Education and Research Hospital, Istanbul were included.

**Intervention:** Sexual function was assessed using the Female Sexual Function Index (FSFI). Depression was evaluated by the Beck Depression Inventory.

**Outcome measures:** A FSFI total score of less than 26.5 was suggestive of sexual dysfunction. BDI was scored as: 11–17 points -

mild depression, 18–23 points – moderate depression, 24 points and more severe depression.

**Results:** Sexual dysfunction prevalence among postmenopausal women was 64.6%. The decrease in total FSFI score and each score in desire, arousal, lubrication, orgasm, satisfaction, dyspareunia domains of FSFI were correlated with the increase in the total score of Beck Depression Inventory. Depression was found in 8% of postmenopausal women without sexual dysfunction, but 92% of postmenopausal women with sexual dysfunction. As time since menopause increases, the total FSFI score decreases while the Beck Depression Inventory score rises.

**Conclusion:** According to our survey sexual dysfunction causes increase in depression of postmenopausal women who applied to our university affiliated teaching hospital. Since our survey medical center which gave medical care service to women from middle and low socioeconomic classes, our results should be confirmed by a large multicenter survey enrolling women from all different socioeconomic classes.

## Erbium YAG laser therapy for pelvic floor dysfunction

Aleksandra Novakov Mikic (RS) and Brigita Bingold (RS)

Poliklinika Novakov et al

**Objective:** The purpose of this study is to evaluate the efficacy and safety of erbium laser treatment for stress urinary incontinence (SUI), pelvic organ prolapses (POP) and vaginal relaxation syndrome (VRS).

**Methods:** In this single center prospective study we performed ErYAG thermo-therapy on a number of patients having SUI, POP and VRS. ICIQ-UI was used for assessment of SUI, POP were graded with Baden-Walker scale and VRS with patients' evaluation of improvement. SUI and VRS patients received 1–2 sessions and POP patients 1–5 laser sessions. Intervals in between the sessions were 1 month. Patients' satisfaction was measured after every session with 10 point numerical scale. Follow-ups were performed at 4 and 12 weeks.

**Results:** 76 patients had SUI, 21 POP and 16 VRS. Some patients had more than one indication – 16 patients had SUI and POP, 2 patients had VRS and POP and one patient had SUI and VRS. Average age of SUI patients was 49.7 yrs (range 21–75) and parity 1.8 (range 1–4); of POP patients 50.2 (range 21–74) with parity 1.9 (range 1–3); of VRS patients 38.1 (range 29–52), parity 2.0 (range 1–3). Average score on ICIQ-UI before the treatment was 12.04 and at the 3 months FU 2.8, showing significant improvement of 9.2 ICIQ points. Only 3 patients (3.95%) didn't improved the ICIQ score. Average prolapse grade before the treatment was 2.0 (range 1–4) and 3 months after the last treatment was significantly reduced to 1.2 (range 0–3). All 16 patients with VRS improved and satisfaction with treatment was very high (in average 9.0 on 10 grade scale). All reported adverse effects were mild and transient.

**Conclusions:** Erbium laser treatment of pelvic floor dysfunction indications (SUI, POP and VRS) showed efficacy in improvement of all treated indications with no major adverse effects noted. Patients' discomfort during the treatment was minimal and satisfaction very high.

## Sexual function and distress in postmenopausal women with medication overuse headache (MOH)

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**Background:** Medication overuse headache (MOH) is a chronic and severe head pain with a significant impact on quality of life and psychosocial functioning.

**Objectives:** To assess the rate of sexual function and distress in postmenopausal women hospitalized for treatment of MOH.

**Methods:** A clinical semi-structured interview and validated questionnaires [female sexual function index (FSFI) and female sexual distress scale-revised (FSDS-R)] were administered to 61 postmenopausal women in a stable relationship, suffering from MOH. The State-Trait Anxiety Inventory and the Beck Depression Inventory (BDI) assessed the presence of mood disorders.

**Results:** Mean age of our study sample was 56.7 ± 6.3 years (range 40–77), mean BMI was 24.6 ± 4.2 kg/m<sup>2</sup> and 40 women had at least 13 years of education (65.6%). Twenty-one women (34.4%) reported no coital activity in the last 6 months. Female sexual dysfunction [FSD (FSFI cut-off score ≤ 26.55)] was diagnosed in 47 women (77%), whereas sexual distress (FSDS-R cut-off ≥ 15) was documented in 37 women (60.7%) and hypoactive sexual desire disorder (HSDD) in 29 women (47.5%). Anxiety (69.9%) and depression (75.4%) were present in the majority of the study sample. Interestingly, 26.2% of women with MOH (n = 16) reported menopause at ≤ 45 years (either naturally or surgically). Years since menopause (p < 0.001) and depression (p < 0.02) significantly predicted FSD, whereas menopause at ≤ 45 years significantly predicted sexual distress (p < 0.001) and HSDD (p < 0.006). Even the number of analgesics used per month predicted both sexual distress (p < 0.03) and HSDD (p < 0.05).

**Conclusions:** This study showed that a high rate of sexual dysfunction and distress is present in postmenopausal women and is part of the headache-related disability. Interestingly, one out of four women with MOH entered menopause prematurely, a finding that deserves further investigation.

## OC9: Sex steroids, menopause and cancer

### *Percutaneous estradiol/oral micronized progesterone versus oral conjugated equine estrogens/medroxyprogesterone acetate. Diverging effects on proliferation, key proteins, tumor related genes and mammographic density*

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**Objective:** Impact of different CHTs on breast cancer risk markers. To elucidate the relations between breast cell proliferation, gene

regulation and mammographic breast density (MD), during natural vs. synthetic CHT.

**Methods:** 77 healthy postmenopausal women were randomized to sequential therapy with two 28-day cycles of either 2.5 g 0.06% (1.5 mg E2) percutaneous E2-gel or of oral 0,625 mg CEE, daily, with the addition of 200 mg of oral micronized P or 5 mg of oral medroxyprogesterone acetate (MPA), daily, respectively, 14/28 days per cycle. Immunohistochemistry was done for Ki-67, Bcl-2, PR B, prolactin and IGF-1 before and after 2 months of treatment as was microarray analysis for 28556 genes on core needle biopsies from eight consecutive patients and this was subject to Ingenuity Pathways Analysis (IPA). Rt-PCR on 16 key genes from 30 patients was used for confirmation. MD was assessed by both Bi-Rads score and digitized assessment.

**Results:** MKi-67 and IGF-1 genes increased (p < 0.03) correlating with Ki-67 protein in CEE/MPA group. Bcl-2 (p = 0.05) and Prolactin (p < 0.05) genes decreased in E2/P group. Prolactin peptide could be detected in breast tissue of many of the women. When PCR data were re-uploaded to IPA, the change in expression of 8 of the 16 genes was shown to augment the IPA-function “mammary tumor” more for CEE/MPA than for E2/P vs. 5/16 genes more for E2/P than CEE/MPA, at a very high significance level (p < E-15). 7/35 women had a digitized MD increase exceeding 15% percentage units in the CEE/MPA group vs. 0/29 women in the E2/P group.

**Conclusion:** There was a more adverse effect on the investigated breast cancer risk markers for CEE/MPA than for E2/P. A significant correlation between the increase in breast epithelial proliferation and the increase in mammographic density gives further insights in the debated biologic nature of MD induced by CHT.

### *Effect of drospirenone (DRSP) and norethisterone acetate (NETA) combined with estradiol (E2) on mammographic breast density and breast cell proliferation – a prospective randomized study*

Eva Lundström (SE) and Angelica Hirschberg (SE)  
Karolinska Institutet

**Objective:** Different hormonal treatments have various impacts on the breast of postmenopausal women. There are so far no previous data on the influence of drospirenone (DRSP) in combination with estradiol (E2) on the human breast. The objective of this study was to evaluate the effects of two surrogate markers for breast cancer – mammographic breast density and breast cell proliferation – in postmenopausal women treated with either DRSP or norethisterone acetate (NETA) in continuous combination with E2.

**Methods:** 120 naturally, apparently healthy postmenopausal women were randomized to either 2 mg of DRSP or 0.5 mg of NETA in continuous combination with 1 mg of oral E2. Women underwent mammography and fine needle breast biopsy at baseline and after six months of treatment for the evaluation of digitized mammographic breast density and breast cell proliferation.

**Results:** There was a significant increase in mammographic breast density after treatment in both groups (p < 0.001 respectively) but no difference between groups. Breast cell proliferation also increased in both groups (p < 0.001, respectively), with a larger increase in the E2/DRSP group (p < 0.05).

**Conclusions:** There was a similar increase in mammographic breast density by treatment with both E2/DRSP and E2/NETA whereas the increase in breast cell proliferation was slightly more pronounced in the E2/DRSP group. There is a need to further investigate the clinical significance of this difference.

## Comparing clinician and patient perspectives in the management of hot flushes in UK breast cancer patients

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Women treated for breast cancer identify vasomotor symptoms, such as hot flushes and night sweats (HFNS), as a serious problem. An estimated 550,000 people live in the UK today with a diagnosis of breast cancer and up to 70% experience HFNS. Oestrogen replacement remains the most effective treatment for hot flushes. However, this is contraindicated in the majority of women with oestrogen-dependent breast cancer.

Fewer than 50% of women with ER+ breast cancer complete the recommended 5 years of endocrine treatment – tamoxifen and AIs. This lack of adherence leads to a 20% excess breast cancer mortality. Much of this lack of adherence is probably due to unacceptable side effects such as HFNS.

Patient members of the National Cancer Research Institute UK Breast Clinical Studies Group identified that there is very little research into the management of symptoms after breast cancer treatment. In response we established a Working Party on Symptom Management. We all have a particular interest in the management of HFNS, and members include: patients; clinical and academic partners representing oncology, psychology, gynaecology, complementary therapies; and the voluntary sector. We gauged current clinical practice of the management of HFNS by surveying breast cancer patients, GPs and health care professionals and we will present this data. There was a considerable mismatch between the three groups, e.g. 40% of patients reported that no HCPs or GPs had asked them about HFNS. Despite over 90% of GPs & HCPs reporting that they prescribed drugs to alleviate HFNS, only 26% of the patients had been offered drugs and fewer than 2% said they helped. 31% of the patients said that the HFNS were severe enough for them to consider stopping endocrine therapy. If women are to be helped to adhere to their life-saving treatment, new approaches need to be developed to ameliorate HFNS.

## Fractional CO2 laser therapy: a new challenge for vulvo-vaginal atrophy in postmenopausal women

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**Objective:** To evaluate the effects of fractional CO2 laser in the treatment of vulvo-vaginal atrophy (VVA) in postmenopausal women.

**Methods:** VVA was assessed in 91 postmenopausal women (mean age 58,7) before and after the treatment with CO2 laser. Tested CO2 laser setup protocol consists of one treatment every 4 weeks for 3 times, including the treatment of vagina, vestibule and vulva. VVA was evaluated with objective (Vaginal Health Index, VHI; and Vulvo-Vaginal Health Index, VVHI) and subjective (Visual Analogic Scale, VAS; and Day-by-Day impact of vaginal aging, DIVA) measures. Patients were evaluated 3 months after the completion of treatment.

**Results:** Preliminary data at the 3 months follow-up visit show that CO2 laser treatment induced a significant decrease of VAS both for dyspareunia ( $p < 0.01$ ) and vaginal dryness ( $p < 0.01$ ), with a significant increase of VHI ( $p < 0.01$ ) and decrease of VVHI ( $p < 0.01$ ). DIVA four multi-item scale addressing symptom impact on activities of daily living, emotional well-being, sexual functioning, self-concept and body image were improved in comparison with baseline ( $p < 0.01$ ).

**Conclusions:** This pilot study demonstrates that CO2 laser induces a significant improvement of both objective and subjective VVA symptoms. Further data from follow-up visit at 6, 9 and 12 months will confirm if the procedure effect is long lasting. The study will be continued to explore the role of laser treatment in the management of VVA in a major number of women.

## OC10: The power of information on menopause

### 'Manage my Menopause' provides post reproductive health guidance – does it achieve the NICE objectives?

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**Objective:** The recently published NICE (National Institute for Health and Care Excellence) guideline on Menopause highlighted the need for clinicians to provide information on 'lifestyle changes and interventions', the 'benefits and risks of treatments' and the 'long-term health implications' of the menopause. The 'Manage my Menopause' advice portal aims to provides this information. Our objective was to establish whether patients find the MmM website useful, whether it achieves the information aims set out by NICE and whether the information provided has an impact on post reproductive healthcare provision.

**Methods:** Users of the Manage my Menopause (MmM) site specify how their data is stored and used. Those users who volunteered to be involved in future research were contacted electronically with a follow up questionnaire.

**Results:** Over the first nine weeks a total of 5042 users accessed the site to generate an advice document. Of these, 459 consented to being contacted about future research work such and this provided 119 responses. Most users found that the design, ease of use and time taken was either good or excellent with 78% finding MmM useful and 74% indicating that the site provided the information they were looking for. It is encouraging that 67% of users had visited their GP and that 24% had done so as a result of the advice on MmM. Our data show that this advice has led to either a change of medication (34%), change of lifestyle (49%) or a change of diet (48%) for a significant number of users.

**Conclusion:** The MmM site is an exciting new development in the field of menopausal health advice and is working well. Although there is unavoidable bias associated with our method of data collection, the initial assessment of the site is encouraging. Web based health resources are becoming increasingly important and this study highlights the impact they can have.

## Pharmacoeconomic and associated cost savings among Premarin® treated US women compared to those without hormone therapy

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**Objectives:** Explore the changes in health care costs among post-menopausal women treated with conjugated estrogens in a commercially insured population.

**Methods:** A retrospective analysis was performed using MarketScan data from 01 Oct 2007 through 30 Sept 2012. Post-menopausal women aged  $\geq 45$  years who initiated Premarin between 01 Oct 2008 and 30 Sept 2011 were identified. The first pharmacy claim date for Premarin was designated as the index date. A comparison cohort of post-menopausal women with vasomotor symptoms (ICD-9-CM: 627.x) without hormone therapy was created, and a random index date assigned. Women had to have continuous medical and pharmacy benefits 6 months pre- and 12 months post-index date. Baseline characteristics were compared using chi-square and t-tests. The 6-month and 12-month incremental change (follow-up minus baseline costs) in direct health care costs was calculated. A difference-in-difference model was used to compare the change in health care costs between the 2 cohorts, adjusting for age, region, Charlson Comorbidity Index (CCI), comorbid conditions, and concomitant medication use.

**Results:** The study included 1,404 Premarin and 3,096 untreated female patients. Women prescribed Premarin were younger (52 vs. 54 years,  $p < 0.0001$ ) and had lower CCI scores (0.29 vs. 0.41,  $p < 0.001$ ) compared to untreated women. After adjustment, Premarin patients showed a greater reduction in total health care costs at 6 months (-\$1,601 vs. -\$503,  $p = 0.044$ ) and at 12 months (-\$1,929 vs. -\$619,  $p = 0.010$ ), with difference driven by inpatient care cost between baseline and follow-up periods compared to the untreated cohort.

**Conclusions:** At 6- and 12-months, women on Premarin had a significantly greater reduction in health care costs after treatment initiation compared to untreated post-menopausal women. Further exploration is warranted to better understand this reduction.

## Information on early menopause: is the internet the place to search?

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**Objective:** Early menopause (EM), menopause occurring before 45 years, affects up to 10% of women. The internet was perceived by women with EM to be the best source of information regarding EM; however, the reality is unknown. The aim of this study was to assess the quality and content of easily accessible websites relating to EM.

**Methods:** Using the keyword 'early menopause' a web search was conducted using Google and different search engines. The first 25 websites listed on www.google.com.au, plus an additional five

websites not appearing in the search results but known to the authors, were assessed for website quality and content by two independent reviewers according to published methodology. Frequencies and inter-observer agreement were calculated.

**Results:** Although different search engines yielded similar results (>84%), different google origins (.au versus .uk versus .com) generated different search results (32–53% congruity). After excluding duplicates, 26 websites were analysed. Commercial websites (10/26) targeting consumers and websites containing advertising (50%) were common. Most (54%) had a readability > grade 8. Few listed authorship (39%) or author qualifications (27%). The overall median score for website content was 9/20 (range 4–20/20) with an observer weighted agreement of 86%. Medical society websites (6/26) did not necessarily rank higher than other types of websites. References were provided in 54% and controversial statements supported by data in 31% of websites. Audio versions of content was available on one and 35% of websites had video content including patient stories (31%). No website addressed culturally specific issues.

**Conclusion:** The top ranked websites regarding EM have significant deficiencies related to both quality and content. This study indicates the need for higher quality internet resources for women seeking EM information.

## The Integrated Women's Health Programme (IWHP) – study design & baseline characteristics of a cross-sectional study identifying the key health issues of midlife Singaporean women attending gynaecology clinics

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**Objective:** Globally, life expectancies are increasing. Singaporean women now live into their mid-80s. The IWHP seeks to identify health issues affecting mid-life women. We report on study methodology & characteristics in the first 500 participants.

**Method:** This cross sectional study enrolls 45–69 year olds attending gynaecology for "well women" checks & symptoms, excluding cancer. Assessment includes standardised questionnaires – menopausal symptoms, incontinence/prolapse, health/function, depression, anxiety, sleep, physical activity & sex; biophysical measures; short physical performance battery/grip strength & dual-energy X-ray absorptiometry scan. Baseline characteristics were analysed (STATA Version 14).

**Results:** With a 56.0% uptake, the mean (+ SD) age of the 512 women is 57.0 (+6.3) years. Racial distribution for Chinese, Malay & Indian is 83.6%, 4.3% & 8.4%, respectively. Majority (79.7%) are married with children (82.2%). The majority (65.5%) are employed with 46.5% completing secondary education. Current smokers comprise 2.3% & 25.1% report no alcohol intake. The mean (+ SD) menarcheal age was 13.2 (+1.5) years. Postmenopausal women, peri-menopausal women and pre-menopausal women constitute 73.0%, 15.4% and 9.6%, respectively. The mean (+ SD) menopausal age was 49.7 (+4.3) years. Main symptoms include joint pain (83.4%), vaginal dryness (47.5%), back pain (43.9%), hot flushes (41.8%) and poor sleep quality (41.0%). Mean (+SD) body mass index was 24.07 (+4.6) with 34.0% overweight/obese. Spinal & femoral neck osteoporosis (OP) was found in 6.8% & 8.2%, respectively.

**Conclusion:** The IWHP provides a holistic health assessment for women attending gynaecology clinics. Examining associations between menopause and age-related health issues should aid the development and implementation of innovative interventions that maximise functional aging in midlife women.

### *Association between knowledge about the climacteric syndrome and use of hormone therapy among Brazilian women – a population-based household survey*

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University of Campinas (UNICAMP)

**Context:** The association between knowledge about climacteric and use of hormone therapy is a poorly explored subject.

**Objectives:** To assess the frequency of use of menopausal hormone therapy among Brazilian women and the factors associated with its use.

**Methods:** A cross-sectional study was conducted in the metropolitan region of Campinas/Brazil. The dependent variable was current or previous use of menopausal hormone therapy. The independent variables were sociodemographic data, health-related problems and knowledge about the climacteric syndrome assessed using a score developed with a questionnaire on various aspects of the menopausal transition. Statistical analysis was carried out by  $\chi^2$  test and Poisson regression.

**Patients:** 749 women aged between 45 to 60 years.

**Intervention:** None.

**Main outcome measure:** Current or previous use of menopausal hormone therapy.

**Results:** The mean age of women was 52.5 ( $\pm$  4.4) years. Regarding the menopausal status, 16% were premenopausal, 16% perimenopausal and 68% postmenopausal. Of all women included, 19.5% reported current or previous use of menopausal hormone therapy. In the final statistical model, being postmenopausal (PR 2.76; 95% CI 1.74–4.38), receive information about menopause from medical and health services (PR 2.73; 95% CI 1.91–3.89), having a higher knowledge about climacteric (PR 1.12; 95% CI 1.05–1.19), history of bilateral oophorectomy (PR 2.18; 95% CI 1.49–3.17), and need to stop working due to hot flushes (PR 1.44; 95% CI 1.03–2.01) were associated with a higher frequency of use of menopausal hormone therapy.

**Conclusion:** The level of knowledge about the climacteric syndrome and how this knowledge is acquired are associated with the frequency of use of hormone therapy. Educational actions promoted by healthcare systems can increase the use of menopausal hormone therapy in women who have indications for treatment.

### *A new screening model may outperform OSTA for prediction of spinal osteoporosis in midlife Singaporean women*

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**Objective:** Globally, 1/3 women risk osteoporotic fracture. The Osteoporosis Self-Assessment Tool for Asians (OSTA) may not perform as well in younger women & while vasomotor symptoms predict osteoporosis in Caucasians, joint pain is more prevalent in Asia. The Integrated Women's Health Programme aimed to evaluate a combination of independent clinical factors vs OSTA to predict spinal osteoporosis (SpOP) in midlife Asian women.

**Methods:** This cross sectional study comprises women aged 45–69 attending gynaecology clinics. Evaluation includes validated questionnaires, biophysical measurements, short physical performance battery/grip strength & dual-energy X-ray absorptiometry. Outcomes were T-scores:  $>0$  (normal),  $-1$  to  $-2.4$  (osteopenia) &  $<-2.5$  (osteoporosis). Univariate and multivariate stepwise multinomial logistic regressions were performed (STATA version 14). Sensitivity, specificity, PPV, NPV were calculated.

**Results:** Mean ( $\pm$ SD) age of the 512 women was 57.0 ( $\pm$ 6.3) years. Spinal OP was reported in 6.8% & significantly associated with increased age [RRR (95% CI): 1.08 (1.00–1.17)], lower weight [RRR (95% CI): 1.84 (1.79–1.89)], menopause [RRR (95% CI): 11.59 (1.15–116.73)], joint pain/stiffness/swelling for more than a month not related to injury [RRR (95% CI): 4.11 (1.53–11.07)] and weaker right hand grip strength [RRR (95% CI): 1.88 (1.81–1.96)]. Our model yielded an area under the curve (AUC) value (95% CI): 84% (77.93–90.29); sensitivity, specificity, PPV & NPV of 2.94%, 99.56%, 0.03 & 0.98, respectively. This was significantly better than the AUC value (95% CI) for OSTA: 79% (71.81–85.31), 'c' statistic p-value was 0.023.

**Conclusion:** A combination of age, weight, menopausal status, chronic joint symptoms and right handgrip strength was significantly better than OSTA at predicting SpOP in midlife Singaporean women. This will be validated in next 500 participants.

## OC11: Menopause and musculoskeletal health

### *Association between adipokine levels and bone mineral density differs according to obesity and menopause in Korean women*

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**Context:** The results of studies assessing the association between adipokines and bone mineral density (BMD) were inconsistent. Little is known about whether the results differed according to menopause and obesity in women.

**Objective:** To evaluate the association of serum levels of adiponectin, high molecular weight (HMW) adiponectin, and leptin with BMD according to menopause and central obesity in Korean women

**Patient(s):** This study included 158 premenopausal and 97 postmenopausal women, from among the attendants of medical examination programs in a hospital.

**Intervention:** This study is cross-sectional.

**Main outcome measures:** Serum levels of adiponectin, HMW adiponectin, and leptin were measured by ELISA. BMD was measured using dual-energy X-ray absorptiometry.

**Methods:** The subjects were divided into groups according to menopause and central obesity. The relationship between adipokines and BMD was assessed in each group.

**Results:** Among women without central obesity, HMW adiponectin levels were positively related with BMDs (lumbar,  $\beta=0.225$ ; total hip,  $\beta=0.233$ ; femoral neck,  $\beta=0.202$ ) in premenopausal women, but negatively related with BMDs (lumbar,  $\beta=-0.360$ ; femoral neck,  $\beta=-0.344$ ) in postmenopausal women. In contrast, no adipokines were associated with BMDs in both pre- and postmenopausal women with central obesity.

**Conclusions:** Adipokines are differently associated with BMD according to menopause and obesity status. The relationship between HMW adiponectin and BMD was significantly positive and negative in premenopausal and postmenopausal women without central obesity, respectively.

### **Assessment of fracture risk in climacteric women with type 2 diabetes mellitus: comparison between Trabecular Bone Score, Hip Structural Analysis and FRAX**

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**Objective:** Patients affected by type 2 diabetes mellitus (T2DM) have an increased risk of fragility fractures, compared with non-diabetic subjects, despite normal or higher bone mineral density (BMD) values. An additional attempt to go beyond the limitations of DXA was the introduction of different DXA-based software, such as Hip Structural Analysis (HSA) and Trabecular Bone Score (TBS), that provide an indirect index of the strength of trabecular architecture and are considered a better predictor of fracture risk than BMD, especially in case of secondary osteoporosis. The aim of the present study was to evaluate the performance of HSA and TBS in well-compensated T2DM climacteric women and their fracture prediction capability, compared to FRAX.

**Methods:** We performed a cross-sectional population-based study, analyzing lumbar spine and femoral BMD, HSA, TBS and FRAX values, in a population of climacteric women consisting of 119 subjects affected by T2DM and 119 controls. The two groups were comparable for age, menopause age, Body Mass Index (BMI). Prevalence of previous clinical fractures was 11.8% and 5.9% respectively.

**Results:** No significant differences emerged between BMD, FRAX and FRAX adjusted for TBS values in the two groups. Multivariate analysis showed that TBS value was the only variable associated with T2DM; in particular, data demonstrated that the lower was TBS and the more probable was the diabetic condition. In addition, the median value of lumbar spine TBS was significantly lower in women with T2DM than in controls (1.174 vs 1.220). No significant differences in HSA parameters were observed between the two subgroups.

**Conclusions:** Our results showed that, between subjects affected by T2DM and controls, the only prognostic factor capable to characterize climacteric diabetic patients was TBS.

### **Should physical activity recommendations for South Asian adults be ethnicity-specific? Evidence from a cross-sectional study of South Asian and white European men and women**

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University of Glasgow

**Context:** Public health guidelines recommend that adults undertake at least 150 min.week<sup>-1</sup> of moderate-intensity physical activity. However, the underpinning evidence has largely been obtained from studies of populations of white European descent. It is unclear whether these recommendations are appropriate for South Asians, who have greater cardio-metabolic risk than white Europeans.

**Objective:** To determine the level of moderate-intensity physical activity required in South Asians adults to confer a similar cardio-metabolic risk profile to that observed in Europeans of similar age and body mass index (BMI) undertaking the currently recommended levels of 150 min.week<sup>-1</sup>.

**Methods:** Physical activity was measured objectively with the use of accelerometers. Factor analysis was used to summarise the measured risk biomarkers into a single underlying latent "factor" describing overall cardio-metabolic risk. Sex did not modify the association between physical activity and the cardio-metabolic risk factor, so data for both sexes were combined and models adjusted for age, sex, BMI and accelerometer wear time.

**Patients:** 148 South Asians and 163 white Europeans aged 18 to 70 years without established cardiovascular disease or diabetes were recruited.

**Intervention:** Objectively measured physical activity.

**Main outcome measures:** Overall cardiometabolic risk.

**Results:** To obtain the same cardio-metabolic risk factor score as a white European undertaking 150 minutes of moderate-equivalent physical activity per week, South Asian adults needed to undertake 234 (95% confidence interval: 200 to 268) min.week<sup>-1</sup>.

**Conclusions:** The present findings suggest that South Asians need to undertake ~230 minutes of moderate intensity physical activity per week, this equates to South Asians undertaking an extra 10–15 minutes of moderate intensity physical activity per day.

### **Dietary protein intake, habitual physical activity, and lumbar spine BMD are associated with skeletal muscle mass in healthy postmenopausal women**

Thais Silva (BR) and Poli Spritzer (BR)

Universidade Federal do Rio Grande do Sul

**Objective:** Declines in endogenous estrogen production during the menopausal transition have been associated with skeletal muscle mass loss. Evidence suggests that older people may require more dietary protein than younger people to prevent this

loss. We investigated the association between skeletal muscle mass and dietary protein intake, habitual physical activity, body composition, and metabolic variables.

**Methods:** One hundred and three healthy postmenopausal women (age  $55.2 \pm 4.9$  years, time since menopause  $6.8 \pm 1.0$  years, body mass index [BMI]  $27.2 \pm 4.6 \text{ kg/m}^2$ ) were enrolled. Protein intake was measured by validated food frequency questionnaire and categorized into lower, moderate or higher levels according to the following cut-off points:  $\leq 0.8 \text{ g/kg BW}$ , following the recommended daily allowance,  $0.81\text{--}1.19 \text{ g/kg BW}$ , as recommended by the PROT-AGE Study Group, and  $\geq 1.2 \text{ g protein/kg BW}$ , following more recent recommendations for older individuals.

**Results:** The prevalence of low lean mass, defined as skeletal muscle mass index (SMI, appendicular lean mass standardized to BMI)  $< 0.512$ , was 7%. Waist circumference, % body fat, trunk fat mass, and blood pressure were higher, whereas SMI and mean daily steps were lower in women with protein intake lower than  $0.8 \text{ g/kg BW}$ . The SMI was positively correlated with physical activity ( $r=0.205$ ,  $p=0.038$ ) and protein intake ( $r=0.334$ ,  $p=0.001$ ), and negatively correlated with waist circumference ( $r=-0.505$ ,  $p<0.001$ ) and % body fat ( $r=-0.808$ ,  $p<0.001$ ). Lumbar spine bone mineral density (BMD) contributed positively and independently to SMI.

**Conclusion:** In our healthy postmenopausal women, SMI was associated with protein intake, physical activity, and lumbar spine BMD.

### Effect of exercise intensity on systemic inflammation in postmenopausal women

Julia Orri (US), Elizabeth Hughes (US) and Deepa Mistry (US)

University of San Francisco

**Objective:** Postmenopausal women (PMW) are at increased risk for cardiovascular disease through endothelial inflammation and reduced heart rate variability (HRV). Endurance training improves HRV but the role of exercise intensity is unclear. The purpose of this study was to evaluate the effects of moderate (MOD) versus vigorous (VIG) exercise intensities on systemic inflammation and perceived stress in PMW.

**Methods:** Thirty-six PMW women who exercised at either MOD (3–5.9 METS;  $n=18$ ) or VIG intensities ( $>6$  METS;  $n=18$ ) participated. C-reactive protein (CRP), HRV, cardiorespiratory fitness, and stress (Perceived Stress Scale) were measured. Participants also completed 3 typical workouts on their own wearing a HR monitor. Energy expenditure (EE) was calculated using the conversion  $1 \text{ MET} = 1 \text{ kcal} \cdot \text{kg}^{-1} \cdot \text{hr}^{-1}$ . Groups were compared using independent-samples t tests, and associations of exercise intensities with CRP and HRV were assessed using multiple regression.

**Results:** CRP, HRV, and  $\text{VO}_2\text{max}$  were similar between MOD and VIG ( $p > 0.05$ ). VIG expended more energy than MOD ( $7.3 \pm 2.8$  vs  $5.1 \pm 2.9 \text{ kcal} \cdot \text{kg}^{-1}$ ;  $p < 0.001$ ). VIG had lower stress sub-scale (negative) scores ( $6.1 \pm 2.9$  vs  $9.7 \pm 4.4$ ;  $p < 0.01$ ) and higher counter-stress sub-scale (positive) scores compared to MOD ( $13.6 \pm 1.9$  vs  $11.7 \pm 2.4$ ;  $p < 0.05$ ). Multiple regression showed a positive association between time spent in VIG exercise and selected HRV time domain indices independent of BMI and menopause years (SDNN,  $b=0.11$ ; rMSSD,  $b=.014$ ;  $p < 0.05$ ).

**Conclusions:** Our findings suggest that VIG exercise may not confer additional benefits in terms of CRP and HRV over MOD, except for stress reduction. However, the more time spent participating in VIG exercise was associated with higher HRV. Therefore, the increased parasympathetic tone achieved with a higher level

of training may provide important cardioprotection after menopause.

### Evaluation of basal bone mass in premature ovarian failure (POF) patients. Preliminary results (Protocol code IIBSP-IOP-2012-109. ClinicalTrials.gov ID: NCT02068976)

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**Goals:** Since 2014, the Spanish Consortium for the study of premature ovarian failure has set up a registry of newly diagnosed cases. This communication presents the information on bone mineral density (BMD) in patients with POF and its relation to different parameters.

**Material and methods:** Bone mineral density has been measured in 48 patients younger than 39 with high gonadotropin and low oestrogen levels. Double energy X ray absorptiometry (DEXA) measurements have been performed at vertebral and femoral neck sites. The results have been analysed in respect to: age at the moment of diagnosis, body mass index, physical activity, smoking habits and climacteric symptoms.

**Results:** The patients have been divided into two groups according to BMD results. G1 included patients with normal BMD whereas G2 include those with T score  $\leq -1$  in any of the two interest points. Mean age at the moment of diagnosis was lower in group 2 but the differences did not reach statistical significance. The incidence of smokers was not different between the two groups (34,5% in group 2 vs. 27,8% in group 1). The incidence of hot flushes was lower in group 1 (27% vs. 67%) but this difference is not statistically significant. Mean BMI in group 1 ( $27 \text{ kg/m}^2$ ) was significantly higher than that of group 2 ( $23 \text{ kg/m}^2$ ) ( $p=0,024$ ). The percentage of patients exercising regularly was higher in group 1 (70% vs. 40%) ( $p=0,22$ ).

**Conclusions:** There is a significant relationship between BMI, regular exercising and BMD at vertebral bone in women with POF. The beneficial effects of exercising on bone health are confirmed in this subgroup of young women. The higher BMI values in women with normal BMD probably reflect an increased ability of peripheral aromatization of androgen precursors to oestrogens. [Other principal investigators: Thomas J, Sosa M, Fernandez J.]

## POSTERS

### Bone

#### P1: Effects of 8 week circuit training on body composition in premenopausal women

Ozden Baskan (TR), Emre Baskan (TR) and Nesrin Yagci (TR)

Pamukkale University

**Objective:** This study is aimed to investigate effects of circuit training on body composition for premenopausal women.

**Methods:** 49 premenopausal women who live in Denizli and were aged between 35-53 (mean age:  $39.32 \pm 4.16$ yr) included to this study. Exercise sessions are supervised by a physical therapist for 30 minutes a day, 5 times a week for 8 weeks. Circuit training includes 9 isokinetic station and aerobic exercises. Subjects worked with the station for 30 seconds and aerobic exercise for 30 seconds. The exercise station includes abdominal, back, knee, hip, shoulder, elbow muscles works. Subjects were evaluated for body composition measurements (breast, waist, hip, upper and lower extremity circumference measurements; body weight, fat, muscle and water ratio with weighing machine) before the training and 8 weeks later.

**Results:** After 8 weeks training women's body weight significantly decreased ( $p = 0,0001$ ). All measurements about their body composition significantly decreased ( $p = 0,0001$ ) except water and muscle ratio ( $p > 0,05$ ).

**Conclusions:** This study shows that circuit training affects body composition positively for premenopausal women. In addition circuit training is an effective exercise method on weight control.

## P2: Prevalence of osteoporosis and fragility fractures in middle-aged women

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Osteoporosis is generally considered to be a disease of the elderly with low bone mineral density (BMD). Hence, age and BMD are the relevant determinants for public health authorities to govern diagnostic and therapeutic measures for managing the disease.

**Objective:** The assessment of the age-related prevalence of osteopenia, osteoporosis and fragility fractures in middle-aged women was the objective of our study.

**Methods:** Using records of their initial consultations, patient characteristics as age and BMI, densitometry results of DXA measurements, as well as previous fragility fractures of the hip, the distal forearm and the vertebrae were evaluated in women 40 years of age and older, who were referred to a menopause and osteoporosis outpatient clinic.

**Results:** 102,501 women were referred to the clinic between 1990 and 2012. 99,399 (97%) were  $\geq 40$  years of age and underwent BMD measurements. 79% of them were younger than 65 years. 52% of the total population showed normal, 34% osteopenic and 14% osteoporotic BMD. 6,540 patients reported fragility fractures; 53% vertebral and 47% distal forearm- and hip fractures. Two thirds of the latter group were younger than 65 years.

**Conclusions:** This analysis confirms the findings of other large real-world population based evaluations supporting the implementation of risk-detecting strategies earlier in life than at age 65. It further promotes the current guidelines for the management of osteoporosis as to use fracture risk assessment, e.g. by FRAX®, rather than solely BMD measurement for making treatment decisions.

## P3: Evaluation of bone mineral density in patients with denoxumab and hormone replacement therapy

Jose Luis Cuadros-Lopez (ES)<sup>a</sup>, Ana Maria Fernandez-Alonso (ES)<sup>b</sup>, Angela Maria Cuadros-Celorrio (ES)<sup>a</sup>, Pilar Morgado-Linares (ES)<sup>a</sup>, Ana Lorca-Blanco (ES)<sup>a</sup>, Nuria Fernandez-Luzon (ES)<sup>a</sup>, Gonzalo Perez-Roncero (ES)<sup>c</sup> and Isabel Maria Fernandez-Alonso (ES)

<sup>a</sup>San Cecilio Hospital, Granada, Spain; <sup>b</sup>Torreardenas Hospital, Almería, Spain; <sup>c</sup>Zaragoza University

**Objective:** Evaluated bone mineral density in postmenopausal women treated with HRT long term (more than 10 years) combined with Denoxumab.

**Material and methods:** A prospective study of 28 patients with osteopenia or osteoporosis treated with hormone replacement therapy for 10 years attending the Menopause Unit of the Hospital Universitario San Cecilio (Granada, Spain) that, properly informed and with your consent, choose to participate in the study. We add denoxumab and we evaluated the BMD after one and two years.

**Results:** A total of 19 patients user estradiol 25mcg and natural progesterone 100mg/daily and 9 patients estradiol 25mcg. The median age was  $65.9 \pm 7.2$ . The results of basal spine and hip BMD were  $-2.3 \pm 0.7$  and  $-1.6 \pm 0.8$  respectively; after 1 year were  $1.9 \pm 0.7$  and  $-1.5 \pm 1.0$  and after two years were  $-1.9 \pm 1.04$  and  $-1.5 \pm 0.8$ . There were significant differences in two cases,  $p < 0.0001$ . There were no vertebral and hip fractures in this period.

**Conclusion:** Denoxumab supplementation of combined hormone replacement therapy seems to produce an improvement in BMD in patients with osteopenia/osteoporosis and decreased risk of fracture after two years of treatment, although larger studies are needed to confirm our results.

## P4: Loss of pubic hair in women over 40 years: prevalence and association with osteoporotic risk

Laura Cucinella (IT)<sup>a</sup>, Francesca Albani (IT)<sup>b</sup>, Ellis Martini (IT)<sup>a</sup>, Silvia Martella (IT)<sup>a</sup>, Lara Tiranini (IT)<sup>a</sup>, David Bosoni (IT)<sup>a</sup>, Amanda Spirito (IT) and Rossella Nappi (IT)

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**Background:** Loss of pubic hair has been associated with the so-called androgen insufficiency syndrome, a clinical entity, mostly occurring after surgical menopause, which comprises other signs and symptoms, including osteoporotic risk.

**Objectives:** To assess the prevalence of self-reported loss of pubic hair in women between 40 and 75 years old who participated to the Menopause Day Campaign for osteoporosis prevention.

**Methods:** A brief questionnaire was filled-in by 2,883 women screened by quantitative ultrasound (Achilles Express apparatus, GELunar Co., Madison, USA) performed at the right calcaneus.

**Results:** In our study population, 1051 women (36.5%) reported loss of pubic hair [67/508 (13.2%) pre/perimenopause, 984/2375

(41.4%) postmenopause]. Being menopausal significantly influenced loss of pubic hair (OR: 4.3; 95% CI: 3.3-5.7). Indeed, women with loss of pubic hair were significantly older ( $p < 0.001$ ) and reported more years since menopause ( $p < 0.001$ ). Bilateral ovariectomy (9.9%) did not seem to influence the occurrence of loss of pubic hair (OR: 0.83; 95% CI: 0.6-1.1), likely due to the low rate (1%) of women who had surgery during the fertile age. However, 45.4% women with surgical menopause reported loss of pubic hair in comparison with 35.5% with natural menopause. Osteoporotic risk [osteopenia/osteoporosis (stiffness  $< 79$ ) was slightly higher (OR: 1.3; 95% CI: 1.05-1.4) in women with loss of pubic hair. Indeed, loss of pubic hair was reported by 50% of women with osteoporosis (stiffness  $< 57$ ), 41.4% with osteopenia (stiffness 57-78) and 32.8% with normal stiffness ( $> 78$ ). **Conclusions:** This study showed that loss of pubic hair is quite common in postmenopausal women, regardless ovariectomy. Moreover, one out of two women reporting loss of pubic hair has an osteoporotic risk and this simple clinical marker may guide screening campaign in the female population.

### **P5: Investigation of the factors effect on low back pain in postmenopausal women**

Tomris Duymaz (TR)<sup>a</sup>, Nesrin Yağcı (TR)<sup>b</sup>,  
Albena Gayef (TR)<sup>a</sup> and Berrin Telatar (TR)<sup>a</sup>

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**Introduction:** The aim of this study was to investigate musculoskeletal pain that may occur during postmenopausal period and its correlation with emotional state and the quality of life of woman.

**Material and Method:** The study was carried out with 405 postmenopausal women, who were aged between 40 and 65 years and applied to the family health centers in Istanbul. Age, height, weight, body mass index, education level, marital status, social insurance, tobacco and alcohol use, medication use, age of menopause onset, presence and frequency of low back pain, and pain severity according to the Visual Analogue Scale were recorded for each participant, they were had to fill out the Anxiety and Depression Scale, Nottingham Health Profile and the Pittsburgh Sleep Quality Index for evaluation of the emotional state, quality of life and sleep quality, respectively.

**Results:** It was recorded that 90.4% of the women had low back pain, and while 31.4% of them suffered from severe low back pain, 37.4% had persistent low back pain. Anxiety, depression, sleep quality and all subscales of the health profile were significantly higher in the women with persistent and worst possible low back pain ( $p = 0.000$ ).

**Discussion:** A great majority of women experiences postmenopausal low back pain, which causes significant problems by negatively affecting their quality of life, emotional state and sleep quality.

**Conclusion:** It was concluded that a great majority of postmenopausal women suffer from persistent and severe low back pain. The presence of low back pain, of which postmenopausal women often complain, has a negative influence on woman's life.

### **P6: The relationship of kidney function and bone marrow density in healthy Korean women**

Jong Kil Joo (KR), Seul Lee (KR), Kyu Sup Lee (KR)  
and Sun Suk Kim (KR)

Pusan National University

**Objective:** In this study, we evaluated the correlation between bone marrow density and renal function with several markers in Korean women without overt nephropathy.

**Methods:** A total of 1,093 women who visited the health promotion center at Pusan National University hospital were included in the cross-sectional study. Bone marrow density was categorized by two groups, osteopenia-osteoporosis group and normal group. The correlation of bone marrow density and renal function markers, such as BUN, creatinine, cGFR and cystatin-C were analyzed. Also, logistic regression of bone marrow density and renal function markers were analyzed.

**Results:** In this study, BUN, creatinine, cystatin-C were correlated with BMD when it was grouped as normal and osteopenia-osteoporosis. In logistic regression analysis, BUN and cystatin-C were correlated with lumbar and femur BMD. However, after adjusting age, menopause and BMI, only creatinine was showed negative correlation with lumbar BMD and cGFR was related positively with femur BMD.

**Conclusions:** Renal function might have an influence on BMD. However, there is conflicting data about renal function marker and BMD. Main cause of these results due to the difference of degree of reduced renal function and renal function marker used in each studies. In this study, we checked the relationship of renal function marker and BMD with normal renal function. Further study about the renal function marker and BMD can make it possible that BMD is predicted with renal function marker.

### **P7: Pregnancy or lactation-related osteoporosis: case series with literature review**

Jong Kil Joo (KR) and Kyu Sup Lee (KR)

Pusan National University

Pregnancy or lactation-related osteoporosis (PLO) is a very rare condition and characterized by the occurrence of fracture during pregnancy or the puerperium. Despite its relative rarity, PLO can be a dangerous condition that causes severe back pain, height loss and disability. Normal physiologic changes during pregnancy, genetic or racial difference, obstetrical history and obstetrical disease such as preterm labor or pregnancy-induced hypertension are presumed to be risk factors of PLO. We found 6 cases of PLO with medical record searching at Pusan National University Hospital from January 2011 to December 2015. Mean age of the patients was 33 year-old and all women were diagnosed PLO after first delivery. The interval of delivery and hospital visit was 1 to 3 month. Chief complaint of all patients was back pain. All patients showed vertebral fracture which were diagnosed mainly by MR vertebrae. Four patients were treated with calcium and vitamin D supplementation and 2 patients were treated with teriparatide. The posttreatment mean BMD was  $-1.7 \pm 0.6$  at L1-L4 and  $-1.4 \pm 0.4$  at femur. The mean BMD change was  $0.8 \pm 0.6$  at L1-L4,  $0.1 \pm 0.4$  at femur in all patients,  $0.5 \pm 0.4$  at L1-L4,  $0.2 \pm 0.1$  at femur in calcium/vitamin D supplementation group and  $1.3 \pm 0.6$  at L1-L4,  $-0.2 \pm 0.81$  in teriparatide group.

The management and natural history are still poorly defined. Traditional medications for osteoporosis such as calcium/vitamin D and bisphosphonate, have been used for PLO patient. But, bisphosphonate carries some concerns with accumulation in bone and exposure to fetus in subsequent pregnancies. Recently, newly developed medication, teriparatide showed good results in PLO patients. We reported 6 cases of PLO with literature review.

### **P8: Epidemiological analysis of postmenopausal osteoporosis by calculating the FRAX index of patients treated in outpatient Gynecology**

Antonio Carballo (ES), María Jesús Cornellana (ES), Silvia González (ES), María Jesús Rodríguez (ES) and Nicolás Mendoza (ES)

CH Jaén

**Objectives:** Determine the current profile of the menopausal woman gynecologist, both public and private schools, considering the sociodemographic and clinical aspects that define us what percentage of them suffer OP and in what situations a treatment is recommended

**Material and methods:** We conducted an observational study in which we include the 3027 women MUMENESP study, and were attended by 18 gynecologists in Spain from 2009 to 2014. Our inclusion criteria will be the same as those planned for the MUMENESP study, this is, postmenopausal women from any cause (early, natural, surgical or iatrogenic) under 70 years should consult a gynecologist. Tests have been applied Kruskal-Wallis and Chi-Square between each of the two variables and each other, in order to observe the differences between variables according to the values that you take one or the other.

**Results and conclusions:** In view of the results of our analysis we can draw as most interesting findings that women with moderate or high risk are older than women with low risk and the greater the risk, the greater the lack of studies and the presence of some pathologies such as hypertension, urinary incontinence and frequency of joint pain, however, is less the frequency of flushing, the rate of physical activity and self-perceived health sexual relationships for patient both physically and mentally

### **P9: Association of green tea consumption with bone health in Korean postmenopausal women**

Ji Hyun Moon (KR)

JEJU National University Hospital

**Objective:** The aim of this study was to analyze the relationship between green tea consumption and bone health in Korean postmenopausal women.

**Methods:** Data were obtained from the Korea National Health and Nutrition Examination Survey 2008–2011. The study population consisted of 3,401 Korean postmenopausal women whose bone mineral density was measured at the femur and lumbar spine and who had completed a standardized questionnaire about the frequency of green tea intake. The cross-sectional relationship between green tea consumption and impaired bone health (osteopenia or osteoporosis) was investigated by bone densitometry.

**Results:** As compared to non-tea drinkers, green tea drinkers had significantly greater total bone density measurements at the femur ( $P=0.038$ ), femoral neck ( $P=0.032$ ), and lumbar spine ( $P=0.015$ ). Green tea consumption and impaired bone health were independently associated after adjusting for age, body mass index, smoking status, alcohol and coffee consumption, frequency of exercise, level of serum vitamin D, and amount of daily calcium intake (odds ratio = 0.62, 95% confidence interval: 0.38–0.99,  $P=0.049$ ).

**Conclusion:** Green tea consumption could help in preventing bone loss in postmenopausal women.

### **P10: “Prevention is better than Cure” – Care in perimenopause, a leap towards aging gracefully**

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Shakuntala Women’s Hospital Sector 3 Airoli Navimumbai, Maharashtra, India

**Aim:** To evaluate bone health status in perimenopausal women & its impact on their postmenopausal bone health and thereby advocating prevention and management methods.

**Materials and methods:** We conducted BMD study in women of age group 45 to 50 yrs. Family history of osteoporosis, obstetric history, calcium intake, amount of physical activity and consumption of tobacco and alcohol were assessed. Serum FSH, calcium and Vit D3 along with DEXA assessment were done

**Results:** Serum FSH was increased in 65%, borderline in 16% and normal in the remaining. Calcium was decreased in 42% and Vit D3 substantially reduced in 64%. BMD showed osteopenia in 72%, normal in 25% and osteoporotic in 3%.

**Conclusion:** The prevalence of osteopenia and declining BMD readings were found to be high in perimenopausal women which is a major health concern. Raised FSH, low calcium and low vit D3 in perimenopausal women should be considered definite markers of osteoporosis risk, which can be easily treated to prevent fracture risks. So goes the saying “Prevention is always better than Cure”.

### **P11: Vitamin D status and its relationship with BMD and incidence of metabolic syndrome in postmenopausal women of Pusan and Gyeongnam province in Korea**

Yong Jin Na (KR), Yong Jung Song (KR), Juseok Yang (KR) and Hwi Gon Kim (KR)

Pusan National University Yangsan Hospital

**Objective:** The aim of this study is to determine the prevalence of vitamin D deficiency and its correlation with BMD and incidence of metabolic syndrome in postmenopausal women of Pusan and Gyeongnam province in Korea.

**Methods:** We recruited a total of 228 postmenopausal women (mean age 54.64 years) who firstly visited Pusan National University Yangsan Hospital from January to December 2015. Plasma levels of 25(OH)D were measured to evaluate vitamin D status. Bone mineral density in lumbar vertebrae and femur was measured with dual-energy X-ray absorptiometry. Blood pressure, waist circumference, lipid profiles including plasma levels of triglyceride and HDL-C and fasting plasma glucose were measured to diagnose metabolic syndrome.

**Results:** Abnormal vitamin D level was defined as plasma 25 (OH)D less than 30 ng/mL, and subdivided into insufficiency ( $\geq 20$  to  $< 30$  ng/mL), deficiency ( $< 20$  ng/mL) and severe deficiency ( $< 10$  ng/mL). Vitamin D deficiency affected 60.9% (139/228) of all studied subjects, including 31.6% (44/139) of severe deficiency. Incidence of metabolic syndrome was 20.2% (46/228). Plasma 25(OH)D levels did not positively correlated with bone mineral density on the lumbar vertebrae and femur.

**Conclusion:** Our results showed an alarmingly high incidence of vitamin D deficiency and metabolic syndrome in postmenopausal women of Pusan and Gyeongnam province in Korea. Further large cohort study is needed to establish the preventive strategy.

## P12: Bone mineral density tests and the risk of fractures and admission: a study of 575,602 community-dwelling older women

Bumjo Oh (KR)

SMG - SNU Boramae Medical Center

**Introduction:** Osteoporosis in elderly is major public health problem as they lead to fracture. We tried to investigate the effectiveness of mass screening of osteoporosis by comparing the rate of diagnosis, outpatient care utilization and admission due to osteoporotic fracture between the examinees and non-examinees.

**Methods:** Data from the NSPTA was used, which offers basal health screening and bone mineral density results of women aged 66 years. Community-dwelling elderly were followed for 4 years (2007-2011) to determine the outcome measures of overall fractures, femoral fractures and admissions for femoral fractures. Chi square and t-tests were used to compare characteristics of subjects whether screening and osteoporosis diagnosis based on bone mineral density test method at baseline. Also we compared drug-related osteoporosis cure rate, admission rate due to osteoporosis-related fractures.

**Results:** Participants comprised 909,869 women aged 66 years; 575,602 (63.3%) screening group. The rate of diagnosis for osteoporosis in the screening group was 45.4%. Determining the odds ratio for prescription drugs based on examination status, obesity and smoking, adjusted odds ratio 1.68, adjusted for comorbidities (95% CI 1.62-1.74) for a prescription drug also increases in BMD Screening Group. Comparing the admission rate for hip fracture, the major complication of osteoporosis, hospitalization is reduced by approximately 17% in the Screening group with adjusted hazard ratio 0.83 (95% CI 0.73-0.96).

**Conclusions:** Osteoporosis is a highly prevalent disease among older women and is associated with a higher risk of hospitalization due to femoral fractures. It is advisable to screen for osteoporosis to early detect and start drug therapy. This can significantly reduce hospitalizations due to hip fracture and therefore leads to cost-effectiveness.

## P13: Osteoporotic fractures prevalence in postmenopausal women

Borja Otero (ES)<sup>a</sup>, Ana Fernandez-Alonso (ES)<sup>b</sup>, Clara Colomé (ES)<sup>c</sup>, Marta Canals (ES)<sup>d</sup>, Ana Castro (ES)<sup>e</sup>, Marcos Cuerva (ES)<sup>f</sup>, Daniel García (ES)<sup>g</sup>, Isabel Níguez (ES)<sup>h</sup>, María José Bravo (ES)<sup>i</sup>, Laura Nieto (ES)<sup>j</sup>, Marcela Serbassi (ES)<sup>k</sup> and Plácido Llana (ES)<sup>l</sup>

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**Objective:** To study the prevalence of osteoporotic fractures in postmenopausal women and the influence of known risk factors for osteoporotic fractures.

**Methods:** Study sponsored by Pfizer and AEEM. An observational multicentric study was designed to recruit 300 patients in 14 Spanish hospitals between November 2015 and May 2016. We present the results for the first 194 patients. Postmenopausal

women signing the informed consent were included. Exclusion criteria included premenopausal women, women on oncological treatment, patients with a severe medical or psychiatric condition, women unable to understand the questionnaires or not signing the informed consent. All the patients had a lateral lumbar spine x-ray evaluated according to Genant scale. Data were analyzed using SPSS Statistics 20.0 software.

**Results:** The median age of the patients was 58,1 years (46-66) and their BMI 26,2 (17,6-39,1). Regarding clinical risk factors for osteoporotic fractures, 0,6% of the patients had a BMI <19, 1% had excessive alcohol consumption, 1,1% had long-term immobilization, 10,7% had hypocalcemia, 19,1% were smokers, 2,6% were on glucocorticoid therapy and 26,8% had a family history of hip fracture. At least one osteoporotic fracture was diagnosed in 21,6% of the patients (n=42). 76,2% of these fractures (n=32) were diagnosed during the present study, 97,6,2% of them being vertebral fractures and 2,4% being Colles fractures. A family history of hip fracture was the only statistically significant risk factor for osteoporotic fracture (HR 3,409; 95% CI 1,7-7,0). Osteoporotic fracture prevalence was 12,5% in women <50 years, 18,2% in women between 50 and 59 years and 27,6% in women >60 years these differences being statistically significant.

**Conclusions:** Up to 75% of osteoporotic fractures can remain unnoticed in postmenopausal women and 97% of them could be diagnosed with a lumbar spine x-ray

## P14: Relation between DXA and osteoporotic fractures in postmenopausal women

Borja Otero (ES)<sup>a</sup>, Ana Maria Fernandez-Alonso (ES)<sup>b</sup>, Clara Colomé (ES)<sup>c</sup>, Marta Canals (ES)<sup>d</sup>, Ana Castro (ES)<sup>e</sup>, Marcos Cuerva (ES)<sup>f</sup>, Daniel García (ES)<sup>g</sup>, Isabel Níguez (ES)<sup>h</sup>, María José Bravo (ES)<sup>i</sup>, Laura Nieto (ES)<sup>j</sup>, Marcela Serbassi (ES)<sup>k</sup> and Plácido Llana (ES)<sup>l</sup>

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**Objective:** To study the relation between the prevalence of osteoporotic fractures and Dual-energy X-ray absorptiometry (DXA) result in postmenopausal women.

**Methods:** Study sponsored by Pfizer and the AEEM. An observational multicentric study was designed to recruit 300 patients in 14 Spanish hospitals between November 2015 and May 2016. We present the results for the first 145 patients. Postmenopausal women signing the informed consent were included. Exclusion criteria included premenopausal women, patients on oncological treatment, patients with a severe medical or psychiatric condition and women unable to understand the questionnaires or not signing the informed consent. All the patients had a DXA and a lateral lumbar spine x-ray performed evaluated according to Genant scale. Data were analyzed using IBM SPSS Statistics 20.0 software. **Results:** The median age of the patients was 58,93 years (47-66). According to DXA values, 18,6% of the patients had normal bone mineral density, 51,7% had osteopenia and 29,7% had osteoporosis. Overall, at least one osteoporotic fracture was diagnosed in 22,1% of the patients. Based upon DXA groups, osteoporotic fractures were diagnosed in 11,1% of the patients with normal DXA, in 22,7% of the patients with osteopenia and in 27,9% of the patients with osteoporosis these differences not being statistically significant. Patients with clinical diagnosis of fragility fractures had normal DXA values in 9,4% of the cases, osteopenia in 53,1%

of the cases and osteoporosis in 37,5% of the cases. Between patients with a lumbar spine fracture, 15,6% of them had normal DXA values in that location, 50% had osteopenia and 34,4% had osteoporosis with a median T score of -2,019 (-3,8-0,9).

**Conclusions:** Radiographic vertebral fractures for fragility are more frequent in women with osteopenia in DXA and lumbar spine x-ray could help to diagnose those fractures.

### **P15: Effects of apolipoprotein E genotype on bone mineral density and response to hormone therapy in postmenopausal Korean women**

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Samsung Medical Center, Sungkyunkwan University School of Medicine

**Objective:** This retrospective cohort study was conducted to evaluate the effect of apolipoprotein E (ApoE) genotype on bone mineral density (BMD) and response to hormone therapy (HT) in postmenopausal Korean women.

**Methods:** One-hundred seventy-four healthy postmenopausal women were divided into two groups according to the presence of the apoE  $\epsilon$ 4:  $\epsilon$ 4 carriers (n= 29) and  $\epsilon$ 4 non-carriers (n= 145). Women received HT for over two years, and BMDs were measured at the lumbar spine (L2-4) and hip by dual energy X-ray absorptiometry at baseline and after 6, 12, and 24 months of treatment. BMD at baseline and changes in BMD after HT were compared between the two groups.

**Results:** No significant difference was found in clinical characteristics at baseline between the two groups. Baseline BMD was significantly lower at the total hip in  $\epsilon$ 4 carriers than  $\epsilon$ 4 non-carriers (0.710 vs. 0.768 gm/cm<sup>2</sup>, p=0.008). BMDs at the lumbar spine and hip increased significantly in both groups after two years of HT (6.1% and 1.0%, p=0.038). Changing pattern of BMD or mean BMD at each time point did not differ between the two groups by repeat measured ANCOVA.

**Conclusions:** This study demonstrated the presence of apoE  $\epsilon$ 4 was associated with lower BMD at the total hip. Nevertheless, BMD response to HT did not differ by the presence of apoE  $\epsilon$ 4 in postmenopausal Korean women.

### **P16: The effect of prolonged breast-feeding on the development of postmenopausal osteoporosis in population with insufficient calcium intake and vitamin D level**

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<sup>a</sup>Severance Hospital; <sup>b</sup>Gil Hospital

**Objective:** The purpose of this study was to determine whether breast-feeding is a risk factor in the development of postmenopausal osteoporosis, especially in highly susceptible population.

**Methods:** The study was performed using data from the 2010-2011 Korea National Health and Nutrition Examination Survey, and it included 1,231 postmenopausal women who were aged

between 45 and 70 years. Osteoporosis was defined using the World Health Organization's T-score criteria, namely, a T-score of  $\leq -2.5$  at the femoral neck or the lumbar spine. The patients' ages, body mass indexes, daily calcium intakes, serum vitamin D levels, exercise levels, smoking histories, and reproductive factors relating to menarche, menopause, delivery, breast-feeding, hormone treatment, and oral contraceptive use were evaluated. Comparisons between the osteoporosis and non-osteoporosis groups were undertaken using Student's t-test, Chi-square test, and logistic regression models.

**Results:** A significant increase in the risk of osteoporosis was apparent in postmenopausal women with prolonged breast-feeding histories ( $\geq 24$  months) (model 1: odds ratio [OR]=2.489; 95% confidence interval [CI]=1.111 to 5.578, p=0.027; model 2: OR=2.503; 95% CI=1.118 to 5.602, p=0.026; model 3: OR=2.825; 95% CI=1.056 to 7.56, p=0.039), particularly in those with inadequate serum vitamin D levels and calcium intakes ( $< 800$  mg/day).

**Conclusions:** Prolonged breast-feeding seems to increase the risk of postmenopausal osteoporosis; however, its impact may not be definitive in women with sufficient vitamin D levels and calcium intakes. Therefore, sufficient calcium intakes and adequate vitamin D levels may be important to prevent osteoporosis in postmenopausal women that is derived from prolonged breast-feeding.

### **P17: BMD is an important tool for post menopausal osteoporosis evaluation**

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<sup>a</sup>Anwer Khan Modern Medical College Hospital; <sup>b</sup>BIRDEM

**Introduction:** Osteoporosis means progressive systemic skeletal disorder of increased bones fragility and susceptibility of fracture. It is a depressing findings in postmenopausal period. Worldwide the lifetime risk for women to have osteoporotic fracture is 30%-40%. BMD means bone mineral density which indicates bone turnover rates and is a diagnostic tool for osteoporosis or osteopenia.

**Objectives:** To assess the importance of BMD for the diagnosis of osteoporosis and reduce the fracture rate by proper treatment and reduce postmenopausal morbidity and mortality.

**Materials and methods:** From our medical college our study group included 20 postmenopausal ladies with age between 45-55 years and clinically and radiologically diagnosed osteoporosis. Control group include 20 postmenopausal non-osteoporotic women in same age. Exclusion criteria: DM, CVD, heart disease, cancer patient, liver or renal disease, patient taking anticonvulsant and HRT. BMD was measured at the midshaft of tibia. All data were expressed as mean SD. Statistical analysis done by z test and paired t test.

**Results:** The mean score of BMD in postmenopausal women was found to be significantly decreased as compared to control group (p < 0.001) and the t-score was in study group  $-2.33 \pm 0.67$  and in control group  $0.246 \pm 0.657$  and z score in study group  $-2.55 \pm 1.03$  and in control group it was  $0.22 \pm 0.522$ . Findings of Menecter et al. and Fohagen et al. support our result. In osteoporosis there may be exaggeration of the imbalance between bone formation and resorption. The remodeling imbalance, however results in permanent decrements in mass and a result BMD will less.

**Conclusions:** BMD measurement are extremely useful in clinical practice to diagnose osteoporosis, assess fracture risk, and aid treatment.

### **P18: Raloxifene administration in women treated with long-term gonadotropin-releasing hormone agonist for severe endometriosis: effects on bone mineral density**

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Satbyul Kim (KR) and Hyuk Jung (KR)  
Chosun University Hospital

**Objective:** To evaluate the efficacy of raloxifene in preventing the bone loss associated with long term GnRH agonist (GnRH-a) administration.

**Design:** A prospective, randomized, observational follow-up study.  
**Setting:** Obstetrics and gynecology department in a Chosun university hospital in the Korea.

**Main outcome measure(s):** Spinal BMD changes in both groups.

**Methods:** Twenty two premenopausal women with endometriosis were treated with leuprolide acetate depot at a dosage of 3.75 mg/4 weeks for 48 weeks. Bone mineral density (BMD) was evaluated at admission and after twelve treatment cycles.

**Results:** Posttreatment BMD differed significantly from baseline lumbar spine and trochanter BMD but not in femoral neck and Wards.

**Conclusions:** In conclusion, raloxifene do not prevents long term GnRH-a related bone loss in premenopausal women with severe endometriosis.

### **P19: The influence of weight loss on bone density in menopausal severely obese women**

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Ljiljana Marina (RS), Zorana Arizanovic (RS),  
Zorana Stojanovic (RS) and Svetlana Vujovic (RS)

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**Context:** Obesity has protective effect on bone metabolism, while menopause has negative impact on it. Physical activity increases, while weight reduction decreases bone mineral density.

**Objective:** The objective of this study was to assess the influence of weight loss after diet and physical activity interventions on bone density in menopausal severely obese women.

**Methods:** Sixteen extremely obese menopausal women aged  $53.00 \pm 5.82$  were involved in the therapeutic program, which consisted of two alternating phases: the three-week of very low calorie diet (VLCD) in hospital conditions and the low calorie diet (LCD) with dosed physical activity in outpatient conditions. Anthropometric parameters and reproductive hormones were measured. All patients were underwent the dual-energy x-ray absorptiometry (DXA). After weight reduction by at least 10%, all mentioned assessments were repeated.

**Results:** The mean weight loss was 18 kg or 14% of the initial weight ( $p < 0.001$ ), which was followed by a significant decrease of other anthropometric parameters (BMI  $48.84 \pm 6.90$  vs.  $41.60 \pm 6.82 \text{ kg/m}^2$  ( $p < 0.01$ ), waist circumference  $132.19 \pm 12.62$

vs.  $118.43 \pm 11.45 \text{ cm}$  ( $p < 0.01$ ), hip circumference  $146.81 \pm 14.86$  vs.  $134.14 \pm 14.42 \text{ cm}$  ( $p < 0.01$ ), neck circumference  $42.96 \pm 2.63$  vs.  $39.67 \pm 1.80 \text{ cm}$  ( $p < 0.05$ )), without the significant change in sex hormones,  $p > 0.05$  (FSH  $40.54 \pm 21.67$  vs.  $59.04 \pm 26.59 \text{ IU/L}$ , LH  $16.73 \pm 8.87$  vs.  $21.33 \pm 10.01 \text{ IU/L}$ , estradiol  $61.60 \pm 38.94$  vs.  $54.75 \pm 32.47 \text{ pmol/L}$ ). Despite the aforementioned weight loss there was not significant change in bone density of the lumbar spine and hip (spine T score  $0.03 \pm 1.42$  vs.  $0.19 \pm 1.38$ , neck of hip T score  $0.50 \pm 0.93$  vs.  $0.19 \pm 0.95$ , total hip T score  $0.92 \pm 0.98$  vs.  $0.83 \pm 0.90$ ).

**Conclusions:** A modest weight loss with dosed physical activity does not change bone density in severely obese menopausal women.

### **P20: Effects of caffeine intake on bone tissue in an animal model of osteoporosis**

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<sup>a</sup>UFCSA/ISCOMPA; <sup>b</sup>UFCSA

**Context:** The animal model of osteoporosis was chosen for mimic the pathophysiological effects of the osteoporosis in humans.

**Objective:** Evaluate the effects of caffeine intake on bone mass in aged female ovariectomized and sham operated rats.

**Methods and interventions:** 16 Wistar female rats of 16 months old were used. The animals were randomized in 4 groups: ovariectomized rats with caffeine intake (Group 1: OVX-caf), ovariectomized rats without caffeine intake (Group 2: OVX-co), rats submitted to sham operation with caffeine intake (Group 3: Sham-caf), and rats submitted to sham operation without caffeine intake (Group 4: Sham-co). The animals "OVX-caf" and "Sham-caf" received caffeine (100 mg/kg body weight) by gavage for 10 weeks, the remaining animals received water as a control. At the end of the experiment, the lumbar spine and right femurs were dissected. Biophysical parameters, quantitative parameters for bone densitometry and quantitative computed tomography measurements were made. The results were presented as means and standard deviations. One-way ANOVA followed by post-hoc Tukey test were employed. Statistical significance was set at  $p \leq 0.05$ .

**Results:** Statistical difference was found in animal body weights and in measurements by tomography in evaluated regions of interest in the intratrochanteric region ( $p = 0.021$ ) in OVX-co group. No significant differences were observed between groups in the other parameters.

**Conclusions:** It seems that caffeine causes no deleterious effect on bone mass in aged rats. More studies are needed to verify the caffeine actions in metabolism.

### **P21: The relationship between spinal mobility and spinal musculoskeletal pain among pre- and postmenopausal women**

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Sevgi Ozkan (TR) and Emre Baskan (TR)  
Pamukkale University

**Objective:** The aim of this study is to show the relationship between spinal musculoskeletal pain and spinal mobility in pre- and postmenopausal women.

**Methods:** In this cross sectional study, the sample consisted of 715 pre- and postmenopausal women aged 35-65 (mean age;  $47.55 \pm 7.97$  years; 419 premenopausal; 293 postmenopausal) living in Denizli, Turkey. Spinal pain intensity was evaluated by Visual Analogue Scale (VAS). Spinal mobility was evaluated by Modified Schober Test (MST), Lateral Bending Test (LBT) and Forward Bend Test (FBT). Fatigue and energy were evaluated by Related to Fatigue Scale Visualization (RFSV).

**Results:** In our study spinal musculoskeletal pain was to determined 67.1% in the premenopausal women (39.5% low back pain; 33% neck pain; 20.5% back pain), 78.7% in the postmenopausal women (56% low back pain; 37.1% neck pain; 28.5% back pain). In postmenopausal women, the mean spinal musculoskeletal pain severity was found as moderate ( $5.50 \pm 2.04$  cm). Postmenopausal women reported significantly greater spinal pain severity, use more painkiller and muscle relaxant than did premenopausal women ( $p < 0.05$ ). Postmenopausal women with spinal musculoskeletal pain were found to decrease spinal mobility in all direction ( $p < 0.05$ ), high fatigue level ( $p < 0.0001$ ) and low energy level ( $p < 0.0001$ ) compared to the premenopausal women.

**Conclusions:** Spinal musculoskeletal pain in postmenopausal women reduces mobility. The planned physiotherapy and exercise programs for pain, we believed that increasing mobility and reduce associated problems.

## P22: Comparison of the osteopathic manipulative therapy and traditional physical therapy program among postmenopausal women with spinal pain

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Pamukkale University School of Physical Therapy and Rehabilitation

**Objective:** The aim of the present study was to determine the effect of osteopathic manipulative therapy (OMT) compared with traditional management of postmenopausal women with spinal pain.

**Methods:** A total of 63 postmenopausal women with chronic spinal pain were randomized into either OMT group ( $n = 37$ ; mean age:  $58.86 \pm 8.04$  yr.; menopause mean age:  $47.72 \pm 4.61$  yr.) or control group ( $n = 26$ ; mean age:  $60.5 \pm 8.72$  yr.; menopause mean age:  $46.53 \pm 5.31$  yr.). OMT group was treated with OMT program (cervical, thoracic and lumbar fascia stretching, soft tissue mobilization, vertebral column mobilization) and Traditional Physiotherapy Program (TPP) (hot pack, ultrasound and Transcutaneous Electrical Nerve Stimulation) (3 days/week; totally 14 sessions). The control group only received TPP (5 days/week; totally 14 sessions). Outcomes were assessed for pain severity using a visual analogue scale, disability level using the Neck Disability Index and Roland Morris Disability Questionnaire and fear avoidance behavior for using Tampa Scale for Kinesiophobia. All evaluation performed baseline and after treatment.

**Results:** Significant differences in measures of pain intensity ( $p = 0.0001$ ), disability level ( $p = 0.002$ ) and, fear avoidance behavior ( $p = 0.026$ ) within each group after treatment. When groups were compared in terms of evaluation parameters, we found significant improvement in pain intensity in OMT group ( $p = 0,001$ ).

**Conclusions:** The results of study show that combination of OMT and TPP were more efficient than TPP alone in the treatment of postmenopausal women with chronic spinal pain.

## P23: Effects of a combined ibandronate and cholecalciferol agent on muscle strength and bone metabolism in postmenopausal women with osteoporosis

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**Objective:** After menopause, muscle mass and strength decrease with bone mineral density (BMD), leading to physical frailty. Osteoporosis and sarcopenia may be the result of common etiologic factors including vitamin D deficiency. Currently, many combined agents of bisphosphonate and cholecalciferol are available. This study was performed to evaluate the effects of a monthly agent combined with ibandronate 150mg and cholecalciferol 24,000 IU on muscle strength and bone metabolism in postmenopausal osteoporosis.

**Methods:** A total of 62 postmenopausal women were enrolled. Serum 25-hydroxy vitamin D [25(OH)D], parathyroid hormone (PTH), C-terminal telopeptide (CTx), and BMD were measured to assess bone metabolism before and after combined therapy. For muscle strength, hand grip strength was measured with a LAVISEN hand dynamometer.

**Results:** At baseline, mean serum 25(OH)D level was  $19.77 \pm 9.19$  (SD) ng/mL, compatible with vitamin D insufficiency and correlated with femur neck BMD ( $r = 0.355$ ,  $p = 0.005$ ). After 6 months of treatment, significant change was found in the variables of bone metabolism (serum 25(OH)D,  $19.77 \pm 9.19$  vs.  $30.37 \pm 8.96$ ,  $p < 0.01$ ; CTx,  $0.32 \pm 0.23$  vs.  $0.12 \pm 0.11$ ,  $p < 0.01$ ; osteocalcin,  $10.48 \pm 2.95$  vs.  $6.88 \pm 2.02$ ,  $p = 0.03$ ; PTH,  $57.03 \pm 14.00$  vs.  $38.93 \pm 13.29$ ,  $p = 0.03$ ), respectively. However, there were no significant changes in average handgrip strength, and lumbar, femur neck BMD. Significant correlations among values of degree of change in serum 25(OH)D, BMD and handgrip strength were not observed after treatment.

**Conclusions:** A monthly combined agent of ibandronate and cholecalciferol is effective in improvement of 25(OH)D and bone metabolism, however, there is no advantage of improvement of muscle strength and BMD in postmenopausal osteoporosis.

## P24: The osteopenic syndrome of patients with ovariectomy

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**Objective:** To assess BMD of patients with ovariectomy.

**Patients and methods:** Assessment of condition BMD on patients with ovariectomy, living in the Moscow Region, was made in the lumbar part L1-L4 and femoris collum on the DEXA (Hologic) included 70 patients (aged  $48 \pm 1,2$ ).

**Results:** In the stage of screening, based on DEXA data all the patients are divided into two groups: the 1 gr. 24 (34%) patients: 22 (92%) of them with an osteopenia and 2 (8%) of women with osteoporosis; the 2 gr.: 46 (66%) women with normal rates of BMD. Based on the results of DEXA in the 1 gr. BMD in the lumbar originally was: T-criteria of L1-L4 =  $-1,5 \pm 0,2$  and T-criteria in femoris collum is  $-1,1 \pm 0,3$ . In the 2 group the values of T-criteria L1-L4 varied from 0,3 to 2,2 and T-criteria in the

femoris collum from 0,4 to 2,0. In 1 gr. 5 patients (24%) received MHT (17 $\beta$ -E2 1 mg + DYD 5 mg or estradiol-gel 1gr), 13 (62%) - MHT in a combination with calcium and 3 (14%) patients calcium only. In 2 gr.: 28 (56%) patients received MHT for the purpose of treatment postovariectomy syndrome: 18 (39%) patients received MHT in a combination with calcium, 10 patients (22%) MHT and 18 (39%) patients, who refused MHT received phytoestrogens with calcium. During dynamic control a year later growth of BMD based on the DEXA data on the background of therapy in 1 gr. was +1,8% of initial level. The BMD rates of patients in the 2 gr. remained in limits of normal state.

**Conclusions:** The patients with ovariectomy living in the Moscow Region allowed to assign to a group of risk on the onset of osteopenic syndrome. MHT in a combination with calcium drugs or without are contributing growth of BMD for patients with ovariectomy and osteopenic syndrome.

### ***P25: The association among irisin, estradiol, and bone mineral density in perimenopausal women***

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West China Second University Hospital

**Objective:** Estradiol (E2) and irisin, a newly discovered myokine, have been proved to take part in bone metabolism and boost bone mass. Perimenopause is characterized by fluctuating serum E2 level, which might relate with bone mass. However, there has been no report on the association among irisin, E2, and bone metabolism in women undergoing menopausal transition. In this study, we investigated the blood levels of irisin, E2 and measured bone mass in perimenopausal women.

**Methods:** Women over 40 years old with decreased ovarian function were included. Those who used hormone therapy (HT) in recent 3 months or diagnosed as menopause were excluded. Fasting blood samples were collected from the 3rd to 5th day of menstruation (early follicular phase). Serum irisin and E2 level were tested by ELISA method, and bone mineral density (BMD) at lumbar spine was also assessed by dual-energy x-ray absorptiometry (DEXA).

**Results:** 60 women, age from 41 to 50 and diagnosed as perimenopausal, were recruited. The serum E2 level was relatively higher in 26 women ( $94.67 \pm 22.13$  pg/ml) than the rest ( $17.14 \pm 5.21$  pg/ml). In women with higher E2 level, the serum irisin level and BMD were  $125.81 \pm 15.40$  ng/ml and  $1.05 \pm 0.17$ . Pearson's correlation analysis showed that the irisin level was positively correlated with E2 ( $r=0.808$ ,  $p<0.01$ ) and BMD ( $r=0.890$ ,  $p<0.01$ ). Such associations were not found in women with relatively lower serum E2 level.

**Conclusions:** Serum irisin level was positively associated with E2 and BMD in perimenopausal women whose serum E2 levels were relatively higher. Larger sample size and further investigations of interactions among irisin, sex hormone, and BMD in perimenopausal women are needed in the future. This project was supported by Scientific Research Projects of The National Natural Science Fund (41473097).

### ***P26: Aging of bone structure in the menopausal transition***

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Eotvos Lorand University

**Objective:** The purpose of the research was to study the relationship between menopausal status and bone structure in the menopausal transition.

**Methods:** A random sample of 1932 Hungarian women (aged 35+) was to be enrolled in the study between 2012-15. Bone mass was estimated by the Drinkwater-Ross anthropometric method. Bone structure parameters were assessed by a quantitative ultrasound (QUS) device (DTU-one). Subjects were divided into pre-, peri- and postmenopausal subgroups on the basis of their menstrual history.

**Results:** The reference quantitative ultrasound data in the studied age-group of Hungarian women for the DTU-one sonometer were determined. By considering the changes in QUS parameters and bone mass by ageing and reproductive ageing an intensive, menopause-related change from the late 40s and then another significant change from the beginning of the 70s were observed in bone structure of women. Both the mass and the porosity of the bone component of the female body decreased by age and by menopausal status. According to the international QUS parameters thresholds for osteoporosis, on average 15-17% of women are at very high risk for osteoporosis in the premenopausal status and after the menopausal transition the decreased level of female sex hormone production doubles this risk of osteoporosis for the beginning of the postreproductive period, and triplicates this risk for the 70s of women. The national and global prevalence of diagnosed osteoporosis patients and osteoporotic fractures confirms this exponential increase in the risk of osteoporosis in females. The premature menopause was found to be accompanied by the increased risk of osteoporosis during the whole studied age interval.

**Conclusions:** The present results emphasize the importance of menopausal status assessment in the screening for this age-related increase of osteoporotic risk.

## **Breast**

### ***P27: Is polycystic ovary syndrome a risk factor for breast cancer?***

Pablo Carpintero (AR), Maria Franchina (AR), Gustavo Litterio (AR) and David Fusaro (AR)

IGBA

**Objective:** To describe the behavior and establish statistical significance correlation between polycystic ovary syndrome (PCO), diabetes, smoking and nulliparity in the possibility of having breast cancer in postmenopausal women (PMW) in our study population.

**Methods:** Retrospective, case-control model, consecutive review of 300 PMW that attended IGBA between 10/1014 and 9/30/15. 267 cases were selected. Exclusion criteria: Patients that had not completed the requested laboratory. Variables: age, menopause, history of PCOs, diabetes, nulliparity, smoking. Statistics: Descriptive comparative statistics were used according to the variable scale and comparative model. Chi2 and odds ratio tests were used for the comparative bivariate model and confidence intervals (CI) of 95% were calculated. Logistic regression method was used for the multivariate analysis. Error  $\alpha$ : 0,05. Error  $\beta$ : 0,10

*Results:* n: 267 PMW Mean: 48.2, SD: +/−9.2. Range: 43–65

*Conclusions:* From 267 PMW, 31 had a history of PCOs (11.6%). We did not find any statistically significant relation between PCOs and the risk of having breast cancer. However, diabetes, smoking and nulliparity showed a statistically significant relation and the logistic regression method demonstrated that they could act as risk factors independently from each other.

## **P28: Advocacy and mass education in breast cancer awareness in Central India – efforts and outcomes**

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*Introduction:* In developing country like India, there is rise in the cases of breast cancer significantly in last decade. Prevention and awareness of breast cancer play an important role at this junction. This essay is an attempt to present our efforts over the past decade in the field of breast cancer awareness.

*Material and methods:* Following are our combined efforts for mass education in breast cancer. We developed a pictorial guide for breast cancer signs and symptoms in regional language. A book titled 'Practical approach to Menopause Management' edited by us, incorporates a chapter on breast cancer. A chapter on breast imaging is also included so as to make clinicians familiar with the imaging appearances of breast cancer. A revolutionary idea of creating a breast cancer app specially for the women of India 'Know yourself' is in pipeline. We have prepared a breast cancer documentary and a skit to be run during various breast cancer awareness programs. Breast cancer screening with the help of mammography is undertaken on large scale free of cost or at very minimal cost with screening of more than 100 patients till now. Special breast models are prepared to demonstrate palpation of various breast lumps to the delegates during the teaching sessions. Various awareness activities for breast cancer like radio talks, television interviews, articles, marathon, cycle rallies on various occasions are arranged on regular basis. Cancer awareness week is celebrated. Breast prosthesis and wigs are given. These efforts showed good results.

*Discussion:* Still efforts taken so far are sparse and do not reach all women. It has to come from government organizations for its long term sustainability.

*Conclusion:* We need dedicated, sustained and combined efforts to make a demonstrable impact towards promoting advocacy for Breast Cancer Awareness and education in the population.

## **P29: Vaginal erbium laser (VEL®): the second-generation thermotherapy for the genitourinary syndrome of menopause in breast cancer survivors**

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*Objective:* The genitourinary syndrome of menopause (GSM) is commonest menopause consequence and tends to be progressive, jeopardizing quality of life and sexual relationships. Local estrogen therapy is the treatment of choice, but has

contraindications, such as breast cancer history. The aim of this study is to evaluate the efficacy and acceptability of a second generation of vaginal laser treatment, the vaginal erbium laser, (VEL®), as a non-ablative photothermal therapy for the management of GSM in postmenopausal breast cancer survivors.

*Methods:* The study was performed using an erbium laser crystal yttrium-aluminum-garnet (XS Fotona Smooth™, Fotona, Ljubljana, Slovenia) with a wavelength of 2940 nm. Forty-three postmenopausal breast cancer survivors were treated with 3 laser applications every 30 days. GSM symptoms were assessed before treatment and after 1, 3, 6, and 12 months, using subjective (visual analog scale, in cm) and objective (Vaginal Health Index Score, VHIS) measures. The procedures were performed on an outpatient basis without anesthesia or drug use before or after the intervention.

*Results:* VAS scores for vaginal dryness and dyspareunia, from basal values of  $8.5 \pm 1.3$ , and  $8.8 \pm 1.3$  cm, respectively, showed a decrease ( $p < 0.01$ ) to  $3.9 \pm 0.6$  and  $3.8 \pm 1.0$  cm 4 weeks after the last VEL; the values remained lower ( $p < 0.05$ ) than corresponding basal values during the follow up period. The VHIS increased from basal levels values of  $10.2 \pm 2.6$  to  $20.1 \pm 2.8$  ( $p < 0.01$ ) after VEL treatment. VHIS values at the end of follow-up period ( $19.1 \pm 3.8$ ) remained higher ( $p < 0.05$ ) than basal values. No adverse events were recorded during the study.

*Conclusions:* This study indicates that VEL® is effective and safe for the long-term treatment of GSM in postmenopausal breast cancer survivors.

## **P30: Didymin, a dietary flavonoid glycoside, reverses phthalate esters-associated breast cancer aggravation**

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<sup>a</sup>Kaohsiung Medical University Hospital; <sup>b</sup>Kaohsiung Medical University

*Objective:* This study investigated didymin, a dietary flavonoid glycoside obtained from citrus fruits, as a potential antidote against phthalate esters-associated breast cancer aggravation.

*Methods:* We treated MDA-MB-231 with butyl benzyl phthalates (BBP), di(n-butyl) phthalates (DBP), or di(2-ethylhexyl) phthalates (DEHP), then harvested the conditioned medium (CM), which was then cultured to monocyte-derived dendritic cells (mdDCs).

*Results:* Cultures of MDA-MB-231 with the conditioned medium of BBP-, DBP-, or DEHP-MDA-MB-231 tumor-associated mdDC (BBP-, DBP-, or DEHP-MDA-TADC-CM) enhanced MDA-MB-231 proliferation, migration, and invasion. Exposure of MDA-MB-231 to DBP caused MDA-TADCs to produce the inflammatory cytokine RANTES, which subsequently induced MDA-MB-231 proliferation, migration, and invasion. Depleting RANTES reversed the effect of DBP-MDA-TADC-mediated MDA-MB-231 proliferation, migration, and invasion. Moreover, didymin suppresses phthalates-mediated breast cancer cell proliferation, migration, and invasion.

*Conclusions:* Our study suggests that didymin is capable of preventing phthalate esters-associated cancer aggravation.

### P31: Breast risk evaluation in 40 plus women

Bipasa Sen (IN)

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**Objective:** 1. Screening and examining breast a step towards early detection of breast malignancy. 2. Assessment of risk factors prior to hormone therapy.

**Methods:** Careful noting of the complaints of women. Through history taking. Physical examination by clinician of – breast, axilla and others.

**Screening:** 1. Mammography: earlier Wolfe introduced 2 types of mammography patterns as index of risk for developing breast malignancy – a) Low risk pattern, b) high risk pattern. Later, The American Cancer Society replaced Wolfe's criteria with BIRADS (Breast Imaging Reporting And Data System). 2. Mammosonography. 3. Fine needle aspiration: major limitation – frequent false positive cytological diagnosis. 4. Core needle biopsy – higher specificity and lower suspicious rate. CNB accurately identifies the grade and type of tumor in most cases. Combined CNB and FNA result in increased absolute sensitivity. 5. Percutaneous imaging guided CNB. 6. Excisional or incisional biopsy.

**Triple Test Score (TTS):**

Scores 1, 2 or 3 is hypothesized for benign lesion, lesion suggestive of malignancy and malignant lesion respectively. TTS is the sum total of all the scores in all three categories. Lesions with TTS 4 or less – benign (even if FNA score is 2). Lesion with TTS 6 or more – malignant. Lesion with TTS 5 - 51% chance – benign, - 49% chance – malignant. TTS allows reduction in open surgical biopsies.

**Results:** Self breast exam helps early detection of any abnormal breast lesion that may direct the clinician towards further investigation and follow up. If HT is to be prescribed, the overall risk evaluation enables the doctor to give it in a tailored way as per individual need.

### P32: The anti-proliferative effects of Maca, Olive Leaf and Spirulina on breast cancer cell lines

Lily Stojanovska (AU), Vasso Apostolopoulos (AU), Kristina Nelson (AU), Stephanie Day (AU) and Todor Vasiljevic (AU)

Victoria University

Cancer is a disorder of uncontrolled cell proliferation. Intake of particular foods and nutrients can be both causative and preventative in cancer. It is estimated that 1/3 of cancers are linked to diet. Obesity, red/processed meat and alcohol are considered risk factors, whereas plant food intake of pulses and vegetables are associated with decreased risk. Popular health food supplements are attributed with health claims, many of which include chemoprevention. Maca, Olive Leaf and Spirulina are popular supplements containing various compounds associated with chemopreventative effects yet their therapeutic mechanisms are not well understood.

**Objectives:** Little is known about Maca, Olive Leaf and Spirulina's effects in cancer; so this study examined their anti-proliferative effects on human breast cancer cell line, MCF-7.

**Method:** We previously demonstrated that Maca reduced symptoms of depression and improved diastolic blood pressure in postmenopausal women. As breast cancer is a risk factor in postmenopausal women, we determined the effects of Maca, Olive Leaf and Spirulina in vitro. Breast cancer cell line MCF-7 was

seeded in 96-well plates and incubated with either crude or artificially digested extracts ranging from 0.01–100 µg/ml. Media alone was used as background control. Proliferation was measured on days 1, 2, 3, 4 and 5 using tritiated thymidine 3H. The difference in the amount of cells/well of the MCF-7 cell line was attributed to the different growth rates of each cell line in vitro.

**Results:** At 100 µg/ml, crude and digested Olive Leaf extracts exerted a striking effect on inhibiting proliferation of MCF-7. Minimal inhibitory effect was observed by Maca or Spirulina in either experiment.

**Conclusions:** Olive Leaf inhibited proliferation of the breast cancer cell line MCF-7 in a dose dependent manner.

## Cardiovascular health

### P33: Anti-Mullerian hormone and stroke prevention

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**Objective:** Increased stroke frequency in postmenopausal women is associated with the development of cardiovascular risk factors in the period of menopausal transition. The premature ovarian aging before menopause, on the background of the continuing need for estrogen, is an additional risk factor for vascular events.

**Methods:** We have evaluated dynamics of reduction anti-Muellerian hormone (AMH) compared with levels of estradiol (E) and follicle-stimulating hormone (FSH) in 29 premenopausal women with essential hypertension (EH). Determined by dynamics of AMH, FSH, E every 3 months for 18 months was also evaluated the severity of climacteric symptoms of Menopause Rating Scale and indicators of blood pressure (BP).

**Results:** The reducing AMS more than 10 times in 3 months occurred in 17.24% of cases (5 patients). In these patients reduction of AMH from  $0,723 \pm 0,0023$  ng/mL to  $0,069 \pm 0,0031$  ng/mL ( $p < 0,05$ ) on average for 1.5 months preceded the appearance of early menopausal symptoms. It should be noted that the severity of vasomotor menopausal symptoms such as hot flushes, heart discomfort and sleep problems was positively correlated with episodes of rise in BP probably due to their synergistic influence ( $rMRS - \uparrow BP = 0,672$ ).

**Conclusions:** Reduced AMH more than 10 times over 3 months is preclinical criteria of premature ovarian aging in premenopause. AMH controls in premenopausal patients with EH will allow time to reveal and correct ovarian hypofunction to save estrogenic protection of vessels and for the prevention of menopausal syndrome, worsening EH - one of the most important risk factors for stroke.

### P34: Aortic size index is a limiting factor for assisted conception in Turner syndrome patient – Case report

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In women with Turner syndrome (TS) we are faced with numerous conjuncted anomalies and diseases. Some of them present a contraindication for procedures of assisted reproduction:

coarctation of aorta, bicuspid aortic valve, previous surgical repair of heart valves or vessels, dilatation of ascending aorta over 2 cm/m<sup>2</sup> (aortic size index – ASI), portal hypertension, body mass index over 30 kg/m<sup>2</sup>, untreated/severe hypertension. We present a case report of a 39-years-old women with TS that was rejected for assisted reproduction trial due to clinically silent but prognostic undesirable significant dilatation of ascending aorta (ASI= 2.1 cm/m<sup>2</sup>, diameter of ascending aorta 34 mm, measured by echocardiography and cardiac MRI). Additionally, she had untreated arterial hypertension, liver steatosis and was overweight (body mass index was 30.5 kg/m<sup>2</sup>). Regarding TS, her genotype was pure X0. She reached menarche at the age of 12 and was secondary amenorrhoeic from the age of 14, receiving hormone replacement therapy after that. In Slovenia, patients with TS entering trials of assisted reproduction are managed interdisciplinarily on the grounds of tertiary medical centre consensus statement.

### ***P35: Effectiveness of a nursing intervention in hypertensive, dyslipidemia and overweight postmenopausal women: a randomized controlled trial with a 12-month post-intervention follow-up***

Alide Salazar (CL)<sup>a</sup>, Vivian Vilchez-Barboza (CR)<sup>b</sup>,  
Katia Sáez (CL)<sup>a</sup> and Tatiana Paravic (CL)<sup>a</sup>

<sup>a</sup>University of Concepción; <sup>b</sup>University of Costa Rica

**Objective:** To examine the effectiveness of a 7-month nursing intervention in hypertensive, dyslipidemia and overweight postmenopausal women in Concepción, Chile in maintaining reductions in cardiovascular risk factors and health quality of life (HRQL) at 12 months post-intervention.

**Methods:** 61 postmenopausal women were recruited from 6 community health centers and were randomized to an intervention group and control group. Nursing intervention: face to face and telephone counseling sessions. Control group received the standard information only. Outcome measures: HRQOL (Physical Component Summary (PCS) and Mental Component Summary (MCS) score), 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), TC/HDL ratio levels and Atherogenic index (IA) were measured as baseline data, immediately post-intervention and at a 12-month follow-up occasion. In follow-up control and intervention group only received the standard information the health center. Statistical analysis: repeated-measures MANCOVA and d-Cohen. Ethics requirements were incorporated.

**Results:** With the exception of the WC ( $F = 3,65$ ;  $P = 0,035$ ) there was no significant differences between-group on outcome measures at posttest and follow-up. In the intervention group decreased significantly at time group: PCS score ( $F = 26,84$ ;  $P = 0,000$ ), MCS score ( $F = 8,8$ ;  $P = 0,000$ ), DBP ( $F = 27,17$ ;  $P = 0,000$ ), WC ( $F = 17,49$ ;  $P = 0,000$ ), TC/HDL ratio ( $F = 18,25$ ;  $P = 0,000$ ) and IA ( $F = 3,27$ ;  $P = 0,046$ ). The control group showed decreased significantly at time group: DBP ( $F = 14,80$ ;  $P = 0,00$ ) and TC/HDL ratio ( $F = 8,25$ ;  $P = 0,001$ ).

**Conclusions:** Waist circumference improved over time. The findings in intervention group should be conducted in primary care to incorporate counseling sessions.

### ***P36: Effects of hormone therapy on serum C-reactive protein level in postmenopausal Korean women***

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**Objectives:** C-reactive protein (CRP) is an established marker of inflammatory status in cardiovascular disease. This study was conducted to evaluate the effects of hormone therapy (HT) on CRP in postmenopausal Korean women.

**Methods:** This retrospective cohort study included 357 healthy postmenopausal Korean women who did not have a history of or risk factors for cardiovascular disease. Two hundred sixty-two women took oral estrogen (conjugated equine estrogen 0.625 mg/day or equivalent), and 95 women applied transdermal estrogen (0.1% 17-β estradiol gel). To prevent endometrial stimulation with estrogen, progestogen was added to 209 women of oral group and 56 women in transdermal group. Serum level of CRP was measured before, 3 and 6 months after HT, and compared according to the route of estrogen administration and addition of progestogen.

**Results:** No difference was found in clinical characteristics between oral and transdermal groups at baseline. In oral group, CRP increased significantly after 3 and 6 months after adjusting for age and body mass index as the confounder of CRP. However, there was no significant change in CRP compared to the baseline in transdermal group. There was also no difference with additional progestogen. Changing pattern of CRP during 6 months was significantly different by the route of estrogen administration.

**Conclusions:** Transdermal estrogen therapy would be more beneficial than oral estrogen in terms of CRP in postmenopausal Korean women. The effects of estrogen are not influenced by adding progestogen.

### ***P37: Effectiveness of a nursing intervention in hypertensive, dyslipidemia and overweight postmenopausal women and middle-aged men: a randomized controlled trial with a 12-month post-intervention follow-up***

Vivian Vilchez-Barboza (CR)<sup>a</sup>, Alide Salazar (CL)<sup>b</sup>,  
Katia Saez (CL)<sup>b</sup>, Tatiana Paravic (CL)<sup>b</sup> and Karin Ferrada (CL)<sup>b</sup>

<sup>a</sup>Universidad de Costa Rica; <sup>b</sup>Universidad de Concepción

**Objective:** To examine the effectiveness of a 7-month nursing intervention in hypertensive, dyslipidemia and overweight postmenopausal women and middle-aged men in Concepción, Chile in maintaining reductions in cardiovascular risk factors and health quality of life (HRQL) at 12 months post-intervention.

**Methods:** 61 women and 33 men were recruited from 6 community health centers and were randomized to an intervention group and control group. Nursing intervention: face to face and telephone counseling sessions. Control group received the standard information only. Outcome measures: HRQOL (Physical Component Summary (PCS) and Mental Component Summary

(MCS) score), 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), TC/HDL ratio levels and Atherogenic index (IA) were measured as baseline data, immediately post-intervention and at a 12-month follow-up occasion. In follow-up control and intervention group only received the standard information the health center. Statistical analysis: repeated-measures MANCOVA and d-Cohen. Ethics requirements were incorporated.

**Results:** Between-group differences on outcome measures at posttest and follow-up time x group for women: WC ( $F=3,65$ ;  $P=0,035$ ) and for men: Emotional role ( $F=4,04$ ;  $P=0,036$ ), Corporal pain ( $F=6,48$ ;  $P=0,008$ ), PCS ( $F=4,13$ ;  $P=0,034$ ), WC ( $F=8,41$ ;  $P=0,002$ ).

**Conclusions:** This findings evidence gender difference in effectiveness of a nursing intervention in hypertensive, dyslipidemia and overweight postmenopausal women and middle-aged men. WC improved over time in postmenopausal women and middle-aged men. Middle-age men also improve some HRQOL Component. It is important to cardiovascular health interventions differentiated by sex.

### ***P38: The risk factors and change of the incidence of CVD in Chinese women during menopausal transition and afterward***

Qi Yu (CN)

Chinese Academy of Medical Science and Peking Union Medical College

Cardiovascular disease (CVD) is the leading cause of death in both men and women in China. It is reported that women of middle age have historically been at a lower risk for overall vascular events than similarly aged men. However, the incidence of CVD among women increases when they are >50 years old, which happens to be the menopausal transition period. Thus, it has been proposed that deprivation of ovarian hormones, specifically estrogen, in menopause is probably related to increased CVD risk in aging women. It is believed that hypertension, hypercholesterolemia, diabetes mellitus, overweight and obesity are main risk factors of CVD. From 1991 to 2002, the prevalence of hypertension in adult women increased from 10.2% to 18.0%, which was higher in men than women <50 years old and equal in women and men above 50 years old. Similarly, the average level of cholesterol and the prevalence of hypercholesterolemia is lower in women than men younger than 45. However, the incidence of women gradually surpasses that of men from 45 to 59 and is significant higher than that of men when they are older than 60 years. The incidence of diabetes mellitus of Chinese women is stated to exceed that of men above 60 years old. It is inevitable that there will be soaring prevalence and death rate of CVD with the increase in incidence of hypertension, diabetes, dyslipidemia and overweight. In a survey conducted in 1994-2000 in Beijing, the annual coronary heart disease (CHD) mortality of male was nearly 3 fold as much as that of female (63/100 000 vs. 22/100 000) when they aged 45-59 year old. As age grows, this gender disparity is narrowing down, accounting 311/100 000 vs. 146/100 000 and 328/100 000 vs. 260/100 000 in the 60-64 and 65-69 age group respectively. The CHD mortality of male is only 1.5-2 fold as much as that of female above 60 years old.

## **Epidemiology/Psychosocial**

### ***P39: Age of menopause and predictors of age of menopause in India***

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Ahuja Health Care Services and Infertility

**Introduction:** Natural age of menopause is when because of ovarian follicle depletion there is amenorrhea. This is a retrospective diagnosis, as there has to be amenorrhea of 1 year before we can say that woman is menopausal 5-6 years preceding menopause of perimenopause. If menopause occurs before 40 years of age it is premature menopause, or can be premature ovarian failure (POF). If menopause occurs between 40 years and predicted age of menopause for that country or race then it is called Early Menopause. Age of menopause is important from clinical point of view and from public health point of view also and also from fertility treatment point of view. There are many determinants of menopause and genetics is the main.

**Methods:** In India in the year 2014, data collection on age of menopause was done and we collected data of about 2108 women and average age of is perimenopause in India =  $44.69 \pm 3.79$  years and menopause is  $45.59 \pm 5.59$  years and natural age of menopause in India is  $46.18 \pm 4.91$  years. As this means fertility loss even in early forties in Indian women is found and more cases of POF and POI are found. So fertility treatment and preservation has to start early in India. This also means that we start all preventive strategies earlier and recommendations for screening for Osteoporosis and CHD and other problems starts much earlier in India

**Conclusions:** We have to start all preventive strategies and even infertility treatment and preservation early .

### ***P40: Knowledge about climacteric syndrome among Brazilian women – a population-based household survey***

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University of Campinas (UNICAMP)

**Context:** Knowledge about climacteric is a poorly explored subject.

**Objectives:** To evaluate knowledge about the climacteric syndrome among Brazilian women and the factors associated with the level of knowledge.

**Methods:** A cross-sectional study was conducted in the metropolitan region of Campinas/Brazil. The dependent variable was knowledge about the climacteric syndrome assessed using a score developed with a questionnaire on various aspects of the menopausal transition. The independent variables were sociodemographic data, health-related habits and problems. Statistical analysis was carried out by the Kruskal-Wallis test, Mann-Whitney test and multivariate analysis. Patients: 749 women aged between 45 to 60 years. Intervention: none. Main outcome measure: knowledge about the climacteric syndrome.

**Results:** The mean age of women was 52.5 ( $\pm 4.4$ ) years. Regarding the menopausal status, 16% were premenopausal, 16% perimenopausal and 68% postmenopausal. The median climacteric syndrome knowledge score was 4 (range 1-11). In the final statistical model, having more years of schooling ( $\beta=0.64$ ;  $p < 0.01$ ), a

higher social class ( $\beta=0.47$ ;  $p<0.01$ ), genital atrophy ( $\beta=0.47$ ;  $p<0.01$ ), social consumption of alcohol ( $\beta=0.61$ ;  $p<0.01$ ), having used some kind of treatment for menopause ( $\beta=0.41$ ;  $p<0.01$ ), having anxiety ( $\beta=0.35$ ;  $p=0.03$ ) and depression ( $\beta=0.31$ ;  $p=0.04$ ) were associated with a higher knowledge about the climacteric syndrome. Having  $\geq 3$  vaginal deliveries ( $\beta=-0.61$ ;  $p<0.01$ ) and higher BMI ( $\beta=-0.02$ ;  $p=0.04$ ) were associated with a lower knowledge about the climacteric syndrome.

**Conclusions:** Knowledge about climacteric is associated with a wide range of factors. Knowing these factors can help identify women who would benefit from educational actions promoted by healthcare systems. A better understanding about climacteric could help these women face this transition phase with a better quality of life.

### **P41: Identifying risk factors associated with severe climacteric symptoms: results from a population-based household survey**

Adriana Pedro (BR), Jeffrey Lui-Filho (BR), Luiz Baccaro (BR), Lucia Costa-Paiva (BR) and Aarao Pinto-Neto (BR)

State University of Campinas - UNICAMP

**Objective:** To determine the prevalence of severe somatic, psychological and urogenital symptoms, and its associated factors in women in a metropolitan region in Southeastern Brazil.

**Methods:** A descriptive, exploratory, cross-sectional study was conducted with 749 women (a population-based household survey). The dependent variable was the intensity of menopausal symptoms assessed by the Menopause Rating Scale (MRS). The independent variables were sociodemographic data, health-related habits and problems, self-perception of health, and gynecological background. Statistical analysis was carried out by the  $\chi^2$  test and Poisson regression using the backward selection criteria.

**Results:** The mean age of the women was 52.5 ( $\pm 4.4$ ) years. With regard to menopausal status, 16% were premenopausal, 16% perimenopausal and 68% postmenopausal. The mean age at the onset of menopause was 46.5 ( $\pm 5.8$ ) years. The intensity of menopausal symptoms was defined according to the median MRS subscales scores. It was considered severe for values above 3, 2 and 1 for somatic psychological and urogenital symptoms respectively. The prevalence of moderate to severe somatic, psychological and urogenital symptoms was 49%, 46% and 44%, respectively. Factors associated with moderate to severe climacteric symptoms in all subscales of MRS were self-perception of health as fair/poor/very poor ( $p<0.01$ ), depression/anxiety ( $p<0.01$ ) and rheumatic diseases ( $p<0.01$ ).

**Conclusions:** This study demonstrates that a high proportion of Brazilian women experience moderate to severe bothersome climacteric symptoms. Despite the considerable symptom prevalence, clinical factors were more related to severity of symptoms showing an evidence of appropriate clinical multidisciplinary care is highly recommended for adequate management of women during climacteric period.

### **P42: Symptoms of menopause in Indian women and their attitude toward MHT (menopausal hormone therapy)**

Sarita Bhalerao (IN)

Wadia Maternity Hospital, Mumbai

**Objective:** To study the incidence and nature of symptoms of menopause in Indian women and their attitude towards menopausal hormone therapy. For the purpose of this study natural menopause is defined as spontaneous cessation of menses for 1 year. Patients who had their ovaries removed are classified as surgical menopause.

**Materials and methods:** Patients were interviewed about their age, age at menopause, symptoms of menopause and their attitude towards menopausal hormone therapy. The patients were classified into different socioeconomic groups. The study was conducted at Nowrosjee Wadia Maternity Hospital which is teaching hospital in Mumbai and at the author's private clinic.

**Results:** Hot flashes and urinary symptoms were the predominant symptoms. Sexual dysfunction due to dryness of the vagina and loss of libido were also common symptoms. Most women were frightened to take menopausal hormone therapy but were keen to try non hormonal medications.

### **P43: The importance and the content of a comprehensive model of care for menopausal patients**

Johannes Bitzer (CH)

University Hospital Basel

**Introduction:** Postmenopausal women suffer from various and multidimensional problems – physical symptoms, mental symptoms, psychosocial problems and stressors. These complaints have a multifactorial origin ranging from genetics, to hormonal changes, aging processes, psychosocial transitions and they are codetermined by behavioral patterns and sociocultural norms. Therefore these women need a biopsychosocial comprehensive concept of care.

**Methods:** Case discussions in group supervision of physicians interested in menopausal medicine. Collaborative proposal for a comprehensive standard of care for menopausal women.

**Results:** The menopausal consultation should be structured and contain the following elements: eliciting the agenda of the patient (her symptoms, her needs and priorities); assessing the biopsychosocial profile (risks and resources); elaborating a shared understanding of the complaints and the health problems by eliciting the patient's health beliefs and providing evidence based information and education; inform and educate patients about all available treatment options including patient adapted risk counseling; making a shared decision regarding solution to problems and treatment.

**Conclusions:** Good clinical practice in the care of menopausal women needs (AUS) – A biopsychosocial perspective, and concept of care; Up to date evidence based knowledge about screening, diagnostic procedures and therapeutic options; Specialized communication skills including patient centred communication, health education and motivational interviewing, risk counseling and shared decision making.

### **P44: Menopause and big data: Word Adjacency Graph modeling of menopause-related ChaCha data**

Janet Carpenter (US), Doyle Groves (US), Julie Otte (US) and Wendy Miller (US)  
Indiana University

*Context:* Pervasive use of social media and mobile applications for health-related searches has created large and complex datasets (i.e. big data) that reflect the public's organic queries and concerns about health. There are 1.9 billion questions asked between January 2009 and November 2012 within ChaCha, a free anonymous question and answer service.

*Objective:* To evaluate salient queries about menopause using ChaCha.

*Methods:* We used Word Adjacency Graph (WAG) modeling to detect clusters and visualize the range of menopause-related topics and their mutual proximity. The subset of relevant queries was fully modeled. Each query was split into token words and stopwords removed. Remaining words were considered in sequence to build summary tables of words and 2- and 3-word phrases. Phrases occurring at least 10 times were used to build a network graph model that was iteratively refined by observing and removing clusters of unrelated content.

*Patients:* A menopause-related subset of 263,363 queries from across the USA was identified by searching for questions containing menopause and menopause-related terms (e.g. climacteric, hot flashes, night sweats, hormone replacement).

*Interventions:* Not applicable.

*Main outcome measures:* Description and depiction of topic clusters.

*Results:* We identified several individual clusters; most highly relevant to the core topic of menopause and fewer considered less relevant. Larger clusters related to hot flashes and hormone therapies. Smaller clusters related to topics such as menopause acne and thyroid function. Clusters are fully described in tables and their proximity depicted in figures.

*Conclusions:* We modeled menopause-related areas about which ChaCha users have asked. Our model provides a foundation for additional, more in-depth analysis of queries and development of patient-centered interventions.

### **P45: The evolution of pregnancy for women with medical thyroid priors**

Eduard Crauciuc (RO), Mariana Bratu (RO) and Dragos Crauciuc (RO)  
University of Medicine and Pharmacy Iasi, Romania

*Objective:* The patients with untreated hypothyroidism have a high rate of unsuccess in getting a pregnancy, even using in vitro fertilization.

*Material and methods:* The study included 26 pregnant women aged between 23 and 45 years old, who were admitted in "Elena Doamna" Hospital of Obstetrics and Gynecology Iasi, Romania: 14 patients had a personal medical history of thyroid problems (Lot I) and 12 who had their first morpho-functional thyroid evaluation (Lot II). To prevent miscarriages, the pregnant women with autoimmune thyroiditis were administered levothyroxine (Euthyrox).

*Results:* Gestational age at the first thyroid evaluation varied from 5 to 34 weeks. Here are some of the signs and symptoms that characterized the diagnosis: heart palpitations at night (26.1%);

tremor of the extremities (23.1%); restless sleep (23.1%); temporal headache (23.1%). The ultrasonographic evaluation shows: hyperechoic structures for 50% of the patients in Lot I and 8.3% in lot II ( $p=0.05$ ). The thyroid was normally vascularized for 57.1% of the patients with a medical history of thyroid illnesses ( $p=0.044$ ). The evaluation of thyroid markers for the patients with hyperechoic changes and increased vascularization showed: TSH $\uparrow$  (1.61  $\mu$ UI/ml;  $p=0.028$ ); FT3 $\downarrow$  (3.98 pmol/l;  $p=0.045$ ); antibodies ATPO $\downarrow$  (11.60 UI/l;  $p=0.001$ ) and ATG $\downarrow$  (15 UI/l;  $p=0.001$ ). Though, according to the cases studied, the only predictable parameter used in determining thyroid damage proves to be FT4 (AUC =0.733; IC95%: 0.452-1.015; cut off 1.10 ng/dl). 2 patients with a medical history of thyroid problems had miscarriages (14.3%).

*Conclusions:* The monitoring of the thyroid function during pregnancy and the prompt treatment administration reduces the risk of complications, both for the mother and for the foetus.

### **P46: Premature ovarian insufficiency and environmental factors**

Ksenija Gersak (SI) and Ziva Gersak (SI)  
University of Ljubljana, Faculty of Medicine

*Context:* Premature ovarian insufficiency is defined as a cessation of spontaneous menstrual cycle before the age of 40 years. The causes are diverse (genetic, autoimmune, iatrogenic, smoking), in most cases they are multifactorial or rather remain unknown. Newer reports also prove a significant causal relationship with environmental factors and endocrine disrupters (ED).

*Objective:* To determine the incidence rate of premature ovarian insufficiency in the statistical regions of the Republic of Slovenia (RS) within an 11-year period (2003-2013).

*Methods:* We used the healthcare statistical data gathered by the non-hospital-based National Institute of Public Health, along with the demographic data from the databases of the Statistical Office of RS. Only women who have been identified as POI at the primary healthcare level were included in the study population.

*Results:* There were 920 newly discovered cases at the primary healthcare level in Slovenia, and the incidence rate was 18/100,000 women per year aged 0-39 years. The highest incidence rate was in the Zasavje region (59/100,000).

*Conclusions:* The explanation for the differing POI incidence between the country's statistical regions can be sought in a multifactorial sample model, which also includes harmful effects pertaining to the environment. In the last 50 years this region was known for its coal-driven thermal power stations, along with factories producing cement, and various chemical agents. Such an environment creates numerous poorly known compounds and combustion by-products on a daily basis. The association has been confirmed for exposure to combustion by-products, polychlorinated biphenyls, and pesticides. Further studies are required to identify their presence in the environment and to understand the mechanisms by which their adverse effects are manifested.

### **P47: Comparison of menopausal symptoms in urban and rural areas using the Menopause Rating Scale**

Elizabet Jusuf (ID) and Andi Tahir (ID)  
Hasanuddin University, Makassar, Indonesia

*Objective:* To compare the menopausal symptoms among women who live in urban (Makassar city) and rural area around South Sulawesi, Indonesia

**Methods:** Cross sectional. This study compares urban and rural women regarding menopause symptoms using the Menopause Rating Scale (MRS). A sample of 140 people was taken by purposive sampling and analyzed by Chi-square test.

**Results:** The average age of menopause women is 49.1 years old in urban areas and 51.09 years old in rural areas. Postmenopausal women (33.9%) and perimenopausal (29.5%) women together experienced significantly higher prevalence of all symptoms than the premenopausal (36.6%) women. The socio-demographic determinants which associated with menopausal symptoms is the level of education. Menopause symptoms are more severe significantly in rural areas than urban areas according to MRS ( $p < 0.05$ ). The most prominent symptoms of menopause from this study is muscle and joint discomfort and then sexual problem.

**Conclusions:** The menopausal symptoms are heavier in women in rural areas than in urban areas. The menopausal symptoms are more severe with who low level of education. Postmenopausal and perimenopausal women experienced significantly higher prevalence of all symptoms than the premenopausal women.

### P48: Factors associated with vasomotor symptoms

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Tiina Siirtola (FI)<sup>c</sup>, Risto Erkkola (FI)<sup>c</sup> and  
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**Objective:** Our aim was to evaluate the associations between vasomotor symptoms and age, socio-economic factors, lifestyle, use of HT, chronic diseases, and self-perception of health (SPH).

**Methods:** This cross-sectional population-based study included 3,421 women, aged 41-54 years (response rate 53.4%). Vasomotor symptoms included hot flushes and night sweats. Symptoms were assessed with two questions, rated on a four-step scale (yes, definitely; yes, sometimes; no, not much; no, not at all). A multivariable analysis was performed to study the associations between the symptoms and age, education, employment, body mass index (BMI), smoking, use of HT, chronic diseases (cardiovascular, neurological, sensory organ, bronchopulmonary, musculoskeletal, gastrointestinal, urological, dermatological, and thyroid disease, diabetes, cancer, and mental health problem), and SPH.

**Results:** Older women had more symptoms than younger women ( $p < 0.001$ ). Lower educational level ( $p = 0.002$ ) and smoking ( $p < 0.001$ ) were associated with more symptoms. The employment status and BMI were not associated with vasomotor symptoms. Former users of HT had more symptoms than non-users and current users ( $p < 0.001$ ). Women who had gastrointestinal disease ( $p = 0.002$ ) or a mental health problem ( $p = 0.021$ ) had more vasomotor symptoms. Musculoskeletal diseases were associated with fewer symptoms ( $p = 0.049$ ). Women with lower self-perception of health had more symptoms than women who defined their SPH as good ( $p < 0.001$ ).

**Conclusions:** In middle-age, vasomotor symptoms increase with aging, although the role of socio-economic circumstances and lifestyle factors is also noteworthy. Thus, to control vasomotor symptoms, it is beneficial to encourage women to avoid unhealthy behavior. Vasomotor symptoms are associated with mental health problems and decreased SPH, but are otherwise quite independent from chronic diseases.

### P49: Cultural pattern for major concerns in perimenopausal patients in Lebanon

Assaad Kesrouani (LB)  
Saint Joseph University

**Objective:** To identify major sources of concern in Lebanese perimenopausal women.

**Methods:** During consultation for a regular check-up, we asked 50 perimenopausal women what they feared most from the menopausal period. Through open end questions we aimed to search for specific concerns and fears. In case the patient didn't address a particular subject, the physician tried to bring it up to see if there were any concerns. Domains investigated include: hot flushes, annoying symptoms, sexual issues, body image, weight gain, family relationships, work relationships, osteoporosis, and illness occurrence.

**Results:** Median age is 46 years [43-50]. All patients accepted to participate in this study. Top concerns expressed by patients were: body image (36%), weight gain (32%), hot flushes (28%), osteoporosis (28%), sexual issues (26%), annoying symptoms of menopause (26%), family (22%) and work relationships (20%) and illness possibilities (20%).

**Conclusions:** Lebanese patients have many concerns for the menopausal period, in regard mainly to their body image, and to a lesser extent to relationships with family or in work.

### P50: Indian menopausal women health characteristics and strategies of interdisciplinary care

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Purushottam Khandelwal (IN)

<sup>a</sup>SMS Medical College; <sup>b</sup>Mahatma Gandhi University of Medical Sciences & Technology

**Objective:** To characterize the menopausal women attending the Centre, assess their health and identify management strategies.

**Methods:** Data collected by retrospective review of initial assessment and follow up record of 2600 menopausal women enrolled (2010-2015) at midlife women health care & Menopause centre. Information was collected on demographic, menstrual, personal, family and medical history using structured interviews. Complete health examination and investigation results documented. WHQ self-risk assessment tool was used to assess the risk and different treatment choices offered.

**Results:** Mean age at initial consultation was  $43.1 \pm 5.8 \pm SD$  (years). 1848 women attained natural menopause at  $48.8 \pm 8.9 \pm SD$  (years), while 752 were surgically menopausal at mean age  $43.3 \pm 2.8 \pm SD$  (years). Awareness regarding menopause was high 85% but for HRT was low 48%. 83% were aware of some form of alternative methods. 90% sample had cluster of problems, commonest was musculoskeletal (52%), hot flushes, sleep problems and depression (44%). Prevalence of chronic medical illness was significantly associated with the presence of menopausal symptoms ( $P < 1.01$ ). There was a positive correlation of BMD & BMI. 70.25% women (47-53 years) took some action to alleviate their symptoms. Women who were regularly seeking help at the centre did show reduced symptom severity with counselling and inter specialty referral, while 436 were lost to follow up.

**Conclusions:** Menopause burden is substantially high in India due to paucity of dedicated Menopause practitioners. Apart from HRT, yoga, acupuncture and lifestyle modification are the emerging

practices adopted by Indian menopausal women. Clinicians should implement preventive health care strategies and manage them comprehensively with individualized multidisciplinary approach based on their culture and holistic views, without or with use of MHT.

### **P51: Use and attitude towards menopausal hormone therapy among Latin-American female gynecologists**

Pablo Lavin (CL)

REDLINK

**Objective:** Evaluate if menopausal status and the presence of menopausal symptoms among female gynaecologists would influence their prescription of menopausal hormone therapy (MHT).

**Methods:** Female gynaecologists of 11 Latin-American countries were requested to fill out the Menopause Rating Scale and a questionnaire for personal information and their perceptions regarding MHT use.

**Results:** 947 female gynaecologists were contacted; 86.4% (n=818) accepted to take part. Mean age  $45.0 \pm 10.7$  years, 32.2% were postmenopausal, 75.3% had a partner and 17.6% were university teachers. 81.8% reported that they would use MHT if experiencing menopausal symptoms, without any influence of their menopausal status. Academic gynaecologists favour personal MHT use (87.5% vs. 80.4,  $p < 0.05$ ) and prescribe it more frequently than non academic ones (55.9% vs. 45.5%,  $p < 0.0001$ ). Postmenopausal gynaecologists prescribe more MHT than premenopausal (50.8%, vs. 45.6%,  $p < 0.01$ ). Additionally, hysterectomized alone prescribe more MHT than those who have experienced natural menopause (62.2% vs. 47.7%,  $p < 0.002$ ). The presence of menopausal symptoms among female gynaecologists does not influence their MHT prescription. A 6.5% of premenopausal gynaecologists and 38.4% postmenopausal ones used MHT (natural menopause: 32.5% users, hysterectomized only: 51.1% and hysterectomized plus bilateral oophorectomy: 59.3%). A 38.5% of surveyed female gynaecologists perceived that breast cancer was the main risk related to MHT use. An 86.4% of physicians prescribed non-hormonal drugs and 84.5% alternative therapies for the menopause.

**Conclusions:** Most female gynaecologists of this Latin American survey will use MHT if they experience menopausal symptoms; however, the presence of these symptoms does not influence their prescription. Postmenopausal physicians used and prescribed MHT in a higher rate than premenopausal ones.

### **P52: Premenopausal Dutch women's attitudes regarding menopause and treatment of severe symptoms influenced by limited education**

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<sup>a</sup>University of Applied Sciences Leiden; <sup>b</sup>ZBC FeM-poli Zwolle

**Objective:** To assess premenopausal women's attitudes toward menopause and treatment options for severe symptoms.

**Methods:** 128 women aged 20 to 35 years living in urban Zuid-Holland completed an internet survey addressing several aspects of menopause transition, control of symptoms and choice of treatments.

**Results:** 79.2% of respondents regarded menopause as a natural non-medical condition. 23.1% showed low sense of control of possible complaints thereby affecting self-efficacy. 75.4% indicated to have insufficient knowledge of menopausal hormone therapy (MHT) and was unable to weigh the pros and cons and make decisions about medication. Only 21.9% of respondents indicated to have sufficient knowledge of MHT. 76.7% assumed general benefit of MHT on happiness and 63.8% expected a positive influence on psychological complaints. 76.6% would not consider use of MHT and 6.1% preferred MHT over homeopathic remedies. 22.2% of women felt social pressure to use MHT in case of severe complaints.

**Conclusions:** Attitude towards menopause and MHT was mainly neutral and seemed determined by lack of knowledge. Respondents were positive about efficacy of MHT, but less so about their sense of control of menopausal complaints. A majority of women would not favour MHT over homeopathic remedies, possibly because of low social pressure to use MHT. Education on the current scientific state of affairs may better prepare premenopausal women to seek adequate treatment for bothersome menopausal complaints.

### **P53: Social capital and eating consciousness and behavior of perimenopausal Japanese women**

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<sup>a</sup>Kinjo Gakuin University; <sup>b</sup>Japanese Red Cross Toyota College of Nursing; <sup>c</sup>Meitetsu Hospital

**Background:** Social capital is a trait that seems to affect health. The amount of evidence indicating the strong relationship between social capital and good health has been increasing.

**Objective:** To investigate the association between social capital and health, menopausal syndrome or eating habits and behavior in perimenopausal Japanese women.

**Methods:** In this study, we defined a woman with rich social capital as an individual with good economic conditions and society's trust and who would participate in a regular workshop or have a health adviser. A self-reported questionnaire that included questions on eating habits and behavior was administered to two groups; one participated in a regular workshop about health, the rich social capital group (RSC; n=26) while the other did not, i.e. the poor social capital group (PSC; n=48). This study design was a cross-sectional study.

**Results:** A greater proportion of the RSC group reported frequent enjoyment when eating meals ( $p < 0.01$ ), thought about nutritional balance ( $p < 0.001$ ), considered the nutritional balance with regard to their eating habits ( $p < 0.01$ ) and reviewed their dietary life ( $p < 0.01$ ).

**Conclusions:** Social capital has a significant effect on the association between eating habits and behavior in perimenopausal Japanese women.

### P54: Does menopause effect body awareness?

Nesrin Yagci (TR)<sup>a</sup> and Sule Simsek (TR)<sup>b</sup>

<sup>a</sup>Pamukkale University, School of Physical Therapy and Rehabilitation; <sup>b</sup>Denizli State Hospital

**Objective:** Our study was designed to determine the effects of menopause on body awareness.

**Methods:** One hundred seventeen premenopausal and one hundred three postmenopausal women was included in the study. Demographic information about menopause was obtained and The Body Awareness Questionnaire (BAQ) was applied to the participant for body awareness. Postmenopausal women were divided into two groups according to time spent in menopausal period (Group I: 1-5 years; Group II: 5 years and over).

**Results:** The average age of menopause is  $48.16 \pm 4.40$  years in women who participated in the study. The average age of premenopausal women was  $40.93 \pm 4.52$  years and postmenopausal women were  $57.20 \pm 6.65$  years. BAQ scores in premenopausal women were  $95.97 \pm 16.97$ , in postmenopausal women Group I was  $99.66 \pm 14.53$ , in postmenopausal women Group II was  $93.05 \pm 17.60$ . There was significant differences between the BAQ scores ( $F = 4.917$ ;  $p = 0.008$ ). As a result of one-way ANOVA with Bonferroni correction, statistically significant difference was found between premenopausal women and postmenopausal women within 5 years and over.

**Conclusions:** The results of our study indicated that body awareness was not affected in early years of menopause. The longer the time spent in menopausal period has been found to decrease body awareness.

### P55: Frequency of menopausal symptoms and their impact on the quality of life of women; a hospital-based story

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<sup>a</sup>Matuail Institute of Child & Mother Health; <sup>b</sup>Green Life Medical College & Hospital

**Objective:** To find out the association of menopause specific quality of life of women with both working status and duration of postmenopausal years.

**Methods:** It was a cross sectional study on 120 postmenopausal women, aged 45-65 years. Study was carried out in outpatient department of Institute of Child & Mother Health, Matuail, Dhaka, Bangladesh during the period from November, 2014 to February, 2016 (16 months). The participants had at least one surviving child, attained natural menopause at least 2 years ago and have never taken hormone replacement therapy. Menopause specific quality of life was measured using self administered standard questionnaire. Additional information on sociodemographic aspect and reproductions history of the participants were collected using a pretested questionnaire.

**Results:** Analysis of the study showed that menopause specific quality of life decrease with increase in duration of postmenopausal years. Working women had a better menopause specific quality of life than their non working counter part.

**Conclusions:** Duration of postmenopausal years had a significant association with menopause specific quality of life of women.

## Gynecological issues

### P56: Postmenopausal choriocarcinoma – it's rare but managed successfully

Sharmin Abbasi (BD), Sehereen Siddiqua (BD), Ehteshamul Haque (BD), Tahminur Rahman (BD) and Suha Jesmin (BD)

Anwer Khan Modern Medical College Hospital

**Introduction:** Choriocarcinoma is a highly malignant potential tumor which usually occurs during fertile period. It is extremely rare during menopause. It is a rare complication of molar pregnancy or normal pregnancy. Choriocarcinoma is less differentiated and more chemo sensitive. We report a case of choriocarcinoma in postmenopausal lady.

**Case:** A patient with 55 years have 4 children and menopause for 3 years came to our clinic with excessive per vaginal bleeding for 2 days. Her age of last child was 8 years. During examination patient was moderately anaemic, per abdominal and per vaginal examination had no abnormality. TVS report showed I increased endometrial thickness with polypoid like structure (43x42)mm in uterine cavity. Hb% was 7.6g/dl, chest x-ray and other investigation profiles were normal. We planned for diagnostic D&C. During D&C excessive bleeding present and vesicle like structure came out with suction and then we decide for laparotomy. And blood sent for beta-hcg. After that total abdominal hysterectomy with bilateral salphingo-oophorectomy done. Grossly uterus was bulky and the cavity filled with polyps. Histopathology report showed haemorrhagic necrosis with clusters of trophoblastic cells having bizarre nuclei among these cells having increase mitotic activity with fibrinoid material. No villus pattern and partial myometrial invasion which was suggestive of choriocarcinoma. According to FIGO it was stage 1. Beta-hcg report was 79234IU/ml. We started EMACO regimen and her Beta-hcg returned to normal in five cycles. The patient is under regular follow up and is doing well.

**Conclusions:** This case indicates that choriocarcinoma can occur in postmenopausal lady. Our patient responded to chemotherapy properly. So by proper diagnosis and management cure rate is very high.

### P57: Postmenopausal pregnancy – it's real not fun

Sharmin Abbasi (BD)<sup>a</sup>, Sehereen Siddiqua (BD)<sup>a</sup>, Mohammad Alam (BD)<sup>b</sup> and Abrar Hasan (BD)<sup>b</sup>

<sup>a</sup>Anwer Khan Modern Medical College Hospital; <sup>b</sup>BIRDEM

**Introduction:** During menopausal period pregnancy is very unusual. In a women when pregnancy occur near 50 years then the duration of climacteric is 2 years. Our patient is 55 years old and she is menopause for 3 years. We report that after 3 years of menopause patient was pregnant.

**Case report:** My patient came to my clinic with the complaints of excessive vomiting and abdominal enlargement. During examination patient was mildly anaemic and dehydrated. P/A examination showed 18 weeks pregnancy sized lump in lower abdomen. We suggested a USG of whole abdomen which showed a 22 weeks live pregnancy with good AFI. Patient wanted termination. But we counselled patient and her husband and the pregnancy was continued. She was in regular antenatal check up. She was GDM and PIH patient. After proper control of blood sugar and blood pressure pregnancy was continued up to 37 completed

weeks. Then elective c/s done and a health female baby with 2.8kg was delivered. Postnatal period was uneventful.

**Conclusions:** Though pregnancy in postmenopausal period is rare. We never exclude it when patient came with vomiting with abdominal distention in postmenopausal period.

### **P58: Malignancy risk in Brazilian women with endometrial polyps**

Cristina Benetti-Pinto (BR), Carolina Ribeiro (BR) and Daniela Yela (BR)

University of Campinas

**Objective:** To determine the prevalence of malignant lesions on endometrial polyps with resection by hysteroscopy in both pre- and postmenopausal women and risk factors for malignant transformation.

**Methods:** A retrospective study with 303 women who were submitted to hysteroscopy-guided polypectomy in 2012 at University of Campinas (UNICAMP), Brazil. Polyps were classified as either benign or malignant. The variables analyzed were age, parity, body mass index, symptoms (asymptomatic, bleeding), associated pathologies (arterial hypertension, diabetes mellitus, breast cancer), endometrial line and size of the polyp. Frequency, medians and standard deviation of the study variables were obtained and risk factors for malignant transformation were submitted to multivariate analysis with odds ratio adjusted to a 95% confidence interval.

**Results:** Women had a median of  $58 \pm 11$  years, were  $9.6 \pm 8.5$  years since menopause. Histopathological analyses showed 6% of malignant and pre-malignant lesions. Risk factors associated with malignancy were age over 60 years (OR: 2.2, IC 95% 1.05-4.71) and postmenopausal bleeding (OR: 4.0, IC 95% 1.92-8.44). Multiparity appeared as a protective factor (OR: 0.3, IC 95% 0.16-0.70).

**Conclusions:** The malignancy transformation in endometrial polyps rate was low. Risk factors associated were postmenopausal bleeding and advanced age. Multiparity was the protective factor found.

### **P59: Development and psychometric properties of a measure of catheter burden with bladder drainage after pelvic reconstructive surgery**

Janet Carpenter (US), Michael Heit (US) and Kevin Rand (US)

Indiana University

**Context:** Catheter burden after female pelvic reconstructive surgery is an important patient-reported quality of life outcome. However, existing tools focus on long-term catheter users rather than short-term postoperative patients.

**Objective:** To evaluate the psychometric properties of a modified version of the Intermittent Self-Catheterization Questionnaire (ISC-Q) in female postoperative pelvic reconstructive patients.

**Methods:** After experts modified the ISC-Q items based on their knowledge of women's experiences in clinical practice, women completed the modified scale and other measures as part of a larger parent study designed to assess health-related quality of life following pelvic reconstructive surgery requiring bladder drainage.

**Patients:** 178 women (108 with transurethral and 70 with suprapubic catheters), mean age of 60 years old, scheduled for

laparoscopic sacrocolpopexy and mid-urethral sling without concurrent hysterectomy.

**Interventions:** Not applicable.

**Main outcome measures:** ISC-Q, a single-item satisfaction scale.

**Results:** During psychometric testing, the modified ISC-Q was reduced to six items encompassing two factors: a 3-item Difficulty of Use factor and a 3-item Embarrassment factor. The new scale was named the Short-Term Catheter Burden Questionnaire (STCBQ). The two-factor model was robust in both subsamples. Due to a lack of scalar invariance, scores within but not between subsamples can be meaningfully compared. Correlations among STCBQ total scores, subscores, and satisfaction indicated good construct validity. Correlations with patient demographics provided further information about the scale.

**Conclusions:** The STCBQ is a short, efficient assessment of short-term catheter burden following female pelvic reconstructive surgery. The scale can be used as an important patient reported outcome measure in clinical practice and research.

### **P60: Comparison of pregnancy exclusion criteria between women in their mid and late reproductive years using the Pregnancy Reasonably Excluded Guide (PREG) prior to intrauterine procedures**

Petra Casey (US), Margaret Long (US) and Stephanie Faubion (US)

Mayo Clinic

**Objective:** To compare criteria for pregnancy exclusion between women in their mid and late reproductive years using a history based tool.

**Methods and patients:** A tool for excluding pregnancy based on the WHO criteria was given at Mayo Clinic to women ages 18-55 years upon presentation for intrauterine procedures. Age and answer to PREG status determination questions including: currently pregnant, negative pregnancy test today, normal menses today, less than 7 days or no coitus since early pregnancy loss, delivery within 4 weeks, no coitus since last menses, consistent use of hormonal contraception, tubal ligation, partner with vasectomy, hysterectomy, menopause, no coitus since delivery or none of the above criteria were abstracted. Chi-square analysis was used for comparison.

**Results and outcomes:** Of 98 women age 45-55 and 232 women age 25-35 included, only 13.3% and 19.4% women respectively required pregnancy testing following the PREG. In women age 45 to 55, the most common pregnancy exclusion criteria were: bilateral tubal ligation (20.4%), vasectomy (14.3%) and no coitus since last menses (13.3%). In women age 25-35 the most common pregnancy exclusion criteria were: no coitus since delivery (21.5%), none of the stated criteria (19.4%) and hormonal contraception (16.8%). Pregnancy was more commonly excluded in the older age group based on BTL ( $p = 0.002$ ), vasectomy ( $p < 0.001$ ), hysterectomy ( $p < 0.001$ ) and menopause ( $p < 0.001$ ) whereas in the younger group, pregnancy was more likely excluded based on no coitus since delivery ( $p < 0.001$ ) and none of the above criteria ( $p = 0.004$ ).

**Conclusions:** Benefits of this primarily history based algorithm for reliable pregnancy exclusion prior to intrauterine procedures include resource cost efficiency and elimination of unnecessary procedural delays associated with point-of-care pregnancy testing.

## P61: Fibroma resection by hysteroscopy with or without treatment before

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Anne Dima (RO)<sup>b</sup>, Cristian Poalelungi (RO)<sup>a</sup>,  
Nicolae Bacalbasa (RO)<sup>a</sup> and Cristian Posea (RO)<sup>b</sup>

<sup>a</sup>Carol Davila University of Medicine and Pharmacy; <sup>b</sup>Dr. I. Cantacuzino Hospital

**Objective:** The aim of this study was to compare the efficacy of ulipristal acetate or GnRH agonist in preparation of the submucosal fibroma for resection by hysteroscopy

**Methods:** The study included 93 premenopausal women treated and followed in the gynecology department of the "Dr. I. Cantacuzino" Hospital, for submucosal fibroma. Inclusion criteria were fibroma visualization at vaginal or abdominal ultrasound with a diagnostic of fibroma tangent or with protrusion in the uterine cavity. The resection was done after no treatment, treatment with ulipristal acetate after 3 months of treatment or GnRH agonist (triptoreline 3,75/month) for 2-3 months of treatment.

**Results:** The main reasons for seeking treatment were uterine bleeding, subfertility, after spontaneous abortion or abortion on demand. The submucosal fibroma were between 2,5 cm and 7 cm. All women undergo biopsy with Pipelle for endometrial safety before treatment. The women were advised for no treatment before if the fibroma were under 2.5-3 cm, or treatment ulipristal acetate or triptoreline if the fibroma were larger than 3 cm or there were multiple submucosal fibroma. During the treatment and evaluation period before, during and after hysteroscopy there were 16 cases loss of follow up or who interrupted treatment for different reasons. 77 patients took part in one of the three groups with no treatment before resection, treatment with ulipristal acetate 3 or triptoreline 2-3 month before hysteroscopy.

**Conclusions:** Success of the hysteroscopic resection of the submucosal fibroma depends of the dimensions, location, protrusion in the cavity and consistency. Treatment before resection with diminishing the dimensions and the vascularization is helpful. Ultrasound is helpful for fibroma visualization and follow up. MRI is useful for multiple fibroma visualization and the vascularization assessment.

## P62: Does age at start of treatment for vaginal atrophy predict response to vaginal estrogen therapy?

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**Objective:** To investigate if age at start of treatment influences response in objective (vaginal maturation index, VMI) and subjective parameters (most bothersome symptom, MBS) of vaginal atrophy (VA) in postmenopausal women receiving ultra-low-dose 10 µg estradiol (E2) vaginal tablets.

**Methods:** Postmenopausal women in a double-blind, randomized, multicenter trial (NCT00108849)<sup>1</sup>, aged ≥45 years and treated with 10 µg E2 for 52 weeks (LOCF), were grouped by age: <60, ≥60 years; symptom intensity was graded on a 4-point scale:

none=0, severe=3. ANCOVA was used to evaluate mean change differences in VMI and MBS from baseline to week 52 between groups.

**Results:** 198 of 205 subjects (<60, n = 143; ≥60, n = 55) had baseline VMI data. There was a lower proportion of parabasal (PB), but higher proportion of intermediate (IM), cells in younger than older women (38% vs 52%; 59% vs 45%, respectively). The proportion of superficial cells (3%) was equal in both groups. After 52 weeks, women <60 years had a lower proportion of PB cells (estimated effect [EE], -3.7; P = 0.0003), and higher proportion of IM cells ([EE], 5.8; P = 0.0002), than those ≥60 years. Overall, VMI across all cell types improved in both groups over time. At baseline, the most reported MBS in younger and older women was dyspareunia (50.7% vs 57.1%), followed by vaginal dryness (30.4% vs 23.2%). Mean [SD] baseline MBS intensity scores in younger and older women (2.35 [0.64] vs 2.40 [0.56]) were comparable, with similar decreases (-1.21 [0.92] vs -1.25 [0.66]) after 52 weeks.

**Conclusions:** 10 µg vaginal E2 therapy led to significant improvement in VMI and MBS in younger (<60 years) and older (≥60 years) postmenopausal women. Reduced responsiveness in PB and IM cell layers in the older group could have clinical significance and supports international guidelines to start VA treatment early.

## Reference

1. Simon *et al. Obstet Gynecol* 2008;12.

## P63: Er:YAG laser efficacy in stress urinary incontinence (SUI) treatment. Fact or fake

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**Context:** Conventional surgical procedures are more likely implemented to cure SUI but are associated with more adverse events. Less invasive operative mesh techniques are relatively effective, but are not immune to complications as well. Initial treatment for SUI should include nonsurgical therapies. Er:YAG laser thermal energy is efficient tool to alleviate/reduce symptoms.

**Objective:** Postmenopausal patient often suffer from SUI. In those patients risks of anesthesia and surgery are high. A minimally invasive laser treatment may play a serious role in SUI and pelvic floor dysfunction treatment as it is compliant, less invasive and low-cost.

**Methods, patients, intervention:** A prospective cohort, single-center study at the Ob/Gyn Clinic, Zagreb, Croatia recruited a consecutive sample of 73 female patients suffering from stress urinary incontinence. The procedure was performed with a 2940 mm Er:YAG laser (XS Dynamis, Fotona, Slovenia). No anesthesia was used before or during the session. The degree of incontinence and its impact on quality of life were assessed with the ICIQ-UI SF. Patients characteristics were analyzed with regard to age, parity, birth weight, BMI, percentage of menopausal patients, perineometry results, residual urine and PISQ-12 score.

**Results:** ICIQ-UI-SF score was reduced to a median of 46% (95% confidence interval 33–67%; p < 0.001). The reduction was significantly higher in women with normal body mass index (67%) than in overweight women (25%), as well as in women younger than 39 years (100%) compared with those older than 60 years (8%) (p < 0.001).

**Conclusions:** The first assessment of efficacy and safety of the Er:YAG laser in the treatment of SUI has shown relevant improvement throughout a short-term period, with minimal adverse events of a transient nature. The improvement was more effective in younger and normal weight patients.

### **P65: Role of transvaginal sonography in evaluation of postmenopausal bleeding**

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Government T D Medical College, Alappuzha, Kerala, India

**Context:** 3-7% of menopausal women have postmenopausal bleeding (PMB) requiring evaluation to exclude malignant/potentially malignant lesions. Standard recommendation is the use of non-invasive transvaginal sonography (TVS) to assess the endometrial thickness with cut-off of 5 mm beyond which invasive sampling techniques are done.

**Objective:** To evaluate the role of TVS in postmenopausal bleeding and correlate any abnormality in it with the histopathological pattern obtained by endometrial sampling taken as gold standard.

**Methods:** On 200 patients between 50-70 yrs with PMB, TVS was done. The characteristics studied were endometrial thickness(ET), quality of endometrium whether echogenic or triple line, regularity of endometrium, presence of fluid in the endometrial cavity, polyp in uterine cavity and distinct demarcation of endo-myometrial junction. Then for  $ET \geq 5$  mm endometrial sampling was done.

**Outcome measures:** To study 1)the efficacy of ET of 7 mm as a cut-off in PMB beyond which invasive sampling techniques need be done. 2)Whether other USG findings has an added benefit when used with ET to rule out endometrial pathology.

**Results:** The sensitivity and specificity of TVS for suspecting endometrial pathology at  $ET < 7$  mm alone is 77.78% and 48.19% respectively but when other USG findings are taken into consideration along with ET, then sensitivity increases to 100%. In comparison, the sensitivity and specificity of  $ET < 5$  mm as cut-off is 88.89% and 13.25% respectively.

**Conclusions:** ET 5 mm is taken as standard for sampling endometrium in PMB. Besides ET, if USG findings like quality of endometrium, regularity of endometrium, presence of fluid in the endometrial cavity, polyp in uterine cavity and distinct demarcation of endo-myometrial junction are considered to decide on endometrial sampling, women with  $ET < 7$  mm need not undergo sampling after the first episode of bleeding.

### **P66: Initial symptoms of pelvic organ prolapse during menopause**

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Saint Joseph University, Obstetrics and Gynecology department

**Objective:** To assess the characteristics of the first symptoms of prolapse in Lebanese menopausal women.

**Methods:** A case series of menopausal Lebanese patients seeking advice for vaginal prolapse during a 3 years period. Occasional prolapsed discovered by the physician during check up were not

included. We studied sociodemographic characteristics, age, parity, initial symptoms, time interval to consultation, type and severity of the prolapsed.

**Results:** 62 patients were included in the study. Median age is 61 years [53–70]. The majority of the population had a high educational level (73%) and a normal BMI (mean of 24.2 [21.2–30.1]). Parity was 0 (5%), less than two (39%) and more than two (56%). Menopause occurred since a mean interval of 9 years [7–12]. Initial symptoms were: vaginal bulging (53%), local soreness or pelvic pain (24%), recurrent urinary infection (11%), recent urinary incontinence (11%) and miscellaneous (1%). The time interval for consultation is three months, with the lowest to vaginal bulging and the most for recurrent infection. Patients reported what they thought the cause for the symptoms as: physical effort (55%), upper respiratory symptoms with coughing (13%), constipation (13%), diet (9%), insufficient fluid intake (9%) and miscellaneous (1%). Among these 62 patients, 52 (84%) considered these symptoms as a major complaint.

**Conclusions:** Initial symptoms of vaginal prolapse are variable and are mainly represented by vaginal bulging few months after physical effort. Physical examination and counseling during prior regular check-ups may have a role in decreasing the importance of prolapse.

### **P67: Characteristics of ovarian fibrothecoma during menopause**

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<sup>a</sup>Saint Joseph University; <sup>b</sup>Saint Joseph University, Obstetrics and Gynecology

**Introduction:** Fibrothecomas are relatively rare (3-4%); they are usually misdiagnosed for uterine fibromas or ovarian neoplasms especially when associated with ascites.

**Methods:** In a 5 years retrospective study we reviewed all cases of histologically proven ovarian fibrothecomas in Lebanese menopausal women. We assessed the characteristics of this pathology and the correlation between clinical presentation, imaging modalities and pathology.

**Results:** 18 patients were included in this study. Mean age is 59 y [50 to 73]. Initial presentation included abdominal pain in 6 cases (33%), bloating in 5 cases (28%), vaginal bleeding in 3 cases (17%) and miscellaneous in 4 cases (22%). Imaging modalities varied among patients, some relying only on ultrasound (28%), while in 17% ultrasound was completed by MRI prior to surgery; 2 cases had a CT-Scan, with in one case an additional MRI. Concordance of the results between the ultrasound and the MRI was 100% in patients having both imaging modalities. Mean size of the tumor was 7.7 cm and in 22% the mass was associated with ascites and that was mainly in case of a size greater than 9 cm. No pleural effusion was noted. The mass was unilateral in 94% (n= 17), bilateral (n= 1) with a right side in 61%. The mass was associated to uterine fibromas in 6 cases, other benign ovarian tumors in 6 cases (mainly cystadenomas), ovarian carcinoma (one case) and endometrial carcinoma (one case). A preoperative diagnosis of uterine fibroma was made in 3 cases, while the diagnosis of a benign ovarian tumor was made in 10 cases (55%) and the specific diagnosis of fibrothecoma was made preoperatively in 22% (4 cases). Pathology results showed a fibrothecoma (n= 16), ovarian fibroma (n= 1) and thecoma (n= 1). CA125 was used in only 3 cases with one elevated value of 60.

**Conclusions:** Fibrothecomas have various presentations in the menopause.

### P68: Perimenopausal endometriosis management with dienogest

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Fortis Escorts Hospital

**Objective:** To evaluate the efficacy and safety of Dienogest treatment in endometriosis complicated with myoma or adenomyosis in symptomatic perimenopausal women.

**Methods:** This single centre prospective study included 20 perimenopausal symptomatic women presenting with dysmenorrhoea, chronic pain, dyspareunia, pain during defecation, menorrhagia and having regular menstrual cycles. Women included had not received any treatment for endometriosis or myoma at least 3 months prior to enrolment. Patients with ovarian, pelvic inflammatory or any other endocrine disease were excluded. Patients received continuous oral therapy of Dienogest (2 mg per day) for 6 months, from day 5 of menstrual cycle and underwent physical examination every 6 weeks. Intensity of pain was monitored using VAS.Hb, CA125 and serum estradiol levels and MRI/USG findings were documented at baseline, 6 months and at follow up of 1 year.

**Results:** Out of 20 endometriosis patients (40-49 years), 11 had coexistent myoma and adenomyosis; 8 intramural (diameter <3 cm), 3 subserosal and 9 adenomyosis. 17 patients continued Dienogest for 24 weeks. Follow up reported significantly reduced pelvic pain as well as CA-125 and estradiol (>50 pg/mL) levels, while in 7 patients went into menopausal phase. Due to worsening of anemia with metrorrhagia, 3 patients discontinued the therapy. 3 women started having hot flashes but did not discontinue the treatment. Dienogest therapy remarkably reduced myoma/adenomyosis volume (upto 67%) from baseline and also intensity of menstrual bleeding. Although the follow up period after end of treatment was too short (6 months) to consider recurrence, but persistent relief in pain and menorrhagia was seen.

**Conclusions:** Use of newer selective progestin Dienogest could be an effective and well-tolerated therapy for long-term management of perimenopausal women leading to natural menopause.

### P69: Correlation of histopathological examination by Pipelle endometrial sampling with endometrial thickness in cases of abnormal uterine bleeding in perimenopausal age group

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Vijayarani (IN) and Kalpana (IN)  
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**Background:** Abnormal uterine bleeding is one of the frequent complaints in the perimenopausal age group who attends the gynaecological OPD. This warrants a thorough evaluation by clinical, ultrasound and histopathology to rule out endometrial hyperplasia and malignancy.

**Aim:** To study the correlation of endometrial thickness detected by transvaginal ultrasound and histopathological evaluation by Pipelle aspiration.

**Materials and methods:** A prospective observational study was conducted in the department of OBG, KMCT Medical college, Kozhikode, Kerala, India for a period of eight months from June 2015 to February 2016. 48 patients were studied and they were

evaluated clinically, by transvaginal ultrasound and histopathologically by Pipelle aspiration.

**Results:** Out of the 48 patients studied, 21 cases (43.7%) belonged to the age group of 40-45 years. 43 case (89.6%) presented with abnormal uterine bleeding. 7 cases were postmenopausal (14.6%). Uterus was enlarged with fibroids in 16 cases (33.3%). According to the thickness of endometrium, this was <10 mm in 26 cases (51.2%) and 10-20 mm in 21 cases (43.8%) and in 1 case (2.1%) showed fluid collection. The histopathology report showed proliferative endometrium in 12 cases (25%), secretory endometrium in 8 cases (16.7%), simple hyperplasia without atypia in 5 cases (10.4%), simple hyperplasia with atypia in 1 case (2.1%), adenocarcinoma in 1 case (2.1%), and tuberculosis in 1 case (2.1%). Surgery was required in 15 cases (31.3%).

**Conclusions:** Pipelle aspiration biopsy is a safer and quick method in diagnosing endometrial pathology and have a good correlation with the endometrial thickness in cases of AUB in perimenopausal women.

### P70: Comparative effects of drospirenone and tibolone on the postmenopausal endometrium

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**Objective:** The aim of this study was to evaluate the comparative effects of drospirenone with 17 $\beta$ -estradiol and tibolone on the histology, immunohistochemistry and expression of estrogen and progesterone receptors and of Bcl-2 protein, in endometrium of postmenopausal women.

**Methods:** Sixty postmenopausal women were divided into three groups of 20 women each as follows: Group 1 (Control) without hormone replacement therapy (HRT); Group 2 (Drospirenone) evaluating oral hormone replacement treatment combining 2 mg/day of drospirenone with 1 mg/day of 17 $\beta$ -estradiol; and Group 3 (Tibolone) evaluating 1.25 mg/day of oral tibolone. The treatment was administered for a 24-week period. The effect on the endometrium was assessed by histology and the apoptosis marker Bcl-2. The immunexpression of estrogen (ER) and progesterone (PR) receptors were also measured.

**Results:** Endometrial histology was atrophic in most biopsies. The drospirenone/estradiol group showed higher expression of PR and Bcl-2 protein in stroma compared to the tibolone group, but the Bcl-2 protein was more immunoreactive in glandular epithelium in the tibolone than in the drospirenone/estradiol group. Compared to controls, drospirenone/estradiol and tibolone users showed higher immunexpression of ER, PR and Bcl-2 protein in both glandular epithelium and endometrial stroma.

**Conclusions:** A twenty-four week course of drospirenone with 17 $\beta$ -estradiol and tibolone resulted in low proliferation and was shown to lead to atrophic endometrium. Drospirenone seems to have favorable effects on the endometrium of postmenopausal women due to its higher immunexpression of PR and Bcl-2 protein in endometrial stroma than tibolone, thereby creating a balance between pro-apoptotic and anti-apoptotic actions.

### **P71: Dyspareunia incidence in Italian women with vulvo-vaginal atrophy**

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**Context:** The decline on oestrogen levels in menopause can negatively impact the quality of life and cause distress. The hormone changes include hot flashes, night sweats, sleep quality changes, fatigue, mood changes, infertility, decreased desire and negative self-image and diminishing sexual function, including vaginal atrophy that entails decreased arousal, dryness and dyspareunia.

**Objective:** This work aims to investigate the dyspareunia incidence in Italian women with vulvo-vaginal atrophy (VVA) and its impact on quality of life.

**Materials and methods:** 300 healthy postmenopausal outpatients (mean age  $\pm$  SD: 63  $\pm$  5 years) classified on the presence of VVA were enrolled. They filled a questionnaire with different items related to sexual desire, vaginal dryness and dyspareunia, poor arousal and orgasm and impaired sexual satisfaction. Smoke, life and food habits were recorded. Anthropometric parameters and biochemical parameters (sex hormones, lipids, glucose homeostasis, kidney function and inflammatory biomarkers) were measured.

**Results:** 85% of total women reported negative consequences of VVA on sex life, 73% reported dyspareunia and 61% indicated VVA symptoms detracted enjoyment of sex.

**Conclusions:** The majority of postmenopausal women with VVA harbour dyspareunia. Therefore the treatment of symptomatic VVA related to sexual activity has to be approached in a stepwise fashion based on the severity of symptoms in order to improve VVA and thereby the quality of sexual life including dyspareunia.

### **P72: Rare case of vaginal bleeding with a normal vault following surgical menopause**

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Nice Hospital for Women, Newborn and Children

Bleeding after hysterectomy is a rare event, there can be varied causes like atrophic vaginitis, stump cancer, infiltrating ovarian tumours, endometriosis of vault. This is a rare case of continuous vaginal bleeding with no lesion in the vault.

A 34yr P2L2 presented with continuous vaginal bleeding for 1 1/2yr following total abdominal hysterectomy and right salpingo-oophorectomy in 2012. Diagnostic laparoscopy in 2013 elsewhere, has revealed dense adhesions between intestines and vault. A cyst of 4  $\times$  3 cms with serous fluid was drained out and the vault was sutured pervaginally. External genitalia were normal, speculum examination revealed bleeding from the vault, no granulation tissue. Nontender mass of 4x4 cms was felt left to the vault. Pap smear, CA125 were normal. High vaginal swab revealed Staph. Aureus. Ultrasound shows left haemorrhagic ovarian cyst of 51  $\times$  40mm with internal ecogenic septae. Appropriate antibiotics and oral contraceptives were given. Patient returns with persistent vaginal bleeding. Laparotomy on March 2014 revealed a 4  $\times$  3cm chocolate cyst in the left adnexal region, adhesions were present at the vault. There was a zigzag tract in the vault which is covered in adhesions. Probing through the vaginal vault revealed the tract with a flap of tissue covering. Vault is closed following left ovariectomy and resection of tract. In

view of young age and possibility for recurrences tibolone was given. Patient is asymptomatic till today.

**Discussion:** Nonclosure of the peritoneum at the conclusion of gynaecological procedure is postulated to be the reason. Failure to diagnose endometriosis, nonremoval of the cyst at the time of laparoscopy and bleeding from chocolate cyst trapping inside the tract which is covered by flap of tissue led to continuous bleeding through vagina. Local wide excision of tract ensures complete treatment.

### **P73: Anorectal symptoms associated static pelvic disorders in women in menopause**

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**Objective:** To present the incidence and therapeutic conduct in case of anorectal symptoms associated with uterovaginal prolapse.

**Methods:** There were included in the study 254 cases with various forms of utero-vaginal prolapse, 31.9% of them being relapses after previous surgical treatment. All patients were evaluated pre- and postoperative through questionnaires in order to identify the associated functional disorders. Of this group were selected the patients with associated anorectal symptoms, anal urgency and fecal incontinence.

**Results:** The anorectal symptoms occurred in 6.7% of cases. Fecal urgency accounted for 75% of cases and was associated with uterovaginal grade I-II prolapse in a rate of 68.3%. Anal incontinence was associated in every case with grade II-III perineal tears. Symptoms of anal urgency resolved by treatment of the medium and posterior compartment defects. For anal incontinence was practiced anal sphincter plasty by suturing the restant sphincter structures or synthetic graft plasty.

**Conclusions:** Anal incontinence is not a common symptom in the pathology of static pelvic disorders, but it is extremely disabling for the patient. Therefore the correct identification through a medical history directed by questionnaires allows the association of a sphincter plasty procedure in the surgical treatment of associated pelvic static disorders.

### **P74: Hysteroscopy in abnormal uterine bleeding**

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Sun Medical Centre

**Introduction:** 25 women from the age group 36 years to 52 years suffering from abnormal uterine bleeding who were evaluated and treated with hysteroscopy by a single operator over 4 years time, from January 2012 to December 2015 were prospectively studied.

**Aim:** To create an awareness of the type of patients who can benefit from hysteroscopic evaluation and treatment, to know the after effects of such surgery and to prognosticate the outcome of hysteroscopy.

**Methods:** 25 patients had undergone hysteroscopic evaluation and treatment during the study period of 4 years. They had been initially evaluated by ultrasonography and were posted for hysteroscopy based on positive findings of ultrasonography. Out of 26, 18 had submucous fibroids and came with regular periods and menorrhagia. 4 had irregular light periods and had non myomatous endometrial polyps. 2 patients came with continuous spotting, one came with postmenopausal bleeding per vagina. After hysteroscopic myomectomy, 10 patients had continuous watery discharge that lasted almost a week. 7 patients with fibroids more than 2 cm had menorrhagia in the immediate cycle following the procedure with dysmenorrhoea. It subsided with the subsequent menstruation. Menorrhagia was accompanied by dysmenorrhoea in 2 patients. There was uterine perforation in one patient, and in one patient, where the histopathology came as adenomyosis, there was recurrence in 4 months time.

**Conclusions:** Hysteroscopic intervention should be offered to patients with abnormal uterine bleeding where ultrasonography shows thickened or irregular endometrium or submucous fibroid is diagnosed. Possible after effects should be discussed with the patient in case of larger submucous fibroids so that they are not alarmed that they did not get a cure after the procedure, in case they have menorrhagia in the subsequent cycle.

### **P75: Secondary uterine inversion with hypovolemic shock caused by uterine bleeding of huge pedunculated submucous myoma: A case report with literature review**

Yong Jung Song (KR), Hyun Sil Yun (KR), Hwi Gon Kim (KR), Ook Hwan Choi (KR) and Yong Jin Na (KR)  
Pusan National University Yangsan Hospital

**Objective:** Submucous myoma is a benign pathology on women in reproductive age causing abnormal uterine bleeding.

**Methods:** A 42-year-old woman visited emergency department with massive vaginal bleeding and drowsy mental status. There was protruding solid necrotic mass out of the vagina.

**Results:** Hypovolemic shock with cardiac arrest was noted. After cardiopulmonary resuscitation, emergent laparotomy was performed with massive volume replacement. Uterine inversion was discovered and restored by manual reduction. Complete resection of myoma stalk through uterine incision was performed. Bilateral internal iliac artery was ligated additionally. After postoperative care at intensive care unit and general ward, she was discharged without any surgical and medical complication.

**Conclusions:** We present here an unusual case of secondary uterine inversion with hypovolemic shock caused by uterine bleeding of huge pedunculated submucous myoma, and a brief review of the literature.

### **P76: Septic shock complicated by intrauterine bleeding and necrosis of adenomyosis: A case report with literature review**

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**Objective:** Adenomyosis is common benign pathology on women in reproductive age. Dysmenorrhoea, heavy menstrual bleeding

and chronic pelvic pain are typical symptoms. It is very rare situation for adenomyosis to be complicated by sepsis or septic shock.

**Methods:** A 42-year-old woman complaining of severe pelvic pain, dyspnea and fever visited emergency department. Pelvic computed tomography showed adenomyosis. Her condition was rapidly aggravated to septic shock in spite of antibiotics treatment.

**Results:** There was moderate amount of pus in pelvic cavity. Total abdominal hysterectomy with both salpingectomy were done emergently. Pathology result was consistent with adenomyosis.

**Conclusions:** After postoperative care at intensive care unit and general ward, she was discharged without any surgical and medical complication. We present here septic shock complicated by intrauterine bleeding and necrosis of adenomyosis and a brief review of the literature.

### **P77: Vaginal Health: Insights, Views & Attitudes (VIVA) – a survey in Latin America**

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**Objective:** The previously reported Vaginal Health: Insights, Views & Attitudes (VIVA) survey, involving 3520 postmenopausal women from seven countries in Europe and North America, showed that respondents generally had little knowledge of vaginal atrophy<sup>1</sup>. Results indicated that healthcare practitioners should proactively initiate discussions with patients, to improve understanding of the condition and raise awareness of treatment options. In addition, it was evident that country-specific approaches may be required. In line with this, and to evaluate women's knowledge of postmenopausal vaginal atrophy in Latin America, where women are often concerned about the consequences menopause can have on their sexual lives<sup>2</sup>, the VIVA survey is being performed in five countries in this region.

**Methods:** A sample of 2500 women resident in Brazil, Mexico, Argentina, Chile and Colombia (500 per country) who are aged 55–65 years, have reached the menopause and have ceased menstruating for  $\geq 12$  months, will complete a structured online questionnaire translated from the questionnaire used in the previous VIVA survey<sup>1</sup>. Data will be summarized descriptively.

**Results:** The primary aim of the study will be to understand the extent to which women report experiencing symptoms of postmenopausal vaginal atrophy. Moreover, their perceptions and knowledge of the condition, including the information sources and treatment options they have used or considered will be also explored.

**Conclusions:** Our data will provide evidence relating to women's knowledge of postmenopausal vaginal atrophy in Latin America. This may help healthcare providers to better understand vaginal atrophy from the patient perspective, thereby assisting management practice, with potential improvements in outcomes.

### **References**

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2. Sturdee DW, et al. *Climacteric* 2010;13:509–22

### **P78: Insulin growth factor (IGF) 1, IGF-binding proteins and ovarian cancer risk: A systematic review and meta-analysis**

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**Objective:** We performed a systematic review and meta-analysis to evaluate the association between insulin resistance and ovarian cancer.

**Methods:** Searches were carried out in 5 database engines for studies evaluating insulin resistance markers (insulin, C-peptide, homeostasis model assessment index of insulin resistance [HOMA-IR], insulin growth factor [IGF] and IGF-binding proteins [IGFBPs]) and ovarian cancer risk. Selection of studies, extraction of data and Newcastle-Ottawa risk of bias assessment was done independently by three researchers. The effect of insulin resistance markers on ovarian cancer was quantified with the standardized mean difference (SMD) or mean difference (MD) and their 95% CIs.

**Results:** Fourteen case-control studies (6 nested) satisfied our inclusion criteria (n=7992). In 11 studies, ovarian cancer was associated with lower IGF-1 levels in comparison with cancer negative controls (SMD -0.37 ng/mL, 95% CI -0.59 to -0.14; p=0.001). Likewise, in 7 studies ovarian cancer was associated with lower IGFBP-3 levels (MD -418.4 ng/mL, 95% CI -539.5 to -297.3; p<0.00001). However, ovarian cancer was associated with higher levels of IGFBP-2 and IGFBP-1 (MD 527.3 ng/mL, 95% CI 473.6 to 581.0; p<0.00001 [3 studies], and MD 3.47 ng/mL, 95% CI 1.42 to 5.52; p=0.0009 [2 studies], respectively). There was scarce information on the effect of insulin levels, c-peptide, or HOMA-IR.

**Conclusions:** Current evidence is suggestive of lower risk of ovarian cancer in women with higher IGF-1 and IGFBP-3 levels.

### **P79: Prevalence of Genitourinary Syndrome of Menopause (GSM) and associated symptoms and signs in a cohort of postmenopausal women in Spain. The GENISSE study**

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**Objective:** The Genitourinary Syndrome of Menopause (GSM) is a very prevalent condition characterized by the presence of urological and vulvovaginal symptoms and signs. It occurs as a consequence of the physiological decline in estrogen production that happens in the menopause. The aim of the Genisse Study was to analyze the prevalence of the GSM and its most relevant

symptoms and signs in postmenopausal women in Spain and to investigate its association with other urogynecological disorders. **Methods:** A multi-centric, transversal, descriptive and observational study was designed. Women consulting for any reason to the gynecologist were in the context of a single visit. Gynecological history, treatments and local symptoms and signs were investigated. GSM was defined as a collection of symptoms and signs that must be bothersome and not accounted for by another diagnosis.

**Results:** 430 women were included (mean age 58.1 years, 9.1 years since last period, 72% sexually active). The prevalence of GSM was 70%. Most prevalent symptoms were: vaginal dryness (93%) and, in sexually active women, lack of lubrication (90%) and dyspareunia (82%), moderate to severe in 68, 67 and 63% of them respectively. Itching (63%), dysuria (28%) and urgency (27%) were also reported. Most prevalent signs were: decreased moisture (93.7%), loss of vaginal rugae (78.4%) and vaginal pallor (74.7%) moderate to severe in 59, 53 and 41% respectively. An association of GSM with urinary incontinence (p<0.01) and prolapse (p=0.02) was found.

**Conclusions:** The GSM is a very prevalent pathology in postmenopausal women in Spain, frequently underreported and coincident with other urogenital pathologies. Genital symptoms are more common than urinary symptoms, being vaginal dryness and lack of lubrication the most frequently described.

### **P80: Impact of vaginal symptoms associated with Genitourinary Syndrome of Menopause (GMS) on women's quality of life. The GENISSE Study**

Mariona Rius (ES)<sup>a</sup>, Luis San Frutos (ES)<sup>b</sup>, Juan Luis Delgado (ES)<sup>c</sup>, Concepción Nieto (ES)<sup>d</sup>, Javier Suárez (ES)<sup>d</sup>, Ibone Huerta (ES)<sup>d</sup> and Syra Velasco (ES)<sup>d</sup>

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**Objective:** GSM is defined as a number of genital and urogynecological symptoms and signs related to the estrogen decline during the menopause, which must be bothersome and should not be better accounted for by another diagnosis. The aim of this study was to evaluate the impact of vaginal symptoms associated with GSM on functioning and well-being in postmenopausal women.

**Methods:** A transversal, descriptive, observational study was designed to analyze the prevalence of the GSM in postmenopausal women in Spain (The Genisse Study). 423 postmenopausal women that presented at least one vaginal symptom were asked to complete the Day-to-Day Impact of Vaginal Aging Questionnaire (DIVA). It consists of 23 items in 4 multi-item domain scales: activities of daily living, emotional well-being, sexual functioning (short and long versions), and self-concept and body image. Items were scored from 0 (not at all) to 4 (extremely) and the mean score on each domain was calculated. An association of the scores with GSM was analyzed.

**Results:** Vaginal symptoms hardly impacted on activities of daily living nor emotional well-being (mean score = 0.7 for both domains); they impacted a bit on women's self-concept and body image (mean score = 1.4). Vaginal symptoms impacted moderately on sexual functioning (mean scores 1.7 -short version- and 1.8 -long version-). When comparing DIVA Questionnaire answers between women with and without GSM, significant

differences were found, being remarkable the impact of vaginal symptoms on sexual functioning ( $p < 0.0001$ ).

**Conclusions:** Vaginal aging symptoms impact the most on sexual functioning and self-concept and body image of postmenopausal women. Women with GMS have a greater impact. Therefore, it is advisable to treat GMS in order to improve postmenopausal women's well-being and quality of life.

### **P81: Erbium YAG laser treatment of pelvic organ prolapses – 3 years follow-up**

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**Objective:** In this paper we are reporting about assessment of efficacy and safety of new ErYAG laser therapy used for treatment of pelvic organ prolapses.

**Methods:** This was a prospective, single center pilot study, included female patients older than 18 years and having cystoceles of grades II–IV were included. Prior to treatment all patients were clinically inspected, and classified by grades using Baden-Walker scale. Patients received two to seven laser treatment sessions with intervals in between the sessions of 2 months. At each visit photographs of prolapses under straining were obtained and graded by two physicians. Treatment discomfort was measured with 10 grade VAS scale and at every follow-up patients were interviewed about their satisfaction with the therapy. Follow-ups were performed at 2, 6, 12, 24 and 36 months after the first laser session.

**Results:** In period of past four years 83 patients having cystoceles of grades II–IV were treated with erbium laser, however 67 of them were followed-up for longer period and included in this study. Patient's average age was 54.9 yrs, parous status 2.2 and BMI of 25.5. The average POP grade before the treatment was  $2.36 \pm 0.62$  and was significantly ( $p < 0.001$ ) reduced already after the first session (to  $1.5 \pm 0.79$ ). The POP continued to improve with sessions, getting reduced to  $0.94 \pm 0.78$  after 6 months and  $0.86 \pm 0.78$  after 12 months. Average grade at 36 months was  $0.86 \pm 0.78$ . Treatment discomfort was very low (average score of 0.4) and patient satisfaction high (median level of 4 on scale 1-5). There were no adverse effects of this treatment reported.

**Conclusions:** Erbium laser treatment for higher-grade cystoceles demonstrated good efficacy in the improvement of cystoceles and minimal patient discomfort during the treatment, with no adverse effects.

### **P82: Molecular characterization of the endometrial actions of ulipristal acetate**

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MCGEL - University of Pisa

**Context:** Ulipristal acetate (UPA) is a Selective Progesterone Receptor Modulator (SPRM) developed for the short term treatment of uterine fibroid. UPA administration is associated with a set of endometrial changes of yet unidentified biological significance, act as a Selective Progesterone Receptor Modulator Associated Changes (PAECs). While PAECs have not been

associated with an increased risk of endometrial hyperplasia or cancer in relatively short clinical trials, their relevance in longer term treatments is unknown.

**Objective:** Study the effects of UPA compared to progesterone on the morphology of endometrial stromal cells and to clarify how these molecules act on actin cytoskeleton rearrangement, regulating the shape and movement of these cells.

**Methods:** Endometrial stromal cells were isolated from biopsies of women younger than 45 and older than 20 years, with regular menstrual cycles for the past 12 months. Before each experiment, cells were kept for 12 hours in DMEM F12 containing steroid deprived fetal bovine serum and treated with 10-9, 10-8 and 10-7 molar of estradiol (E2), progesterone (P4), UPA and P4 or UPA + E2. Cell lysates were separated by SDS-PAGE and analysed through western blot against pY397-FAK, FAK, pT558-Moesin, Moesin and GAPDH. Cell migration was assayed with razor scrape, and was monitored for 48h in presence of ARA-C, an inhibitor of DNA synthesis.

**Results:** Cells treated with E2, P4 and P4 + E2 increased protein phosphorylation levels of FAK and Moesin with a correlation in cell migration respect to control cells. UPA at different concentrations not stimulate stromal endometrial cell migration. Cells treated with UPA + E2 10-9 M decreased stimulatory E2-effects.

**Conclusions:** UPA in combination of E2 reduce its stimulatory effects, however, UPA alone does not affect stromal endometrial cell migration.

### **P83: Postmenopausal bleeding it's alarming**

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**Introduction:** Postmenopausal bleeding is alarming and make fear in mind. Cervical cancer is one of the most common malignancy in Bangladesh. It is one of the important cause of postmenopausal bleeding. It is a silent killer sometimes. Cervical cancer screening can help for the prevention but screening is not all time confirmatory. We present a case of post menopausal bleeding due to cervical cancer.

**Case report:** Our patient is 58 years old with history of menopause for 4 years. In our clinic she came with postmenopausal bleeding. She had no history of post coital bleeding. During her evaluation she was anaemic and hypertensive. Pelvic examination showed broad hypertrophied cervix with bulky uterus. TVS report showed normal endometrial thickness. Paps smear and colposcopy report showed CIN-I. Biopsy report also showed CIN-I. We advised the patient for regular follow up. But the patient was unable for regular follow up. So decision for hysterectomy was taken. At the time of operation we found that the uterus and cervix was very fragile and near the cervical area tissues are not very healthy. On spot we decided for extended hysterectomy. Histopathology report showed poorly differentiated invasive squamous cell carcinoma. Endometrium, both sides parametrium free from invasion and metastasis. She was referred to radiotherapy department for further management.

**Conclusions:** By this case our take home message is we should be careful when we deal with postmenopausal bleeding. Though colposcopy and biopsy report showed cervical intraepithelium neoplasia but cancer never be excluded.

## P84: Clinical Guide to probiotic products available in Canada: 2016 edition

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**Objectives:** This Guide is designed to translate scientific evidence available for probiotic supplements to practical, clinically relevant information, enabling clinicians to easily select the appropriate product, dose, and format for a specific indication.

**Methods:** Published data on the indications for probiotic products was searched, using inclusion criteria as listed on the Guide (product available in Canada, specific strain listed, having assigned Natural Health Product Number, clinical studies in humans published). The inclusion criteria was used to evaluate the strength of the recommendation for each product. Once this information was compiled into a comprehensive chart form, it was assessed by independent reviewers.

**Results:** The Guide itself comprises 4 tables comparing brands of probiotics available in Canada with regards to the bacterial strains in these products, dose, colony forming units (CFU) per dose, administration format, indications, and the level of evidence found in the literature. Tables in the Guide are listed as 1. Adult Health; 2. Pediatric Health; 3. Vaginal Health; 4. Functional Foods with Probiotics added. Vaginal Health table includes vulvovaginal candidiasis and bacterial vaginosis as indications.

**Conclusions:** This guide is meant to bridge the clinical and commercial implications of probiotic products available in Canada, based on published evidence for efficacy, strain specificity and approval by Health Canada. As of 2016, this guide has widely been used in general practice, clinical care, and emergency medicine.

## P85: Conization with "T" technique to diagnose invasive cancer in menopausal woman

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LLETZ cone analysis in menopausal patients in the service of the Lower Genital Tract Pathology in the SOLCA Oncological Hospital, Quito-Ecuador, between: 2003 to 2015. In Ecuador, the female life expectancy is 78 years; menopause begins around 46 years that corresponds to 18% of women. The rate of invasive cervical cancer of in Ecuador is 17.5/100,000. According to the National Cancer Registry in 2013, the average age of invasive cancer in woman is 53 years (22-99 years).

**Objective:** Evaluate the "T" technique in conization, to diagnose invasive cancer in menopausal woman.

**Materials and methods:** Development of a cross-sectional descriptive epidemiological study of patients diagnosed with cone between: 2003-2015 in SOLCA Oncological Hospital. Evaluation of two techniques: biopsy versus T technique with cone, which consists of pulling the cervix and removing the bladder and posterior fornix of the vagina.

**Results:** From 2790 cones, 893 were from menopausal woman of 46-98 years (32%) with previous biopsies with lesions of CIN II and CIN III or cancer without definition of invasion. Biopsy versus cone: Invader adenocarcinoma 2 (0.2%) vs 8 (0.8%); Adenocarcinoma In Situ 3 (0.3%) vs 8 (0.8); Invasive Carcinoma 12

(1.3%) vs 30 (3.3%); Microinvasive carcinoma 11 (1.2%) vs 2 (0.2); Chronic Cervicitis 54 (6.04%) vs 214 (23.9%); CIN I 86 (9.6%) vs 105 (11.7%); CIN II 302 (33.81%) vs 170 (19.03%); CIN III 291 (32.5%) vs 246 (27.5); See and treat 36 (4.0%); Carcinoma in situ 83 (9.2%) vs 82 (9.1%); Leiomyoma 6 (0.6%) vs 7 (0.7); Polyp 6 (0.67%) vs 4 (0.44); Endometrial stromal sarcoma 1 (0.1%) vs 1 (0.1%). Invasive cancer biopsy was found in 25 (2.7%) vs cone 40 (4.5%). Borders free of neoplasia 838, residual neoplasia 65 (7.3%).

**Conclusions:** The diagnosis of invasive cancer in cone 4.5% is higher than in biopsy 2.7%. The "T" technique shows 92.7% free edges, that is an important incidental treatment.

## P86: Vulvar invasive cancer and vulvar intraepithelial neoplasm in menopause

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**Background:** During menopause there is vulvar regressive changes in the epithelial's trophism, particularly at cutaneous levels and it is due to hyperestrogenism. Invasive cancer of vulva represents worldwide 4% of all gynecological tumors. In Ecuador, incidence is 0.7 x 100,000 women while worldwide ranges between 0.5 and 1.5. Human papilloma virus is found in 25.1% of vulvar invasive cancers (VIC) and in 87.7% of vulvar intraepithelial neoplasia (VIN).

**Aim:** To identify frequency of vulvar invasive cancer and vulvar intraepithelial neoplasia in Ecuadorian menopausal women for early diagnosis and timely treatment.

**Material and methods:** In a descriptive and epidemiological study, all patients older than 46 years old attending to the Oncological Hospital "Solon Espinosa Ayala" (SOLCA Quito), between 2003 and 2015, with diagnosis of VIC and VIN confirmed by histopathological analysis in biopsy or surgical piece.

**Results:** There were 229 menopausal women between 46 to 97 years old with these diagnosis. A total of 111 lesions were benign (48.4%), while 35 (29.71%) corresponded to VIN, including 13 (37.1%) carcinoma in situ, 12 cases of VIN III (34.2%), nine (25.7%) VIN II and one Paget's disease (2.8%). The remaining 70.3% (n=83) were vulvar invasive carcinomas, including 67 (80.7%) squamous; 7 basal cell (8.4%), 4 Melanoma (4.8%); 1 Dermatofibrosarcoma (1.20%), 1 caseous (1.20%), 1 Ecrino (1.20%), 1 Neuroendocrine (1.20%) and 1 Mucinous (1.20%).

**Conclusions:** Vulvar tumor pathology is more frequent in menopausal women. More common varieties are squamous cell carcinoma and its precursor lesions, i.e. Ca in situ and VIN (III). Diagnosis of vulvar pathology is done only by histopathology, therefore biopsy is essential for proper treatment.

### ***P87: miR-199a-5p and miR-34a-5p modulated by steroid hormones in endometrial mesenchymal stem cells***

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**Objective:** We investigated whether the most widely used steroid hormones, namely danazol, progesterone, and medroxyprogesterone acetate (MPA), regulate endometrial miRNAs.

**Design:** We used endometrial mesenchymal stem cells (EN-MSCs) and a mouse model of endometriosis.

**Setting:** Kaohsiung Medical University, Kaohsiung, Taiwan.

**Animal:** C57BL/6NCRj mice.

**Intervention(s):** Steroid hormones were added to cultured ectopic EN-MSCs; after incubation, the cells were harvested for in vitro studies and mRNA was collected for measurements.

**Main outcome measure(s):** We used a global miRNA expression profile microarray to evaluate miRNA expression following treatment with 1  $\mu$ M of danazol, progesterone, or MPA. Ingenuity Pathway Analysis helped to predict the functions of miRNAs. The miRNAs were assayed using quantitative reverse transcription-PCR. Cell viability was evaluated by the WST-8 assay.

**Results:** We selected candidate miRNAs whose expression changed more than five-fold following the addition of danazol, progesterone, or MPA in ectopic EN-MSCs. We found 13 upregulated miRNAs in ectopic EN-MSCs. To study the function of these 13 miRNAs, we subjected their sequences to Ingenuity Pathway Analysis. We found that miR-199a-5p and miR-34a-5p correlate with molecular and cellular functions associated with endometriosis. The steroid hormones we added elevated the levels of miR-199a-5p and miR-34a-5p. For further confirmation, the levels of miRNAs in endometrial lesions after hormone treatment were concurrent with those data in vitro.

**Conclusions:** Steroid hormones can regulate miRNA expression in EN-MSCs and in vivo mouse model. These findings contribute to our understanding of the molecular mechanisms underlying endometriosis and illustrate the mechanism of the steroid hormones treatment in endometriosis.

### ***P88: Impacts of S-equol supplement (SE5-OH) on vaginal conditions of postmenopausal women***

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**Objective:** In the management of vaginal atrophy during menopausal transition, some women concern about receiving hormone therapy because of their side effects. The objective of this study was to evaluate the effect of S-equol supplement (SE5-OH) on reproductive health in postmenopausal women.

**Methods:** One hundred five postmenopausal Japanese women who were equol non-producer were assigned to one of four groups; 2 mg/d S-equol (n=26), 6 mg/d (n=25), and 10 mg/d (n=27) and a placebo (n=27). The study consisted of 12 wks intervention and 4 wks follow up periods. The subjects visited a hospital at baseline, 6 wks, 12 wks, and the end of 4 wks follow up. In each visit, physical examination, blood and 24 hrs urine collections were conducted for later analysis. Gynecological cytology and endometrial thickness were determined at baseline and 12

wks. For gynecological cytology test, vaginal smears were collected from the upper one third of the lateral vaginal wall using cotton swabs and were stained by standard Papanicolaou's technique. To assess the maturation values in vaginal epithelium, 200 cells were examined to determine the percentage of the parabasal, intermediate or superficial cells. Transvaginal sonography was performed to evaluate endometrial thickness.

**Results:** Change of superficial cells percentage on vaginal wall during the 12 wks of S-equol intervention was increased dose-dependently. Then, 10 mg/d S-equol group showed a trend of the higher percentage of superficial cells compared to placebo (P=0.05). In the vaginal cytology and endometrial thickness at 12 wks, the number of abnormality was not increased in all subjects.

**Conclusions:** This study suggests that S-equol exerts estrogen like actions on the vaginal epithelium assessed by maturation value. Daily 10 mg S-equol supplement may contribute to improve the reproductive health and QOL of postmenopausal women.

### ***P89: Evaluation of women over 40 with abnormal uterine bleeding***

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**Context:** A large majority of women present with Abnormal Uterine Bleeding (AUB) to the Gynaecologist. Evaluation aims at establishing a specific diagnosis in the least invasive manner.

**Objective:** To correlate symptomatology with Transvaginal Ultrasound (TVS), hysteroscopy and histopathological findings in women with Abnormal Uterine Bleeding

**Methods:** Women over 40 years, who presented to Jehangir Hospital, Pune, India with abnormal uterine bleeding between 1 January 2015 and 31 December 2015 were included. Women with bleeding disorders, known genital tract malignancy and those on anticoagulants were excluded. A detailed history was taken and a thorough clinical examination was done. A TVS and diagnostic hysteroscopy were performed. Endometrial samples were taken. Biopsies were taken from focal lesions. Endometrial polyps and sub mucous myomas were resected and sent for histopathology.

**Results:** 78 women were enrolled. The most common complaint (39.7%) was postmenopausal bleeding (PMB). 49% of premenopausal women had menorrhagia. One third of women with PMB had atrophy. Endometrial polyps were the major cause of AUB. 36% of those with menorrhagia, 55% of women with metrorrhagia and 60% of those with menometrorrhagia had polyps. Almost 50% of women with polyps were not reported to have an intra-cavitary lesion on TVS. Majority of postmenopausal women with ET >12mm had a polyp and two women had Carcinoma endometrium. Hysteroscopy had a sensitivity, specificity, PPV and NPV of 100% for detection of all endometrial pathologies.

**Conclusions:** Hysteroscopy remains the gold standard as a significant number of women with AUB have endometrial polyps, which may be missed on TVS. ET more than 12 mm in postmenopausal women does not necessarily indicate a malignancy.

### **P90: Immunohistochemical assessment of symptomatic postmenopausal endometrial polyps in tamoxifen users and no users**

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**Introduction:** Although endometrial polyps are common in postmenopausal women occurring in 16–54% of women with postmenopausal bleeding, there is still no consensus in the literature regarding the pathogenesis and the effect of tamoxifen on the hormone receptor (HR) profile of these polyps.

**Objective:** Evaluate the expression of hormone receptors (ER and PR) and markers of proliferation and apoptosis (Ki-67 and Bcl-2) in endometrial polyps of postmenopausal nonusers and users of tamoxifen.

**Methods:** Forty-six postmenopausal patients between 47 and 86 years old were included. All patients presented postmenopausal bleeding and underwent hysteroscopic resection of endometrial polyps. Fourteen were on tamoxifen and 32 did not use hormonal medications. We used immunohistochemical analysis of tumor tissue fixed in formalin and embedded in paraffin to detect Ki-67, Bcl2, RE and RP with the ADVANCETM HPR kit (DakoCytomation®).

**Results:** We evaluated the glandular component of the polyps and found an expression of 96.9% of PR in polyps of non-users tamoxifen and 92.3% in users ( $p=0.499$ ). Regarding ER all polyps in the tamoxifen nonusers group were positive when compared to 92.3% in the tamoxifen users group ( $p=0.295$ ). We found a 75% expression of Ki-67 in tamoxifen users and 82.8% in nonusers. All showed expression of Bcl-2 in endometrial polyps.

**Conclusions:** The use of tamoxifen, despite its risk for endometrial polyp, did not alter the expression of HR significantly compared with nonusers of tamoxifen. Both groups showed inhibition of apoptosis demonstrated by the expression of Bcl-2 in all cases included in the study. This finding reinforces the theory that polyps grow by inhibition of apoptosis and not by cellular proliferation.

### **P91: Profile of patients with deep endometriosis in a Gynecologic Clinic from a University Hospital in the south of Brazil: initial experience**

Carla Vanin (BR), Noadja França (BR), Sonia Fior (BR) and Raquel Dibi (BR)

UFCSA/ISCOMPA

**Objective:** Evaluate the profile of the patients with deep endometriosis from a specialized Gynecology Clinic in a University Hospital of the South of Brazil.

**Methods:** Retrospective analysis of the medical records from the patients with the diagnosis of deep endometriosis seen at the Endocrinological Gynecology Clinic of Irmandade Santa Casa de Misericórdia de Porto Alegre.

**Results:** The records from 17 patients were reviewed. The average age was 38.3 years-old (range: 18–52 years old). Seven patients (41.1%) were nulliparous. Chronic pelvic pain was the most frequent symptom, described in 11/17 patients. Three of these patients also had infertility. Only 3 patients were asymptomatic. Only one patient presented hematuria. Intestinal involvement was the most often finding (76,4%). Vaginal, bladder and ovarian

lesions were found in 23.5% of the cases. Five of the 17 patients had already been submitted to a surgical procedure. In one case we found uterosacral ligaments involvement agreeing with previous imaging studies that was realized before surgery and another case had parametrial involvement that was not registered by previous imaging tests. The frequency of these findings are more often seen during surgical procedures than described by pre-operative imaging tests.

**Conclusions:** The profile of patients studied in our University Hospital with deep endometriosis corroborates with the literature data. The most frequent symptoms were chronic pelvic pain and infertility and most of the lesions involved the intestinal segment.

### **P92: A new synergistic treatment with a moisturizing, lubricant and healing effect in vulvovaginal discomfort**

Franco Vicariotto (IT)

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Genitourinary syndrome of menopause (GSM) referred to symptoms related to the menopause, including vulvovaginal atrophy (VVA). It can occur at any time in a woman's life cycle, although more commonly in the postmenopausal phase. A novel pharmacological treatment easy to administer by women with symptoms of VVA was studied.

**Objective:** To assess the effectiveness in treatment of VVA symptoms of a new medical device in gel based on the synergic combination of Nioskin™ Red Clover Extract niosome (NRC), a unique ultra-deformable vesicles effectively delivering the concentrated isoflavones aglycones of Red Clover, and SylTech™ system (SB), a complex of silicium microcrystals covalently bound with silver ions associated with hyaluronic acid, in the supportive treatment of VVA.

**Methods:** Observational open study. 40 menopausal women with a diagnosis of VVA and any hormone therapy for at least 3 months before, received a 12-weeks treatment, as gel applied internally in vagina and externally on the vulvar, once a day. Main outcomes at baseline, at month 1 (V1) and after 3 months (V2): clinical VVA symptoms (VAS scale); dyspareunia (Marinoff score); secondary end points: vaginal trophism (Vaginal Health Index), vestibular trophism (score).

**Results:** The positive results suggest that this new medical device gel was significantly effective in reducing symptoms consequent to VVA, at 3 months of follow-up. The innovative gel formula contributes to restore and promote the maintenance of the physiological vaginal environment. An high compliance and full tolerability was recorded.

**Conclusions:** The study shows that the application of the Nioskin (NRC) SylTech synergistic gel can be an effective treatment for the reduction of VVA, with moisturizing, lubricant and healing effects, indicating also an use as a preventive agent in any predisposing condition of vulvovaginal discomforts.

### **P93: Codon 72 polymorphism of the p53 tumor suppressor gene is not associated with idiopathic recurrent pregnancy loss**

Sang Ho Yoon (KR)

Dongguk University Ilsan Hospital

**Objective:** The balance of apoptosis and proliferation is an important part in the embryonic development during pregnancy. It has been reported that the p53 gene plays a significant role in angiogenesis and placental development, namely in reproduction and is suggested as a potential mediator of pregnancy. This study was performed to investigate whether the genetic polymorphism of the p53 gene is associated with idiopathic recurrent pregnancy loss (RPL).

**Methods:** We conducted a case-control study. Study subjects consisted of 294 patients with idiopathic RPL and 300 postmenopausal controls. The genotyping for the p53 codon 72 polymorphism was performed using a Taqman assay. Continuous variables were compared using Student's t test and the  $\chi^2$  test was used to evaluate differences in the genotype distributions between the RPL and the controls.

**Results:** The median number (range) of spontaneous miscarriages was 3 (2-13) in RPL patients and 0 (0-0) in controls. There were no significant differences in the genotype distributions or allele frequencies of the p53 codon 72 polymorphism between the RPL and control group (Arg/Pro rates; 65.3/34.7% in the RPL vs. 64.8/35.2% in the control group,  $p=0.864$ ). There was also no significant association between the p53 codon 72 polymorphism and RPL risk in both recessive (Pro/Pro vs. Arg-carriers,  $p=0.314$ ) and dominant model (Pro-carriers vs. Arg/Arg,  $p=0.383$ ). For further analysis, if RPL patients were divided according to the numbers of pregnancy losses ( $\geq 2$  and  $\geq 3$ ), neither group was significantly different compared with controls.

**Conclusions:** The codon 72 polymorphism in the p53 gene did not show any correlation with idiopathic RPL in Korean women, implying that it may not be susceptible allelic variants or be insufficient to cause RPL.

### **P94: Does salpingectomy have a deleterious impact on ovarian response in IVF cycles?**

Sang-Hee Yoon (KR)<sup>a</sup>, Ji-Young Lee (KR)<sup>b</sup> and Hyo-Jin Lee (KR)

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**Objective:** To investigate the impact of salpingectomy in patients with in vitro fertilization treatment on ovarian response. Design: Meta-analysis. Setting: All countries.

**Patient(s):** Patients under treatment for infertility, during the cycles before and after treatment by salpingectomy for hydrosalpinx or ectopic pregnancy.

**Intervention(s):** PubMed, MEDLINE, EMBASE databases, and CENTRAL in Cochrane Library up to July 2015. Either a fixed- or a random-effects model was used to calculate the overall combined risk estimates. The subgroup analysis was planned a priori before data were collected and analyzed.

**Main outcome measure(s):** The amount of gonadotropin administered, the peak estradiol level, the number of oocytes retrieved, and the number of pregnancies.

**Results:** After the final screening, twelve of the studies were retrospective and six were prospective. In this meta-analysis, 1482 patients were enrolled including a total of 657 patients with salpingectomy and 825 without salpingectomy. The comparisons before and after salpingectomy of the peak estradiol level

(SMD = -0.182, 95% CI: -0.166 - 0.101, I2: 85.45%,  $p$ -value = 0.208), the total gonadotropin dose used for stimulation (SMD = 0.127, 95% CI: -0.054 - 0.308, I2: 84.49%,  $p$ -value = 0.169), and number of oocytes retrieved (SMD = -0.060, 95% CI: -0.189 - 0.070, I2: 63.93%,  $p$ -value = 0.365) did not find any significant differences. The number of pregnancies before and after salpingectomy did not differ significantly (OR = 1.180, 95% CI: 0.854 - 1.630, I2: 34.01%,  $p$ -value = 0.315).

**Conclusions:** The salpingectomy in infertile patients does not have any negative effect on their subsequent fertility treatment, but further studies should be performed before this result can be considered definitive.

## **Hormones and the brain**

### **P95: Social factors fact of depression disorder in menopausal women**

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Sebelas Maret University/Dr. Moewardi Hospital Surakarta

**Objective:** To understanding depression disorder in menopausal women and investigating many factors such as age, occupation, income, domicile demographics, that influence it significantly.

**Methods:** Dependent variable of our study is depression disorder that measure with Hamilton Rating Scale (HARS) Modification Questionnaire as tools to establish depression disorder. Independent variable of our study is age, occupation, income, domicile demographics, sleep disorder, and intelligence disorder. The samples are 100 menopausal women that agree to participate in this study. We observed 22 menopausal women with <5 years long of menopause period as control, and compare to 78 menopausal women with  $\geq$  than 5 years long of menopause period then perform bivariate and also multivariate analysis to determine all factors that significantly influence depression disorder in menopausal women.

**Results:** The age variable increase the risk of depression OR = 0,07; CI 95% = 0,018 - 0,274;  $p=0,00$ . We found that occupation increase 3,49 times the risk of depression, with the OR = 3,499; CI 95% = 0,089 - 13,780;  $p=0,07$ . Income variable OR = 0,708; CI 95% = 0,201 - 2,501;  $p=0,59$ . Urban domicile demographics increase 1,49 times the risk of depression with the OR = 1,494; CI 95% = 0,396 - 5,640;  $p=0,55$ .

**Conclusion:** Age, occupation, income, and domicile demographics, statistically influenced the depression disorder in menopausal women.

### **P96: Evaluation of depressive symptoms in mid-aged Latin American women using the CESD-10: report of a multicentric study**

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**Background:** Previous reports among Latin American mid-aged women have shown an effect of altitude and ethnics over the severity of menopausal symptoms; however, these factors have not been studied in the same population in relation to depressive symptoms.

**Objective:** To evaluate depressive symptoms and related factors among mid-aged women.

**Methods:** This was a cross-sectional multicentric study in which women aged 40 to 65 from various Latin American sites were surveyed with the CESD-10 and a questionnaire containing personal data.

**Results:** A total of 857 women were surveyed from Cartagena, Colombia (n = 215, Afro-Colombian), Guayaquil, Ecuador (n = 195, Mestizo), Cusco, Perú (n = 231, Quechua and high altitude) and Asunción, Paraguay (n = 216, Mestizo). Median age of the whole sample was 48 years, with women from Guayaquil being older. There were no differences in the rate of being postmenopausal among studied sites. Median total score for the CESD-10 was 7.0. Higher scores (indicating more depressed mood) were significantly correlated with being postmenopausal and Afro-Colombian. There were no differences observed in terms of living in high altitude or being indigenous (Quechua).

**Conclusions:** In this large mid-aged female sample, depressive symptoms correlated to menopausal status and race.

### **P97: The impact of the androgen steroids level on cognitive function in climacteric women**

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Clinical Center of Montenegro

**Objective:** Climacterium is period in women's life characterized by changes in steroids level, which decreases in its latest stages. Testosterone decrease has a negative impact on cognitive functions. Some of steroids, which influence mental health, are androgen steroids and their decrease has negative impact on cognitive functions.

**Methods:** Two groups of women aged between 45 and 55 were analyzed; in both groups of 30 subjects episodes of oligo/amenorrhea were present. The psychological testing (mini-mental state exam) was done with a maximum score of 30. The first group had 25 and less, the second group scored above 25. Afterwards in both groups the blood samples were taken for FSH, LH, estradiol, total and free testosterone and DHEAS. LH, FSH, estradiol, DHEAS were measured by chemiluminescence, total and free testosterone via RIA method.

**Results:** In both groups gonadotropins levels are typical for climacterium. For the assessment of differences in estrogen, total and free testosterone and DHEAS between the two groups, the t-test was applied for independent samples. Value of total testosterone was statistically significantly lower in the first group, with less points (t = 3.423, p = 0.002), while in the value of estrogen, free testosterone and DHEAS there is no statistically significant difference (p < 0.05).

**Conclusions:** Climacterium brings with itself changes in steroid level that is not the same for all women. Decrease in the level of testosterone has a negative impact on cognitive functions what indicates the necessity of its substitution. On the other hand maintaining the level of free testosterone in both groups could be a compensatory mechanism of nature in order to preserve cognitive functions.

### **P98: Association of physical activity and sleep quality in premenopausal and postmenopausal women**

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Istanbul Bilim University

**Objective:** The aim of this study was to examine the individual and combined associations of physical activity and sleep in premenopausal and postmenopausal women.

**Material and methods:** 65 premenopausal (mean age: 45.50 ± 2.10) and 65 postmenopausal (mean age: 60.27 ± 3.03) women were evaluated. We compared age, body mass index (BMI), education, marital status, age at menopause, jobs, medical conditions, smoking, physical activity and sleep quality using the Women's Health Initiative Insomnia Rating Scale between groups. The SPSS 22.0 program was used for statistical analysis of the research data. Frequency and percentage (average, standard deviation) were used as descriptive statistics of the study. Non-parametric tests (Mann-Whitney U, Kruskal-Wallis, Spearman correlation test) were preferred for comparison of the variables, which did not comply with normal distribution. Significance was accepted as p < 0.05.

**Results:** Sleep quality scores had better in premenopausal women when compare with premenopausal women (p = 0.000). No significant differences were found in BMI (p = 0.691). Mean age at menopause were 47.56 ± 4.91 in postmenopausal women. Postmenopausal women's physical activity and sleep quality worst than premenopausal women's. 17 premenopausal (7 of them walking, 4 of them swimming, 6 of them fitness) and 6 postmenopausal (4 of them walking, 2 of them swimming) women had physical activity. In whole women, exercise training participants had better sleep quality. Who exercised in both group had better sleep quality (p = 0.000). No significant differences were found in sleep quality between who exercised premenopausal and postmenopausal women (p > 0.05).

**Conclusions:** Objective sleep measures differed significantly between the pre- and postmenopausal groups. These findings provide strong evidence to sleep qualities are more favorable in highly active women relative to less active women.

### **P99: Suicidal ideation and suicidal behaviour in postmenopausal schizophrenia women: the relevance of suicide risk assessment**

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**Objective:** The main aim of this study was to investigate whether postmenopausal and premenopausal women and men with schizophrenia differ in suicidal ideation and behaviour

frequencies, suicidal ideation intensity and potential lethality of suicide attempts.

**Methods:** Psychopathology was assessed by using the Positive and Negative Syndrome Scale, the Personal and Social Performance Scale and the Columbia-Suicide Severity Rating Scale (C-SSRS). Univariate differences were investigated by applying Analysis of Variance using the C-SSRS variables as dependent factors and group as fixed-factor. Antipsychotic doses, age at onset, DUP, number of psychotic episodes and social support were introduced into the model as covariates. In a further step, logistic regression analyses were performed.

**Results:** Among 169 schizophrenia patients (men, 74; premenopausal, 32; postmenopausal women, 63), 73 (43.2%) reported lifetime suicidal ideation and 43 (23.7%) attempted suicide at least once. When uncorrected, men needed higher doses of antipsychotics ( $p=0.037$ ), showed earlier age at onset ( $p<0.001$ ) and higher number of psychotic episodes ( $p=0.014$ ) than pre- and postmenopausal women. Postmenopausal women showed lower deterrents that definitely stopped them of committing suicide ( $p=0.017$ ) and a tendency toward higher potential lethality of actual attempts ( $p=0.062$ ). Postmenopausal women had higher suicidal ideation intensity, even after correction for confounding factors ( $p=0.039$ ). Differences in deterrents from attempting suicide did not change after adjustment ( $p=0.004$ ).

**Conclusions:** Postmenopausal schizophrenia women showed higher suicidal ideation intensity and deterrents were less likely to stop them from attempting suicide compared to men and premenopausal women. Hormonal status should be considered a potential neurobiological underpinning of suicidal behaviour in schizophrenia.

### ***P100: Menopausal women sleep disorders: integrative and interdisciplinary care***

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Universidade Federal de São Paulo

**Objectives:** The Women's Sleep Disorders Ambulatory is a non-profit of integrated and interdisciplinary care in sleep disorders for menopausal women accordingly with the principles of integrative medicine. Our aims were: to treat sleep disorders and improve quality of life; to promote training activities and continuing education for human resources in health; to carry out research activities in the field of sleep disorders in women's health within the Scientific, Postgraduate and Medical Residence Programs.

**Methods:** Patients undergo a medical care (anamnesis, general and exams) followed by specific tests of sleep (e.g. polysomnography, actigraphy and multiple sleep latency test) and answer the questionnaires: Insomnia Severity Index, Pittsburgh Sleep Index and Epworth Sleepiness Scale on each appointment. The physician team referrals to specific treatments (along with pharmacotherapy or not), such as manual therapies (postural global re-education, chiropractic, myofascial release), urogynecological physiotherapy, kinesiotherapy, Pilates exercises, psychotherapy, nutrition, flower therapy, meditation and acupuncture. Sessions are individual or in groups and include sleep hygiene.

**Results:** The Women's Sleep Disorders Ambulatory has attended 108 patients in medical appointment, and 26 in integrative therapies weekly: 11 in physiotherapy, 5 in psychotherapy, including psychotherapy emergency care, 2 in nutrition, 6 in meditation and 13 in acupuncture, between August and December of 2015. Patients report improvement in sleep patterns and comorbidities that may influence sleep (e.g. pain, anxiety, and obesity).

**Conclusions:** The Women's Sleep Disorders Ambulatory provided knowledge of the specific medical area of sleep in order to improve the knowledge of the population about good sleep habits and its importance and interference in our lives.

### ***P101: Effects of Bach Flower Remedies on menopausal symptoms and sleep pattern: a case report***

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Universidade Federal de São Paulo

**Objectives:** This investigation aims to evaluate the effects of Bach Flower Remedies on sleep pattern (i.e. sleep perception and objective sleep) and on menopausal symptoms in one postmenopausal woman, who had an insomnia diagnosis, according to the American Academy of Sleep Medicine (2007).

**Methods:** This study received prior approval by UNIFESP Ethical Committee (# 638.935/2014). It was conducted at Ambulatory of Women's Sleep Disorders of the Department of Gynecology of the Federal University of São Paulo (UNIFESP), São Paulo, Brazil. A 53-year-old single woman at postmenopausal stage was diagnosed with insomnia and climacteric symptoms. The patient underwent a treatment with a blend of Bach Flower Remedies, replaced every 15 days for 4 months. Beck Anxiety Inventory, Beck Depression Inventory, Menopause Specific Quality of Life Questionnaire, Blatt-Kupperman Menopausal Index and Sleep questionnaires (Epworth Sleepiness Scale, Pittsburgh Sleep Quality Index and Insomnia Severity Index) and a full night polysomnography were performed, before and after treatment.

**Results:** Both sleep perception and objective sleep were improved. Anxiety and menopause symptoms were reduced after the Bach Flower Remedies treatment, which could affect secondarily subjective sleep parameters. Sleep latency, rapid eyes movement (REM) sleep stage, sleep latency, stage N3 of non-REM (NREM) sleep, arousal index and apnea-hypopnea index decreased; while total sleep time, sleep efficiency and stage N2 of NREM sleep increased significantly. These findings indicated an overall positive change in sleep architecture due to the Bach Flower Remedies treatment.

**Conclusion:** The indication of Bach Flower Remedies as a therapeutic strategy to relief menopausal symptoms, such as anxiety, mood changes, and insomnia is consistent and can help improving quality of life of women in postmenopausal stage.

### **P102: The effects of a mindfulness meditation training on postmenopausal women with insomnia: a randomized clinical trial**

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**Objectives:** Investigate the effects of training in mindfulness for insomnia, vasomotor symptoms and overall quality of life in postmenopausal women.

**Methods:** Thirty postmenopausal women 50-65 years insomniacs (DSM-V) without hormonal therapy were randomized in two groups: intervention (n = 19) in mindfulness for 8 weeks and control group (n = 11). Women were evaluated by questionnaires: Pittsburg Sleep Quality Index - PSQI, Severity of Insomnia-ISI, Menopause Specific Quality of Life-MENQOL, Kupperman Menopausal Index-KMI, level of attention (Mindfulness Awareness Attention Scale-MAAS) and polysomnography(PSG) before and after treatment. Intervention group attended once a week 30 minutes with a trained instructor, control group only for informal conversations. Mindfulness group were instructed to meditate 3 times a day using audio technique.

**Results:** PSQI in the meditation group decreased from (12.5 ± 1.6) to (4.3 ± 1.8), control group from (12.6 ± 1.4) to (10.4 ± 2.2); p = 0.0001. ISI in the meditation group decreased from (18.3 ± 2.7) to (3.2 ± 2.8), control group from (18.8 ± 2.8) to (15.0 ± 5.1); p = 0.0001. MENQOL Vasomotor domain in the meditation group was (4.3 ± 2.3) before and (2.2 ± 1.4) after intervention, in control group (4.2 ± 2.2) before and (4.6 ± 03.0) after; p = 0.005. A decrease in menopausal symptoms occurred in mindfulness group, KMI in intervention group went from (27.8 ± 7.5) to (10.1 ± 6.6) and control group was (25.7 ± 11.2) before and (21.45 ± 9.55) after; p = 0.001. MASS scale for meditation group increased from (59.0 ± 12.6) to (69.3 ± 8.1) while in control group it was decreased from (61.1 ± 14.9) to (60.8 ± 12.8); p = 0.007. There was no difference for PSG between groups.

**Conclusions:** The training of mindfulness meditation improved the quality of sleep, the overall quality of life in postmenopause, the level of mindfulness and reduced vasomotor symptoms in postmenopausal women with insomnia.

### **P103: A cognitive behavioral therapy self-help intervention for menopausal working women with bothersome vasomotor symptoms: MENOS@WORK trial protocol**

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<sup>a</sup>King's College London; <sup>b</sup>University of Nottingham

**Objectives:** This paper describes the protocol for a randomised control trial of a self-help cognitive behavioural therapy (CBT) intervention, the main aim of which is to reduce the impact of bothersome vasomotor symptoms for working women.

**Methods:** 100 working women aged 45-60 years, experiencing bothersome vasomotor symptoms (hot flushes/night sweats (HFNS)) for two months or longer, are being recruited from several large UK-based organisations. Upon completion of a baseline

questionnaire, participating women are randomly allocated to either a CBT treatment group or treatment as usual group (TAU). The four week self-help intervention, found to be effective in previous MENOS trials, was modified for working women. The TAU group will receive the intervention at the end of the study. Follow-up questionnaires will be completed by all participants at 6 and 20 weeks post-randomization. Treatment group participants will also be invited to a telephone interview to provide additional feedback about the intervention.

**Results:** Quantitative and qualitative analyses will be conducted to assess the effectiveness and feasibility of implementing the proposed intervention. The primary outcome of this study is problem rating of HFNS and secondary outcomes include HFNS frequency, mood, quality of life, attitudes to menopause, HFNS beliefs and behaviours, work outcomes such as work absence, presenteeism, job satisfaction, job stress, job performance, disclosure to managers, and turnover intention.

**Conclusions:** Women tend to report that menopausal symptoms are particularly troublesome in work settings; yet few employers offer information or have policies for the menopause. This study aims to provide an evidence-based intervention for employers to help staff with bothersome menopausal symptoms and difficulty at work.

### **P104: Symptom clustering across the menopausal transition: Study of Women's Health Across the Nation (SWAN)**

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**Objectives:** Perimenopausal women who experience symptoms in one domain are frequently symptomatic in other domains. Among women who were initially pre or early perimenopausal, we assessed symptom clustering longitudinally across the menopausal transition and evaluated risk factors for being highly symptomatic.

**Methods:** 3289 women from the multiethnic Study of Women's Health Across the Nation reported on 58 symptoms including emotional, physical, pain, vasomotor, sleep symptoms and sexual desire at baseline and 7 follow-up visits. We conducted latent transition analyses to assess symptom clustering and to model symptomatology across the menopausal transition (pre, early peri, late peri and post). Regression analyses were used to determine risk factors for baseline latent class membership.

**Results:** Symptoms cluster into 6 latent classes. At baseline, 9.2% of women are in the highly symptomatic class reporting very high symptom levels across all domains. Two classes (12.0 and 14.4% prevalences) report high levels of physical, fatigue and pain symptoms with the first also reporting emotional and sleep symptoms. The least symptomatic class (18.6) reports very low symptom levels across all domains. Intensity of vasomotor symptoms and sexual desire differ minimally by latent class. Women in the highly symptomatic class are more likely to be white, overweight, current or former smokers, have difficulty paying for basics, and have less than a high school education. Over time, women exhibit considerable movement between symptom classes, but transition probabilities do not differ significantly by current menopausal stage.

*Conclusions:* Symptom clustering among midlife women may suggest common underlying mechanisms amenable to interventions. That women transition across classes over time provides evidence that timely interventions may improve women's long-term well-being.

### ***P105: Neuroprotective strategies of Cimicifuga racemosa (CR): update***

Susana Garcia De Arriba (DE), Hans-Heinrich Henneicke-Von Zepelin (DE) and Klaus-Ulrich Nolte (DE)

Schaper & Brümmer GmH & Co. KG

Menopause has been associated with microglia-brain inflammation, loss of neuronal activity and severe oxidative stress. All these changes may lead to progressive decline in cognition, attention, memory, as well as behavioral changes. iCR treatment restored neuronal function (c-fos expression) in hypothalamic areas affected by estrogen deprivation. The extent of this efficacy was similar to that of estrogen. iCR caused selective changes in brain activity similar to those exerted by drugs used to treat degenerative diseases, mood and cognition impairment. iCR reduced brain steroid sulfatase (STS) activity in human hippocampus tissue, while in human neuroblastoma cells an inhibition was followed by a stimulation. Depending on the substrate, inhibition (dehydroepiandrosterone sulfate) or stimulation (estrone sulfate) of the STS activity, may lead to a protective effect, which may contribute to reduce degenerative processes. Now, we evaluated CR activities, which may contribute to the prevention of climacteric-related neurodegenerative processes.

*Methods:* Literature in reference databases (e.g. MEDLINE, EMBASE, BIOSIS) was collected till 2015. The CR protective effects were classified in 3 groups: 1) anti-inflammatory; 2) antioxidant/radical scavenging; 3) mitochondrial protection.

*Results:* Eighteen in vitro/in vivo studies were included in order to update the different protective effects of CR extracts and distinct constituents. Anti-inflammatory activities emerged by decreasing TNF $\alpha$ , IL-6, IL-4, IL-5, IFN- $\gamma$ , IL-8 and NO production. Hydroxyl, superoxide anion and DPPH radical scavenging properties as well as mitochondrial protection was also evidenced.

*Conclusions:* Inhibition of neuroinflammatory and pro-oxidant processes by CR may prevent or delay the progression of degenerative processes in climacteric women. Further research is needed to support this hypothesis.

### ***P106: Melatonin in treatment of climacteric symptoms and sleep problems***

Denis Burchakov (RU) and Irina Kuznecova (RU)

I.M. Sechenov First Moscow State Medical University

*Objectives:* During menopausal transition many women develop vasomotor and psychosomatic symptoms. These symptoms stem both from estrogen deprivation and hypothalamic-pituitary-ovary system aging. Melatonin is a hormonal circadian regulator, working at every level of reproductive system down to receptor level. It also regulates sleep, and sleep disorders are numerous in menopausal transition. We aimed to investigate whether

melatonin is effective at alleviating climacteric symptoms and improving sleep quality.

*Methods:* In course of this open-label randomized controlled trial 53 women (age 45-62) took 3 mg of melatonin each day before sleep for 3 months. Control group included 40 age- and weight-matched women. To avoid confounding from sleep apnea, which is also a common condition at middle-aged women, we did not include women with body mass index above 29.9. All participants completed Greene Climacteric Scale (GCS) and Pittsburgh Sleep Quality Index (PSQI) at the day 1, day 45 and day 90 of the study. We considered results statistically significant at  $p < 0.05$ .

*Results:* In treatment group mean GCS score decreased from 40.96 to 21.36 ( $p < 0.001$ ) and median PSQI score decreased from 16 to 7 ( $p < 0.01$ ). Women in control group did not show any significant changes in GCS and PSQI scores. Between-group comparisons proved to be significant. No significant difference was found regarding side effects between treatment and control groups ( $p = 0.14$ ).

*Conclusions:* 3 mg of melatonin improve subjective sleep quality and alleviate climacteric symptoms. It is still unclear whether melatonin should be prescribed along with menopausal hormonal therapy (MHT), but in women with contraindications to MHT and women refusing to take MHT melatonin can be a viable option, either alone or in combination with another method.

### ***P107: Depressive mood is more associated with insomnia in postmenopausal women***

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*Objectives:* The most common symptoms of menopause are depressive mood and insomnia. Meanwhile, their association may be changed in postmenopausal women. This study aimed to compare the association of depressive mood and sleeping hours between premenopausal and postmenopausal women.

*Methods:* We investigated the data obtained from the Korea National Health and Nutrition Examination Surveys (KNHANES) V conducted from 2010 to 2012. KNHANES is a nationwide cross-sectional study, which includes self-reported questionnaires and some laboratory test results. We compared the probabilities of depressive mood according to sleeping hours between premenopausal and postmenopausal women.

*Results:* This analysis included 13,918 women, wherein 5188 and 8730 subjects were postmenopausal and premenopausal women, respectively. As sleeping hours increase by 1 h, the possibility of depressive mood lowered significantly, and the association remained after adjustment for age (adjusted odds ratio [aOR], 0.92; 95% confidence interval [95% CI], 0.87–0.96) in postmenopausal women. However, the association was not significant in premenopausal women (aOR, 0.99; 95% CI, 0.93–1.05).

*Conclusions:* Short sleeping hours might increase the possibility of depressive mood in postmenopausal women more significantly than in premenopausal women. Active insomnia management for postmenopausal women might help relieve their depressive mood.

### ***P108: Depression and its link to other symptoms in menopausal transition***

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**Objectives:** Menopausal transition is a period happened between 45-55 years old. This transition may take three to nine years. During this transition, the hormonal changes may contribute to the physical and psychological complaints in women. One of the psychological complaints is sign of depression. However, not all of the women will experience those complaints. Thus, the evaluation is needed to assess the relationship between depression in menopause transition and other menopausal symptoms and factors contribute to depression among Indonesian people.

**Methods:** Cross-sectional study on 107 female subjects between 45-55 years old. All baseline data, depression score, and menopausal symptoms were collected using validated questionnaires. Beck Depression Inventory-II (BDI-II) and Menopause Rating Scale (MRS) were used to evaluate depression and menopausal symptoms among subjects. The comparison and relation were assessed for every aspect regarding depression and menopausal symptoms.

**Results:** From 107 subjects, depression was found in 11 subjects (10.3%). Depression was more common on low-educated subjects ( $p=0.014$ ). Somato-vegetative and urogenital symptoms were complained by 46.2% and 73.8% subjects, respectively. There were no correlation between depression and somato-vegetative as well as urogenital complaints among women who underwent menopause transition ( $p=0.169$ ;  $p=0.065$ ). However, there were significant correlation between BDI-II scores and MRS scores for somato-vegetative and urogenital complaints ( $p<0.001$ ;  $p<0.001$ ).

**Conclusions:** Depression on menopausal transition do not correlate with the complaint of somato-vegetative and urogenital symptoms among women.

### ***P109: Sleep difficulty in women at midlife transition and menopause***

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**Objectives:** Sleep difficulty is one of the hallmarks of menopause which has consequences to health including reduced quality of life, impaired mental health, and increased physical health morbidity. Aim of this study was to find prevalence of sleep difficulty at various stages of the menopausal transition, its consequences and its impact on quality of life.

**Methods:** Cross sectional, observational prospective study conducted at Saveetha Medical college Obstetrics & Gynaecology Outpatient Department. One hundred and twenty women aged 40 to 70 years were categorized into five groups: premenopausal 21, early perimenopausal 27, late perimenopausal 31, naturally postmenopausal 33, surgically postmenopausal 8. These women were asked whether they had experienced difficulty sleeping in the past 2 weeks. Sleep quality was objectively measured by self-reported sleep problems by questioner (validated tool).

**Results:** Difficulty sleeping was reported by 48%. Rates were highest in the late perimenopausal 22%, naturally postmenopausal

17%, and early menopausal 9%. Most commonly encounter sleep disorder is insomnia 32%. Symptoms of difficulties in initiating sleep in 8%, maintaining sleep in 12%, both in 7%, vasomotor symptoms in 5%, psychological symptoms 8%, arthritis 3%. Sleep disordered breathing (SDB) was seen in late perimenopause 12%, in menopause 14%. Other associated sleep disorders are nil. All cases reported that they had impaired occupational, social functioning in day time.

**Conclusions:** In our study self reported sleep difficulty is more during menopausal transition. Hence treatment for sleep disorders to be considered in midlife women.

### ***P110: Serotonin receptor targeting activities for Cimicifuga racemosa dry extract (BNO 1055) as active component of Klimadynon®***

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Bionorica SE

Extracts from Cimicifuga (syn. Actaea) racemosa (CR, black cohosh) proved to be an effective phytotherapeutic agent against climacteric complaints such as hot flushes. Earlier studies suggested an agonistic effect of CR towards serotonin receptors 5-HT<sub>1A</sub> and 5-HT<sub>7</sub> resulting in modulation of vasomotor activity as potential mechanism of action against hot flushes.

We analyzed BNO 1055, a dry extract from CR and active component of Klimadynon®, for its binding affinity and functional activation of serotonin receptors 5-HT<sub>1A</sub>, 5-HT<sub>2A</sub> and 5-HT<sub>7</sub> in vitro using radioligand binding assays and second messenger (cAMP) activation assays. This approach revealed that BNO 1055 dry extract contains substances with the capacity to bind serotonin receptors 5-HT<sub>1A</sub> (IC<sub>50</sub>: 2 µg/ml) and 5-HT<sub>7</sub> (IC<sub>50</sub>: 6 µg/ml) rather than 5-HT<sub>2A</sub>. Binding was biologically functional as revealed by second messenger assays (EC<sub>50</sub>: 5 µg/ml for each, 5-HT<sub>1A</sub> and 5-HT<sub>7</sub>). In addition, serotonin receptor activation of BNO 1055 and Klimadynon® was analyzed in comparison to four other best-selling CR-containing products available in Germany. Binding of BNO 1055 and Klimadynon® was considerably more efficacious than most of the competitors' products as reflected by EC<sub>50</sub> values of 5 µg/ml (5-HT<sub>1A</sub>) and 1-3 µg/ml (5-HT<sub>7</sub>) for BNO 1055 and Klimadynon® as compared to EC<sub>50</sub> values ranging from 10 to 98 µg/ml (5-HT<sub>1A</sub>) and from 2-26 µg/ml (5-HT<sub>7</sub>) for the competitors. In summary we demonstrated that Klimadynon® contains herbal substances with selective agonistic serotonin receptor activity. Moreover, Klimadynon® is one of the most effective of all tested CR dry extract-containing phytotherapeutics regarding serotonin receptor 5-HT<sub>1A</sub> and 5-HT<sub>7</sub> activation. Thus, we hypothesize that the well documented therapeutic effect of Klimadynon® is due, at least in part, to substances that activate serotonin receptors.

### ***P111: Diagnostics algorithm of anxiety-depressive disorders in perimenopausal women***

Hanna Tabolina (BY)

Belarusian Medical Academy of Post-Graduate Education

**Context:** The development of reliable criteria for diagnostics of anxiety-depressive disorders (ADD) in perimenopausal women allows the doctor and the patient in a timely manner carrying

out a complex of measures aimed at maintaining the health of women, form risk groups that require special attention on the part of gynecologists and psychotherapists.

**Objectives:** The purpose of the study is to define the criteria for the diagnostics of ADD in perimenopausal women.

**Methods:** Modified menopausal Kupperman-Uvarova index (MMI), Greene Climacteric Scale (GCS) and a statistical module "Classification Trees" (CT) were used in the study. The study involved 127 perimenopausal women and was conducted at "Gynecological City Hospital", Belarus.

**Main outcome measures:** The algorithm of the module "CT" allowed reducing the number of significant analyzed parameters, allowed determination of their threshold values and ranges, as well as a sequence of incremental assessment to diagnostics of ADD in patients.

**Results:** The correct forecast of diagnostics of ADD according to CT was received in more than 95.0% women. Based on the CT 4 groups of perimenopausal women with ADD were emphasized: 1 group - moderate or severe severity of psychoemotional component of MMI (>8 points); 2 group - age ≤45 years and decreased sex drive; 3 group - age >50 years, absence of sexual relations, while maintaining sexual desire; 4 group - age >45 years, depression according to GCS >5 points in conjunction with anxiety according to GCS ≥7 points.

**Conclusions:** The proposed algorithm will improve the quality of diagnostic procedures for assessing the risks of ADD in perimenopausal women already during gynecological examination. In the test sample predictive efficiency was 84.0%. High values of information capacity allow to qualify the proposed algorithm as good.

### **P112: Complex treatment of mental disorders at women in perimenopause**

Hanna Tabolina (BY)

Belarusian Medical Academy of Post-Graduate Education

**Context:** Estrogen deficient states and various stressful factors at women in perimenopause are the cornerstone of development of mental disorders for which treatment application of methods of psychotherapy is important.

**Objectives:** Increase of efficiency of delivery of health care to women in perimenopause with mental disorders.

**Methods:** Beck's Depression Inventory, State-Trait Anxiety Inventory, Modified Menopausal Kupperman-Uvarova Index, The Utian Quality of Life Scale were used in the study. Examination and treatment of 65 women included in 2 groups was conducted: in the first (main) group (n=26) the complex treatment including the hormonal replacement therapy (HRT) - Femoston 1/10 mg film-coated tablets and psychotherapy, (including the developed method of mental self-regulation with sub steps system of self-control) was carried out; patients of the second group (control group) received (n=39) only HRT - Femoston 1/10 mg.

**Main outcome measures:** Therapeutic efficacy of comparable approaches to treatment was assessed immediately after the psychotherapy (3 months after the beginning of supervision) and after 9-12 months by the change in approach indicators manifestations of climacteric syndrome, mental disorders and quality of life.

**Results:** The positive dynamics of the mental and vegetative disorders as well as improving of the quality of life were more expressed in patients of the main group than in women, who were treated with the use of HRT only. Therapeutic effect of complex treatment was maintained for one year after the start of treatment.

**Conclusions:** Designed psychotherapeutic method makes it possible not to increase the HRT dose, contributes to improve the quality of life of perimenopausal women without significant increase in financial expenses.

### **P113: Palpitation in middle-aged women is associated with anxiety**

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Tokyo Medical and Dental University

**Objectives:** Palpitation is included in most of menopausal symptom inventories, whereas the precise underlying mechanism is not known. This study aims to investigate factors associated with palpitation in middle-aged women.

**Methods:** The records of 305 women aged 40 to 59 years who enrolled in a health and nutrition education program at a menopause clinic were analyzed cross-sectionally, approved by institutional review board. The prevalence of palpitation was estimated based on women's response to the Menopausal Symptom Scale. Effects of background characteristics, including age, menopause status, body composition, basal metabolism, cardiovascular parameters including heart rate variability, physical fitness, life style, and psychological symptoms, on palpitation were assessed using multivariate logistic regression analysis.

**Results:** Palpitation was reported by 35.8% of women. Factors associated with palpitation were: resting energy expenditure; systolic blood pressure; pulse rate; cardioankle vascular index; hand-grip strength; body ante-flexion; regular exercise; depression and anxiety. Multiple logistic regression analysis revealed independent association between palpitation and Hospital Anxiety Subscale (adjusted odds ratio 1.22 [1.15-1.32]).

**Conclusions:** Palpitation is highly prevalent in middle-aged women, and is associated with anxiety. Treatment of anxiety could relieve palpitation in this population.

### **P114: Breakout the myths of sleep and intelligence disorder in menopausal woman**

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Sebelas Maret University

**Objective:** To understanding Sleep Disorder and Intelligence Disorder in menopausal woman and breakout the myths of many factors such as age, the long of menopause period, occupation, income, domicile demographics, that influence it significantly.

**Methods:** Dependent variable of our study are Sleep Disorder and Intelligence Disorder that measure with Hamilton Rating Scale (HARS) Modification Questionnaire as tools to establish Sleep Disorder and Intelligence Disorder. Independent variable of our study is age, the long of menopause period, occupation, income, domicile demographics. The Samples are 100 menopausal woman that agree to participate in this study. We perform bivariate and also multivariate analysis to determine all factors that significantly influence Sleep and Intelligence Disorder in menopausal woman.

**Results:** From this study, we found 35% menopausal woman had sleep disorder, and 30% had intelligence disorder. The long of

menopause period had a significant impact on sleep disorder ( $p=0,030$ ). For intelligence disorder, age ( $p=0,017$ ), long of menopause ( $p=0,02$ ), and also occupation ( $p=0,02$ ) had statistical significant impact. After considering all external variables, from multivariate analysis, we found all independent variable had no significance in sleep disorder ( $p=0,386$ ) but occupation had significance in intelligence disorder in menopausal woman ( $p=0,043$ ).

**Conclusions:** Menopausal woman had sleep disorder and also intelligence disorder, the long of menopause period had a significant impact both on sleep disorder, and also intelligence disorder. Age, and occupation only had statistical significant impact on intelligence disorder.

### ***P115: Sleep disorders in Singaporean postmenopausal women: a cross-sectional survey***

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**Objective:** NIH State-of-the-science Panel in 2005 had indicated that 35-60% of postmenopausal women reported sleep problems. Both age and the menopause can contribute to sleep disorders in women. There are few studies on sleep disorders in postmenopausal women in Singapore. A sleep survey was conducted in 2008 in Singapore General Hospital amongst the postmenopausal women in our menopausal clinic to understand the problems in our local patient population.

**Methods:** Postmenopausal women attending the menopause clinic in Singapore General Hospital were invited to fill up a questionnaire to identify any sleep disorder and relevant associated factors. Analysis was made in 227 postmenopausal women surveyed.

**Results:** Their mean age was 60 years and majority of them were Chinese (93%). Mean age of menopause was 48 years and mean BMI was 23.5. Twenty two percent of the women were on HRT. Sleep initiation difficulty (difficulty in falling asleep) was reported in 49% (62/127) of women. Sleep maintenance difficulty (frequent awakenings) was reported in 65% (83/127) of women. More than 50% of women surveyed also reported unrefreshing sleep and snoring. There were no significant differences in sleep disorders between women on HRT and those who were not except for increased symptoms of insomnia and decreased snoring in women on HRT.

**Conclusions:** In conclusion, symptoms of sleep disorders are frequent in Singaporean postmenopausal women and their resulting health effects may require further attention.

## **Menopause management**

### ***P116: Comparison of the effects of methotrexate and ginger extract on reproductive parameters in female rats***

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Woman's Reproductive Health Research Center

**Objective:** Methotrexate is an anticancer drug used in chemotherapy. The purpose of this study was to evaluate the effect of

ginger extract on sex hormones of female rats treated with methotrexate.

**Methods:** In this experimental study, 56 female Wistar rats (10-12 weeks old) weighing 200-220g were randomly divided into control and experiment groups. Experiment group 1 was administered 5mg methotrexate intraperitoneally daily, experiment groups 2 and 3 were administered 20mg and 40mg of ginger extract orally daily, and experiment groups 4 and 5 received methotrexate and ginger extract. Sex hormones were measured after 8 weeks. One-way analysis of variance (ANOVA) was used data analysis.

**Results:** The results showed that serum concentrations of follicle stimulating hormone (FSH), luteinizing hormone (LH), decreased significantly in the group receiving methotrexate compared with the control group. The concentration of these hormones in experimental groups 2 and 3, which received ginger extract, increased compared with the control group. The serum levels of these hormones in groups 4 and 5, which received methotrexate and ginger, increased compared with the group receiving methotrexate.

**Conclusions:** Ginger extract reduced the adverse balance effects of methotrexate on sex hormone-producing cells. This effect is probably due to the antioxidant property of ginger.

### ***P117: Cimicifuga racemosa (CR) therapy in Asian patients: efficacy, safety and additional benefits***

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A double-blind, randomized controlled trial (RCT) in 244 Chinese patients showed a 3-month treatment with isopropanolic CR extract (iCR) to be as effective as tibolone, even for moderate to severe climacteric symptoms. Due to its better safety, the benefit-risk profile of iCR was significantly superior to that of tibolone ( $p=0.01$ ). A subset of 62 patients had at least one myoma at study start. Three-dimensional myoma diameters were measured with transvaginal ultrasound for pre-post comparison. With iCR treatment ( $n=34$ ) volume was reduced by 30.3%, which differed significantly ( $p=0.016$ ) from the increase by 4.7% under tibolone. Responder rates (volume reduction) were 70% for iCR and 36% for tibolone. Confounder-adjusted logistic regression showed a 4.7 times higher probability of myoma reduction under iCR compared to tibolone ( $p=0.008$ ).

Efficacy and safety of iCR in Asian patients were confirmed by further trials. One RCT demonstrated improvement in climacteric complaints and another in sleep disorders and quality of life, each with significant differences to placebo. GnRH-a induced symptoms in endometriosis patients were similarly reduced by iCR as by tibolone, yet iCR was safer. Combining iCR with SSRI was more effective than SSRI alone for perimenopausal depression. 6-month use of iCR significantly improved menopausal symptoms in patients after endometrial cancer surgery, accompanied by a significant increase in bone mineral density. The entity of these trials also shows that iCR is well tolerated and does not influence hormones, estrogen-sensitive tissue or liver function. In Asian patients iCR is effective and safe. First data suggest additional benefits for patients who not only suffer from climacteric complaints but also have myoma or an increased risk for osteoporosis.

## ***P118: Traditional Indian medicine and the menopause***

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The traditional Indian form of medicine is known as Ayurveda a Sanskrit word which means 'the science of the preservation of life'. Ayurveda is believed to have originated several thousand years ago. It is said to be the oldest form of medicine available. It is from India that this form of medicine travelled to China and formed the basis of the traditional Chinese medicine. Ayurveda is a comprehensive form of medicine that believes in the interconnectedness of the body and mind in maintaining the internal milieu of the body and consequently promoting good health. In recent times there has been an interest generated in bridging the gap between the traditional and modern medicine.

The current paper explores the relevance of this form of medicine in management of the climacteric. It looks at the science behind this form of medicine and how it can be used in the effective management of the menopause. However, we must be aware that traditional medicine is also viewed with mistrust and fear due to the side-effects reported in some cases. Toxic effects of such formulations used in traditional medicine have also been reported. Studies have also reported the presence of unacceptable high levels of heavy metals in such formulations. These issues will also be addressed in this paper. We need to look at the evidence in an objective manner and promote practices which are not detrimental to the health of the patient and only serve to improve the quality of life.

## ***P119: Daidzein isoflavone supplementation on IL-4, IL-6, IL-10, and TNF- $\alpha$ levels, in equol-producer and nonproducer postmenopausal women***

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**Objective:** Reducing level of estrogen in postmenopausal women causes immunosenescence state and daidzein isoflavone, one form of phytoestrogen, has effect as immunomodulatory in equal-producer human. Isoflavone was given as intervention and was expected to create effect in Th1 and Th2 cytokines level. This research was aimed to observe IL-4, IL-6, IL-10, and TNF- $\alpha$  level in postmenopausal women who produces equol and does not after treatment given.

**Methods:** Subjects were 50 women who underwent natural menopause with FSH >30 mIU/ml and E2 < 20 pg/ml in Persahabatan General Hospital. This study was an experimental research with randomized controlled trial (RCT). Blood equol from isoflavone and control groups were withdrawn to distinguish equol producers and non-producers. Different intervention applied for each group; one tablet consists of isoflavone 30 mg, calcium glycerophosphate 125 mg, and Vitamin D3 35IU and placebo for 6 weeks. IL-4, IL-6, IL-10, and TNF- $\alpha$  levels were determined using ELISA method. T-test analysis for two independent group was done to discover intervention's effect in isoflavone and control

group, then linear and logistic multivariate analysis was done to determine clinical characteristic of subjects.

**Results:** No significant difference found in IL-4, IL-6, IL-10, and TNF- $\alpha$  post Daidzein treatment ( $p > 0,05$ ). Yet, significant differences were observed in IL-6 level of control + equol nonproducer group and TNF- $\alpha$  in Daidzein + equol nonproducer, control + equol producer, and control + nonproducer groups.

**Conclusions:** Within only 6 months of research, there was no significant difference in the outcome of IL-4, IL-6, IL-10, TNF- $\alpha$  post Daidzein administration in equol producer and equol non-producer groups.

## ***P120: Cimicifuga racemosa for non-hormonal treatment of climacteric complaints – an overview***

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University of Barcelona

The European Medicines Agency approved a positive benefit-risk-ratio for Cimicifuga racemosa (CR) medicinal products (MP). Thereof, best documented and most thoroughly investigated in experimental and clinical studies including more than 12,000 patients is the isopropanolic CR extract (iCR).

Randomized controlled trials (RCT) consistently demonstrate iCRs efficacy and safety: climacteric complaints are significantly reduced compared to placebo. Efficacy is equal to low-dose hormone therapy or tibolone. Yet, compared to tibolone iCR shows a better safety profile. High-dosed iCR combined with St. John's Wort demonstrates its efficacy vs. placebo – extending therapeutic options for patients with more severe or pronounced psychic climacteric complaints. iCR is well tolerated, does not affect estrogen-sensitive tissue, and no evidence for hepatotoxicity could be found in clinical trials. Breast cancer survivors using iCR have a reduced risk for tumour recurrence. A large case-control study suggests breast cancer protective effects for iCR.

A Cochrane Review questioned the benefits of CR for improving Menopausal Symptom Scores. However, the review has critical shortcomings: missing differentiation between extract qualities and on-label/off-label use, incomplete identification of RCT and incorrect exclusion of RCT from the analysis. An updated meta-analysis including all appropriate RCT demonstrates CR to be significantly superior to placebo. However, only MP of CR with confirmed quality have proved efficacy for menopausal complaints and are accepted by medical regulatory agencies.

Regarding phytotherapy for climacteric complaints, clinicians should only recommend approved MP instead of plant preparations of unknown origin, since MP of CR are effective and safe, with iCR exhibiting the highest level of evidence.

## ***P121: The effects of treatment with Riselle in surgical menopause***

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**Objective:** The study was performed in "Elena Doamna" 3rd Clinic of Obstetrics- Gynaecology Iași, Romania and it proved that

hormone therapy in menopause causes a major improvement in the climacteric symptoms.

**Material and methods:** Study groups: 45 women with surgical menopause treated with Riselle (25 mg estradiol every 6 months-subcutaneous implant) aged between 35 and 56 years old and 20 women with surgical menopause, untreated, aged between 40 and 60 years old, mainly coming from towns and cities (76% vs 70%;  $p=0.910$ ). Inclusion criteria: amenorrhoea that was surgically induced at least for 1 year through bilateral ovariectomy/oophorectomy; the absence of a hormone treatment for at least 1 year.

**Results:** At the beginning of the study, the group without treatment recorded significantly more cases with migraines (14 vs 50%;  $p=0.014$ ), flushes (20 vs 45%;  $p=0.033$ ) and instability/agitation (8 vs 50%;  $p=0.005$ ). The patients treated with Riselle recorded, after 6 months, significantly more cases with libido (32 vs 5%;  $p=0.024$ ). At the end of the study, the untreated group recorded significantly more cases with flushes (0 vs 30%;  $p=0.012$ ); instability/agitation (0 vs 25%;  $p=0.030$ ); insomnia (0 vs 30%;  $p=0.012$ ) and pollakiuria (0 vs 15%;  $p=0.045$ ). For the patients treated with Riselle, flushes are mainly present (96%) at the beginning of the study, but their frequency decreases below 20% after 12 months of treatment ( $p=0.001$ ); the libido appears after 6 months of treatment for 28-36% of the women ( $p=0.012$ ); stress urinary incontinence was found in 24% of the cases at the beginning of the study, but its frequency diminished and almost disappeared by the end of the study ( $p=0.026$ ).

**Conclusions:** After 2 years of treatment, the patients with surgical menopause that were treated with Riselle restored their libido and had remarkably less flushes and urinary symptoms.

### **P122: Evaluation of vasomotor symptoms after 20 years with hormone replacement therapy**

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**Objective:** To evaluate vasomotor symptoms with consensual self-administered scale containing 30 items in menopausal women over 20 years of treatment.

**Material and methods:** This was a cross section study of 135 patients with cyclic combined HRT (54 patients), continuous (37 patients) or estrogen alone (44 patients), adequately informed and your consent, decide to participate in the study. They complete a scale of climacteric symptoms at initial year, at 5, 10, 15 and 20 years of treatment.

**Results:** The age of patients was  $48.7 \pm 6.8$  years and they were menopausal last an average  $3.3 \pm 3.8$  years. The test has a Cronbach alpha of 0.802. The baseline result was  $7.3 \pm 4.3$ ,  $3.2 \pm 3.7$ , at year are  $4.2 \pm 3.8$ ,  $4.0 \pm 3.3$  at 5 years,  $15 3.9 \pm 3.5$  at 15 years and  $20 \pm 3.7 4.4$  at 20 years. We found a significant improvement at one year of treatment,  $p < 0.0001$ , which remains at 20 years ( $p < 0.0001$ ).

**Conclusions:** Hormone replacement therapy improves the climacteric symptoms and quality of life is maintained through 20 years of treatment.

### **P123: Non-hormonal treatment of vasomotor symptoms in female patients with and after breast carcinoma**

René Druckmann (FR)

ANEMO Menopause Center

The tumour is hormone-sensitive in around two thirds of all cases. Restoring the quality of life of these patients is key to their well-being. The innocuousness and harmlessness of a purified cytoplasm of pollen (PCP) obtained from selected pollen grains by a patented procedure, free of allergens, has been demonstrated in numerous studies. The effectiveness in the treatment of VMS was demonstrated in a randomised, double-blind, controlled study against a placebo. It is effective in the case of vasomotor symptoms (VMS) during the peri- and postmenopause, especially in women with and after breast cancer. PCP contains no phytoestrogens nor hormones. It therefore has no hormonal effects, does not activate the oestrogen receptors and does not stimulate the proliferation of cancer cells. No oestrogenic effect could be demonstrated in a further assay in which the capacity of the PCP to bind to the oestrogen receptors was tested using MCF7 and 293T cells. Blood tests on FSH, oestrogens, testosterone and SHBG in further studies showed no change in concentrations in female patients who were treated with PCP.

The vasomotor symptoms are reinforced and/or intensified by Tamoxifen. Tamoxifen is broken down by the cytochrome P450 2D6 to form 4-hydroxytamoxifen and other active metabolites. Anti-depressants (Fluoxetine and Paroxetine) and selective serotonin reuptake inhibitors (SSRI) have been prescribed to mitigate Tamoxifen-induced VMS. However, SSRI are powerful CYP2D6 inhibitors and can reduce the effectiveness of Tamoxifen. In contrary, there are no pharmacological interactions between the pollen extract and the CYP2D6 enzyme system. No inhibition of the enzymes was found at up to five times the daily dosage.

These PCP appear to be a non-oestrogenic alternative to hormone therapy for women with VMS, even for women with and after breast cancer.

### **P124: Custom compound HT - a window of opportunity for special cases**

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**Objective:** Although the use of commercially manufactured HT to treat menopausal symptoms has declined during the past 12 years in response to the now well-known safety findings of the Women's Health Initiative trials, use of custom compounded hormone therapy seems to have increased.

**Methods:** Woman (at age of 39) with refractory anemia, following bone marrow transplantation and primary hyperparathyroidism, sustained premature ovarian failure (POF). After systemic biologic treatment (azacitidine) and corticosteroids therapy, beside extreme climacteric symptoms (Green climacteric scale =59) and impaired QoL, she had elevated liver enzymes. Therefore, she was not a candidate for p.o. HT.

**Results:** We started with FDA approved 17-beta estradiol patch 0,5 mg (Climara) together with micronized progesterone intravaginally 2x100 mg (utrogestan) for 3 months. She was not satisfied which was proved with Green climacteric scale =54. The custom

compound HT started with 17-beta estradiol 0,5mg gel 2x/day and micronized progesterone in liposomal gel 100mg/daily. She was much better but she complained of low libido, still decreased sex drive and emotional instability. Testosterone 1% gel (10 mg/g gel) was added. She was completely satisfied, Green climacteric scale =8. Liver enzymes were normal except gamma-GT which was still a bit elevated but almost 4 times lower than before the treatment (7,49  $\mu$ kat/L vs. 2,13  $\mu$ kat/L).

**Conclusions:** Custom compound HT has possibility of tailoring and adjusting the therapy upon the individual need, which was the everlasting goal in menopause medicine. No matter there were some problems such as: lack of scientific evidence, no FDA oversight, so safety and efficacy were not tested, there was definitively a window of opportunity for special circumstances.

### **P125: Factors affecting complementary and alternative medicine use by women experiencing menopausal symptoms in Korea**

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**Context:** The use of CAM (complementary and alternative medicine) has been increasing throughout the world. However, the prevalence, exact definition and the effectiveness of CAM during menopause are not been fully evaluated.

**Objectives:** To describe prevalence rates of CAM use for the relief of menopausal symptoms among Korean women and to investigate the factors affecting CAM use.

**Methods:** Women aged 45-65 years attending public health centers completed self-administered questionnaire. Data on general demographics and health characteristics, menopause related symptoms and the use of CAM and pharmaceutical treatments during previous 12 months were collected.

**Results:** A total of 391 (87%) questionnaires were collected back for analysis. All of the responding women stated that they have been experiencing menopausal symptoms and 48.3% were categorized into 15 and more of Kupperman index. Symptoms ranged from vasomotor symptoms, psychological and physical symptoms to sexual discomfort. 70.8% of the responding women had used CAM interventions average 3.9 type of CAM. Among the CAM user, 29.6% had used both hormone replacement therapy and CAM. Popular CAM interventions were dietary supplementation, herb medicine, mind-body medicine and traditional Chinese medicine including acupuncture. The significant variables between user and non-user of CAM were age, BMI, parity, level of happiness and satisfaction of income, dietary habits, concerning about menopause, menstrual status, Kupperman index and severity of menopausal symptoms. In the logistic regression analysis, age, BMI, menstrual status and severity of menopausal symptoms were revealed as significant factors affecting CAM use. **Conclusions:** High prevalence of CAM use by women experiencing menopausal symptoms should encourage clinicians to be willing to provide risks and benefits of CAM to the menopausal women.

### **P126: Hyperprolactinemia in women at peri- and postmenopause: a diagnostic dilemma**

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**Introduction:** Pituitary prolactin secreting tumors (50-60% - microadenomas, 40-50% - macroadenomas) are the most often causes of pathologic hyperprolactinemia. The highest prevalence of microprolactinomas is observed in young women aged 25-30 years though half of macroprolactinoma cases are found in women over 50 years.

**Discussion:** During reproductive age menstrual irregularities and infertility are clinical markers for hyperprolactinemia. However hyperprolactinemic amenorrhea in women 40-50 years can be considered as premature or early menopause. Hence diagnosis of prolactinomas is overlooked. Hyperprolactinemia signs in these women are absence of vasomotor symptoms (which experience most of the women with premature/early/natural menopause) and FSH levels lower than usually in postmenopause. So it is essential to evaluate the prolactin levels in an amenorrheic woman aged 40-50 years with FSH levels <25 mU/l and without climacteric symptoms. Other clinical symptoms may be visual disturbances and headache that are caused by macroadenoma which is the most frequent hyperprolactinemia reason in women over 50 years. So these complaints constitute an indication for pituitary magnetic-resonance imaging. If pituitary tumor is revealed (including incidentally discovered cases) prolactin levels should be also evaluated. Early treatment in patients with macroprolactinoma is necessary not only for restoration of physiological hormonal balance but also for control of tumor volume and prevention of visual field impairment and severe headache due to further growth of macroprolactinoma.

**Conclusions:** Diagnosis of prolactinomas remains a challenge in women at peri- and postmenopausal age due to absence of common reproductive symptoms. Indications for prolactin measurement in women over 40 years are amenorrhea with FSH <25 MU/l and diagnosed pituitary tumor.

### **P127: Stage of reproductive aging and hypogonadotropic hypogonadism: does 'central menopause' exist?**

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**Introduction:** Natural postmenopause can be defined as a "physiological hypergonadotropic hypogonadism". According to STRAW +10 the main menopausal signs reflect a loss of a follicular reserve. However standard criteria of reproductive aging cannot be applied to women with hypogonadotropic hypogonadism when amenorrhea and low FSH levels are consequences of hypothalamo-pituitary dysregulation and does not reflect an ovarian aging.

**Discussion:** Hypogonadotropic hypogonadism (HH) can be caused by genetic disorders, organic lesions of hypothalamo-pituitary region as well as functional factors including weight loss, excessive physical exercises and stress (so called functional hypothalamic amenorrhea - FHA). HH is reversible in the most of the FHA cases and is persistent in genetic and organic cases.

We analyzed clinical symptoms and metabolic parameters of 161 women (24 [19; 44] y.o.) with permanent HH, 45 healthy women

of similar age (25 [20; 42] y.o.) and 53 healthy postmenopausal women of middle/old age (56 [50; 66] y.o.)

The frequency of the physical and psychoemotional problems, urogenital disorders, increased body mass index, hypercholesterolemia, hypertriglyceridemia and osteopenia was significantly higher in untreated young women with HH compared to healthy women of similar age, however, was similar to what was observed in postmenopausal women. The main difference was the rate of vasomotor symptoms (low in HH and high in natural postmenopause). Taking into account all these clinical and biochemical features of CH we conclude that it is corresponded to postmenopausal stage of reproductive aging independently of their chronological age, FSH and AMH levels.

**Conclusions:** The irreversible central hypogonadism (due to genetic or organic disorders) can be considered as a "central postmenopause" with characteristic variances from natural postmenopause.

### ***P128: A study on the effect of postmenopausal estrogen plus progestin, tibolone and Raloxifene therapy on vaginal bleeding and endometrial thickness***

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Chosun University Hospital

**Objectives:** To study the effect of low-dose estrogen-progestin therapy (EPT), tibolone and raloxifene on the incidence of vaginal bleeding and endometrial thickness over a 3-year period.

**Methods:** 273 postmenopausal women were studied in retrospective design. Vaginal spotting/bleeding and endometrial thickness as assessed by transvaginal ultrasonography. Women received tibolone 2.5 mg (N=81), raloxifene HCl 60 mg (N=58), estradiol hemihydrate 1.03 mg/drospirenone 2mg (N=86), and no therapy (controls, N=48). Women with suspected endometrial pathology were performed endometrial sampling for confirm endometrial malignancy.

**Results:** Bleeding/spotting incidence was highest (28,6%) among EPT users compared to controls ( $p < 0.001$ ). The incidence under tibolone and raloxifene was 14.9% and 1.6%, respectively, while 1.9% of women not receiving therapy reported vaginal bleeding. Mean endometrial thickness was not significantly affected in any of the groups studied. The drop-out rate due to bleeding was higher EPT regimens.

**Conclusions:** EPT, tibolone and raloxifene do not appear to associate with significant changes in endometrial thickness in the majority of cases. But Raloxifene associated with the lowest incidence in vaginal spotting and bleeding

### ***P129: Automedication and supplement treatment in menopausal women***

Assaad Kesrouani (LB) and Alain Daher (LB)

Saint Joseph University

**Objective:** To determine the modalities of supplementation therapies in Lebanese menopausal women.

**Methods:** In a cohort study done in Beirut over one year, menopausal women that presented for a regular check-up were asked

about automedication and supplements that they were taking. Questions included type and duration of treatment, reason for taking the supplement, who advised the patient to take it and possible adverse effect that it exerted. We also searched for the expectations of the patient for the treatment and how long would she consider taking it. Data were analyzed at the end of the study

**Results:** Among the 836 patients, 804 women (96%) accepted to take part in this study. The mean age was 62 years [47–72]. Calcium intake was already prescribed to 95% of the women by her physician and 91% were indeed taking it. In 354 women (44%), other products were used and were represented by multi-vitamins (14%), Iron (11%), vitamin E (8%), Magnesium (7%) and fish oil derivatives (3%) and miscellaneous (1%). The main person that advised for these medication is reported as follows: Friend (34%), pharmacist (31%), family (25%), suggested by media (10%). The mean duration of treatment is three months [two weeks to one year or ongoing]. The product that led to the most adverse effects is the fish oil derivative (23%) and the least the magnesium (4%). The main reason for stopping treatment is based on compliance issues. Most people stated that treatment gives them 'more energy' (52%). Only 6% reported no benefit at all.

**Conclusions:** Menopausal patients tend to have a trend for automedication with many supplements. Despite satisfaction, compliance rate is relatively low and many of them stop the treatment following few months. Physicians should spend more time to address benefits and adverse effects of supplements in the menopausal period.

### ***P130: Perceptions of postmenopausal symptoms and treatment options among Korean middle-aged women***

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**Context:** Korean society is a fast-ageing society and increasing number of Korean women suffers from postmenopausal symptoms.

**Objective:** This study aims to investigate how Korean middle-aged women perceive postmenopausal symptoms and its treatment options.

**Methods:** A cross-sectional study was conducted by surveying 2330 Korean women with a structured questionnaire including sociodemographic data and information regarding the menopause and its treatment. 2330 Korean women aged from 45 to 65 years old were included. After stratified sampling, random quota sampling of the participants was done.

**Main outcome measures:** The number of women seeking medical treatment was low and proper knowledge of hormone therapy (HT) was lacking.

**Results:** More than half (65%) of all participants perceived postmenopausal symptoms as a disease, and 66.8% have heard about HT. 30.9% positively considered having HT, while relatively smaller number (7.3%) had the opposite views. The most common reason for those with negative views about HT was the concern of side effects (47.3%), especially worrying about the risk of developing cancer (41.1%). Hot flush was the most commonly experienced symptom (75.4%), and vaginal dryness, fatigue, insomnia were next in sequence. Hot flush was also the most difficult to endure (33.1%), followed by insomnia and fatigue. For managing the symptoms, 36.5% tried non-medical treatments such as diet therapy or exercise, and only 19.7% had HT. Few

people (29.9%) visited OBGY clinics for consultation and treatment due to the idea that the symptoms may be managed enough by simple lifestyle modification.

**Conclusions:** HT use in Korea was rather low compared to non-medical treatment options. Education about the safety and positive effects of HT, and seeking professional healthcare from physicians should be encouraged.

### ***P131: A 12-week, multi-center, double-blind, randomized, placebo-controlled clinical trial for the evaluation of the efficacy and safety of PAC-EX01 (EstroG-100®) on menopausal symptoms***

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**Objective:** The aim of this study was to assess the efficacy and safety of PAC-EX01 (Herbal extract, EstroG-100®) on menopausal symptoms compared with placebo.

**Methods:** Multicenter, double-blinded, randomized, placebo-controlled clinical trial was performed between March 2014 and August 2014 for 105 women with menopausal symptoms. Patients were randomly assigned into two groups (study group: 51 patients vs. control group: 54 patients). The study group was administered with PAC-EX01 (2 tablets, a total of 514mg/day), and the control group with placebo. Modified Kupperman index was used to assess the menopausal symptoms. E2, FSH, and endometrial thickness was evaluated for the safety of PAC-EX01.

**Results:** Significant decrease of Kupperman index was found in study group administered with PAC-EX01 (EstroG-100®). There was significant difference in nervousness, depression, vertigo, fatigue, arthralgia, and hand and foot numbness. But there was no significant difference in hot flush, insomnia, headache, and palpitation and vaginal dryness between two groups. There was no significant difference in E2, FSH, endometrial thickness.

**Conclusions:** The PAC-EX01 (EstroG-100®) is effective in various menopausal symptoms and improves the quality of life in women with menopausal symptoms without any adverse effects.

### ***P132: The effects of Black Kohosh root extract on the vasomotor symptom and bone of postmenopausal women***

Hongbae Kim (KR)<sup>a</sup>, Young Lim Oh (KR)<sup>a</sup>, Heung Yeol Kim (KR), Wan Ku Eo (KR)<sup>b</sup> and Hyuck Jung (KR)<sup>c</sup>

<sup>a</sup>Kosin University College of Medicine; <sup>b</sup>Kyunghee University College of Medicine; <sup>c</sup>Chosun University College of Medicine

**Objectives:** To evaluate the effect of black cohosh root extract (BCRE) on vasomotor symptoms and bone mineral density in postmenopausal women.

**Methods:** This prospective randomized clinical trial examined the effects of BCRE on vasomotor symptom, bone mineral density, and biochemical markers of bone turnover in 90 postmenopausal women. Treatment included BCRE (group I, N=30) or 0.625 mg Conjugate Equine Estrogen (CEE) (group II n=30) for 6 months. Kupperman Index, BMD, and biochemical bone marker were measured at 0, 3, and 6 months.

**Results:** Kupperman index decreased significantly at 3 months and 6 months of the treatment in group I and group II (P < 0.05). BMD of lumbar spine increased significantly during the treatment in group I and group II (P < 0.05). Urinary deoxypyridinolin decreased significantly at 3 months and 6 months of the treatment in group I and group II (P < 0.05).

**Conclusions:** BCRE appears to be a safe and effective alternate to hormone therapy for vasomotor symptoms and may be especially useful in women with intolerance or contraindication to traditional hormonal therapy.

### ***P133: Efficacy of porcine placental extract on wrinkle widths below the eye in climacteric women***

Koji Koike (JP)<sup>a</sup>, Chikako Yoshikawa (JP)<sup>b</sup>, Tiger Koike (JP), Fumihide Takano (JP)<sup>c</sup> and Nobutaka Suzuki (JP)<sup>b</sup>

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**Objective:** Injections of human placental extract, which is known to play a role in skin regulation, have long been used for the treatment of skin wrinkles and nonhealing wounds. Porcine placental extract (PPE), an oral supplement, was recently developed for this purpose. The aim of this study was to assess whether PPE has a positive effect on the improvement of fine wrinkles below the eye in climacteric women.

**Methods:** We first noninvasively measured wrinkle widths with a skin analyzer in a cross-section of 185 healthy adult Japanese women. Next, 44 climacteric women with mild or few climacteric symptoms were enrolled into an open-label, randomized, controlled study of the effect of PPE on wrinkle widths. A retrospective comparison of wrinkle widths with or without PPE treatment in 123 climacteric women with climacteric symptoms was also performed.

**Results:** Wrinkle widths below the eye in women ≥30 years of age were significantly higher than in women 20 to 29 years of age. Treatment with three capsules of PPE per day was significantly (P < 0.05) effective in reducing wrinkle widths at 24 weeks compared with control subjects. Retrospective analysis showed that subjects treated with three (P < 0.05) and six (P < 0.01) capsules of PPE per day observed a significant reduction in wrinkle widths compared with untreated subjects.

**Conclusions:** Oral PPE treatment is possible option for improvement of fine wrinkles below the eye in climacteric women.

### ***P134: Pharmacologic rationale for beneficial effects of *Vitex agnus castus* on infertility and outcomes in polycystic ovary syndrome***

Susana Garcia De Arriba (DE)<sup>a</sup>, Jennifer-Christin Kuchernig (DE)<sup>a</sup>, Stephanie Pickartz (DE)<sup>a</sup>, Raluca Grigore (RO)<sup>b</sup>, Belal Naser (DE)<sup>a</sup> and Klaus-Ulrich Nolte (DE)<sup>a</sup>

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**Objective:** Polycystic ovary syndrome (PCOS) is characterized by anovulation or cycle irregularities and hyperandrogenism. It affects up to 10% of reproductive women and may result in infertility. Hormonal imbalance rise from elevated LH levels. Current therapies (like oral contraceptive, clomiphene) often have adverse effects and are not always effective (low pregnancy rates). Thus, demands arise for alternative and safer therapies. *Vitex agnus castus* (VAC) has proven clinical efficacy against cycle irregularity, luteal phase dysfunction, and female infertility. This pharmacological update evaluates published data for pharmacodynamic VAC actions and their positive impact on PCOS.

**Methods:** Literature in reference databases (e.g. MEDLINE, EMBASE, BIOSIS) was collected till 2015. Preclinical and clinical data regarding the possible beneficial effects of VAC in PCOS were classified in 4 groups: 1) irregular menstrual cycles; 2) chronic anovulation; 3) luteal-phase dysfunction; 4) hyperandrogenism.

**Results:** Preclinical studies confirmed the binding of VAC constituents to dopamine and  $\mu$ -opioid receptors in the pituitary anterior lobe and hypothalamus. Dopaminergic modulation of pituitary gland function lowers prolactin secretion and balances the level of LH and FSH. In a rat PCOS model, VAC increased progesterone and decreased testosterone levels. Clinical data corroborate that VAC restored pituitary hormone balance, ovarian function and balance of progesterone to estrogen levels during luteal phase. VAC lowers LH, prolactin and testosterone levels.

**Conclusions:** Current studies suggest that VAC modulates menstrual cycle and balances hormone profiles in PCOS women. Accordingly, the use of VAC in PCOS patients may have beneficial effects by enhancing fertility and improving outcomes.

### ***P135: Non-inferiority, multi-center, double-blind, randomized, prospective clinical trial for the comparison of the efficacy and safety of the *Unicenta* and *Melsmon* injection for the menopausal symptoms***

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**Objectives:** The purpose of this study was to evaluate the efficacy and safety of *Unicenta* (placental extract) compared to *Melsmon* (placental extract) in women with the menopausal symptoms.

**Methods:** This study was a non-inferiority, multi-center, double-blind, randomized, prospective clinical trial. A total of 104 patients were included in two different academic medical centers from April 2013 to January 2014. Patients were randomly assigned into two groups (52 patients injected with *Unicenta* vs.

52 with *Melsmon*). The changes of the Kupperman index and the hormonal level were analyzed.

**Results:** The effect of *Unicenta* injection was not inferior to that of *Melsmon* as measured by the change of Kupperman index 12 days after administration of each injection in both intent-to-treat ( $p=0.95$ ) and per-protocol populations ( $p=0.49$ ), respectively. There was no significant difference in the adverse effects between the *Unicenta* group (11.76%) and the *Melsmon* group (7.84%) ( $p=0.51$ ). Statistical significance was not found in the hormonal levels (FSH, E2), endometrial thickness, and vital signs.

**Conclusions:** The results of study indicated that *Unicenta* is not inferior to *Melsmon* in terms of the efficacy and safety using the Kupperman index and hormonal levels. Compared to the *Melsmon*, *Unicenta* administrations improved the menopausal symptoms

### ***P136: Safety and tolerance of a natural supplement containing glucosinolates, $\beta$ -sitosterol and citrus flavonoids in healthy adult women***

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**Background:** Although menopausal hormone therapy is still the most effective option to treat symptoms, after a decade of the WHI study its use is still low. There is an increasing trend among patients and doctors to seek alternatives.

**Objective:** To determine the safety and tolerance of a natural supplement containing glucosinolates,  $\beta$ -sitosterol and citrus flavonoids (Warmi®: W).

**Methods:** This was a phase I, randomized, double-blind, placebo-controlled study in which sixty otherwise healthy regularly cycling women aged 18 to 40 randomly receive W= 1.65 gr/day ( $n=17$ , W1) or W= 3.3 gr/day ( $n=19$ , W2) or placebo ( $n=17$ ) for three months. Clinical and laboratory parameters were measured before and after treatment.

**Results:** No differences in socio-demographic, clinical and lab parameters were observed at baseline among studied groups; however, all women displayed an increased mean body mass index (BMI). The W2 group displayed a significant decrease of baseline blood glucose levels. Total cholesterol levels significantly decreased in the W1 group. At the end of the trial no adverse effects were reported among groups W1 and W2; and there was no effect on menstrual cycles and serum hormonal profile (estradiol, LH, FSH and progesterone) and also BMI index and blood pressure values.

**Conclusions:** The studied compound in both dosages demonstrated to be safe and tolerable in adult healthy women; there is a need to perform a trial among mid-aged women.

### ***P137: Treating menopausal symptoms with Cimicifuga racemosa is safe for the breast***

Mary Minkin (US)

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In clinical practice, frequently questions arise whether climacteric complaints in breast cancer patients can be treated with *Cimicifuga racemosa* (CR) extracts. Recent research has shown extracts of CR rootstock to be free of phytoestrogens. Furthermore, intake of CR medicinal products does not influence hormones.

Almost all data regarding breast safety have been generated with a special isopropanolic CR extract (iCR). 6-month intake of iCR affects neither mammographic breast tissue density (visual and digitized assessment) nor breast epithelial cell proliferation. This was confirmed by mammograms of patients treated with CR for 12 months. There were also no changes in breast ultrasounds in two studies investigating the 6-month use of iCR, one including a 12-month follow-up. Nipple aspirate fluid of CR treated patients showed neither changes in morphology nor in estrogen or estrogen regulated protein values.

Breast cancer survivors using iCR had a reduced risk for tumour recurrence compared to non-users. A large case-control study sponsored by the German Cancer Aid e.V. found exclusively the intake of iCR to be associated with a reduced risk for breast cancer, while other CR extracts did not influence breast cancer risk. These results were confirmed by two further case-control studies. The clinical data are substantiated by a wide range of experimental studies. They showed that iCR inhibited the growth of breast cancer cells and the production of estrogen in breast tissue. Additionally, iCR did not stimulate and even reduced breast cancer growth and enhanced the effects of tamoxifen.

The data show collectively and coherently that treatment of climacteric complaints with iCR is not only safe at breast tissue but is even associated with reduced risks for breast cancer and breast cancer recurrence.

### ***P138: Menopausal symptoms and quality of life after isoflavone daidzein supplementation for menopause women with non-equol producer status***

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*Objective:* Physiological changes during menopause contribute to symptoms of vasomotor, physical, psychological, and sexual dysfunction in women. Every woman may experience different symptoms with different severity regarding menopause. Many ways to deal with those symptoms have been established, including soy-germ supplementation. Daidzein is a form of isoflavone found in soy-germ that produces equol metabolite similar to estrogen. Daidzein supplementation is believed may reduce the symptom of menopause. This study was conducted to assess the effect of isoflavone daidzein supplementation toward menopausal symptoms and quality of life on postmenopause women with non-equol producer status.

*Methods:* This is a single-blind randomized controlled clinical trial to assess the impact of isoflavone daidzein supplementation compared to placebo on postmenopause women. Menopausal symptoms were assessed using MENQOL questionnaire on the beginning and the end of trial. 8 weeks course of daidzein supplementation and placebo were given to each group.

*Results:* Nineteen subjects were on daidzein group and twenty subjects were on placebo group. Equol producer was not found on the subjects. There was significant mean reduction of all domain of menopausal symptoms and quality of life improvement in after 8 weeks course of daidzein supplementation ( $p < 0.05$ ). However, those findings were not different between intervention and control groups ( $p > 0.05$ ).

*Conclusions:* Soy-germ isoflavone daidzein supplementation was not superior compared to placebo to improve menopausal symptoms and quality of life on menopause women with non equol producer status.

### ***P139: Cimicifuga racemosa for treatment of vasomotor symptoms: update of mode of action***

Susana Garcia De Arriba (DE), Stephanie Pickartz (DE), Belal Naser (DE) and Klaus-Ulrich Nolte (DE)

Schaper & Brümmer GmbH & Co. KG

*Objective:* *Cimicifuga racemosa* (CR) has shown its efficacy against vasomotor symptoms (VMS). Although numerous studies have been conducted, the mode of action is still controversially discussed because the pathophysiology of VMS is still unclear. Nowadays circulating levels of estrogen are no longer considered as triggers for VMS. The hypothalamic thermoregulatory center, rather than the pituitary locus, appears to be the most likely site of thermoregulatory dysfunction. Estrogen fluctuations affect several neurotransmitter systems and cause imbalances of serotonin- and noradrenalin-levels in the hypothalamic thermoregulatory center, which have been shown to result in VMS. The aim of this pharmacological update is to discuss the relevant pharmacological properties of CR, which may contribute to the mechanism of action for the relief of VMS.

*Methods:* Literature in reference databases (e.g. MEDLINE, EMBASE, BIOSIS) was collected till 2015. For the purpose of this analysis, we classified the effects of CR in 2 groups: 1) interaction with brain receptors; 2) modulation of brain activity and brain metabolism.

*Results:* Several publications verified that CR contains substances, which bind to serotonin, dopamine, GABA and  $\mu$ -opioid brain receptors leading to receptor-mediated functional activity. In addition, CR is also able to modulate the ratio of cerebral monoamines and metabolites, brain activity, especially serotonergic and dopaminergic systems and  $\mu$ -opioid receptor availability.

*Conclusions:* The current data suggest that alleviation of VMS by CR is not due to estrogen-agonistic effects. The hypothesis of an association between CNS receptor-mediated effects and an efficacious relief of VMS have become more plausible, since iCR has been shown to bind to CNS receptors, modulate brain function and metabolism involved in thermoregulation and brain ageing.

### **P140: Role of MRT in management of sleep disturbance of menopause**

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**Background:** Beside vasomotor symptoms sleep disturbance is very distressing condition in menopause. The insomnia leads depression and poor quality of life for menopausal women. Sleep disorder is 3.4 times more in menopause than pre-menopause. 500 million women will enter in menopause within 5-10 years. So effective therapy is needed to prevent insomnia and its related morbidities for this huge population. To have good sleep and quality life is the right of menopausal women

**Objective:** To investigate the effect of MRT on sleep disturbances in menopause.

**Study design:** Randomized, double blinded, placebo controlled study carried out in Sikder Women's Medical College Hospital, Dhaka from Jan 2015 to Jan 2016.

**Methods:** 320 menopausal women with insomnia were enrolled for 6 months of treatment of estradiol 2mg + MPA and placebo. Sleep quality like sleep efficiency, total sleep time, number of awakenings were compared before and after treatment. The Insomnia Severity Index (ISI) questionnaires were used for sleep quality assessment. Hot flushes, sweating and palpitation were asked for Vasomotor domain using MENQOL. Women with psychiatric illness or any severe diseases were included from the study.

**Results:** Our study fails to show any significant difference in sleep efficiency improvement between women having MRT and placebo. The sleep time <4 hours (28% vs 31%,  $p=0.663$ ), sleep efficiency (31.3% vs 25.0%,  $p=0.463$ ), no. of awakenings >3 (69.7 vs 48.7,  $p=0.028$ ), patient satisfaction rate (21.1% vs 9%) were not different with MRT. But the vasomotor symptoms improved (50% vs 18.6%,  $p<0.001$ ) in MRT group.

**Conclusions:** MRT did not ameliorate the sleep disturbances in menopausal women. Future research are needed to reach a comprehensive understanding of its mechanism in dealing with sleep disturbance in menopause.

### **P141: The association between premenopausal syndrome and climacteric disorders**

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**Objective:** Premenstrual syndrome (PMS) occurs in the premenstrual phase. Women who suffer from PMS usually have normal menstrual cycles and their hormone levels are basically normal. On the other hand, climacteric disorders occur in the perimenopausal transition. These symptoms are brought about by hormonal changes, especially the decreasing of estrogen. Though it seems that these are quite different, these symptoms have a lot in common. Thus we investigated the association between premenopausal syndrome and climacteric disorders.

**Methods:** Participants were 28 women in menopause transition. 16 women who were treated for climacteric disorder by hormone replacement therapy or kampo therapy were labeled "the climacteric group". 12 women who were aged 40 to 60, came as

outpatients for gynecological checkup and didn't suffer from climacteric disorders were divided into "the control group".

We used two interview sheets. One was a questionnaire about their experiences of premenstrual symptoms, another was a climacteric score made by the Japanese Society of Obstetrics and Gynecology.

**Results:** 1. Regarding the frequency of experiences of premenstrual symptoms, there was equal percentage in both groups. 2. The percentage of women who experienced PMS symptoms that bothered their daily life was higher in the climacteric group than the control group.

**Conclusions:** The results suggested that there is an association between the severity of premenstrual symptoms and the occurrence of climacteric disorders.

### **P142: Does the menopausal status of female gynecologists affect their prescription of hormone therapy?**

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**Objective:** To evaluate if menopausal status and symptoms among female gynaecologists would influence their clinical behaviour related to menopausal hormone therapy (MHT).

**Methods:** Female gynaecologists of 11 Latin American countries were requested to fill out the Menopause Rating Scale and a questionnaire containing personal information and that related to MHT use.

**Results:** 818 gynaecologists accepted to participate (86.4%). Overall, mean age was  $45.0 \pm 10.7$  years, 32.2% were postmenopausal, and 17.6% worked in an academic position. An 81.8% reported that they would use MHT if they have symptoms; regardless of menopausal status. Academic gynaecologists favour personal MHT use in a higher rate ( $p=0.04$ ) and have a higher MHT prescription rate as compared to non academic ones ( $p=0.0001$ ). Same trend was observed among post- as compared to premenopausal ones ( $p=0.01$ ) and among those who had hysterectomy alone as compared to those experiencing natural menopause ( $p=0.002$ ). The presence of menopausal symptoms did not influence their MHT prescription. Current MHT and alternative therapy use was higher among post- than premenopausal gynaecologists (both,  $p=0.0001$ ) and among those who had undergone hysterectomy than those experiencing natural menopause. A 38.5% perceived breast cancer as the main risk related to MHT and an 86.4% prescribed non-hormonal drugs or alternative therapies (84.5%).

**Conclusions:** Most female gynaecologists of this survey would use MHT if menopausal symptoms are present. Postmenopausal physicians use MHT and prescribe it to their symptomatic patients in a higher rate than premenopausal ones.

### **P143: Safety of the isopropanolic Cimicifuga racemosa extract (iCR) on the endometrium**

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The isopropanolic Cimicifuga racemosa extract (iCR) is widely used in climacteric women as an alternative to classical hormone replacement therapy. Preclinical data from several animal studies

show that iCR does not possess any uterotrophic activity. The uterine weight remains unchanged and there is no upregulation of estrogen responsive genes. What is more, in the histological evaluation the endometrium remains atrophic and the expression of the proliferation marker Ki67 is not affected. In animal models of endometrial cancer, treatment with iCR does not enhance tumor growth or metastatic potential. Beyond that, 12 months of iCR treatment resulted in an attenuated tumor malignancy, as evident in uterine gland and endometrial morphology. In clinical trials, the use of iCR in climacteric women does not affect the endometrial thickness and therefore does not evoke postmenopausal vaginal bleedings, which is in contrast to tibolone. Also in women with uterine pathologies such as fibroids or even endometrial cancer, the use of iCR turns out to be safe. A reduction of the myoma volume was observed in women taking the iCR for 3 months; whereas, in the tibolone group a slight increase was noted. In patients treated with the GnRH-agonist goserelin due to endometriosis, the endometrial thickness was also not influenced by the concomitant use of the iCR. In women after surgical treatment of uterine cancer, there was no recurrence of the disease or changes in the serum Ca-125 concentrations during 6 months treatment with the iCR and after 1 year follow-up. In summary, the use of iCR in climacteric women is devoid of estrogenic effects in the endometrium and appears to be safe even in women with uterine pathologies such as fibroids, endometriosis and even endometrial cancer.

### ***P144: Estradiol pharmacokinetics following Lenzetto application and the effects of skin-to-skin contact, washing of the application site and sunscreen use on estradiol pharmacokinetics***

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**Objectives:** Lenzetto® is an estradiol metered-dose transdermal spray approved in the US and in Europe to treat postmenopausal vasomotor symptoms. The pharmacokinetics (PK) of estradiol and factors that may affect estradiol absorption were assessed in two clinical pharmacology studies.

**Methods:** Study 1 was an open-label (OL) study in 72 healthy postmenopausal women aged  $\geq 40$ – $\leq 64$  years, randomized to one-, two-, or three-spray doses of Lenzetto once daily (q.d) for 14 days. Estradiol PK following Lenzetto application were assessed. Study 2 was an OL study in 20 healthy postmenopausal women aged 40–65 years treated with three sprays of Lenzetto q.d for 18 days. Healthy males (n=20) provided skin-to-skin contact but were not treated with Lenzetto. Estradiol PK and geometric mean ratios (GMRs) were assessed following Lenzetto application, washing of the site and sunscreen application in female subjects, and skin-to-skin contact in male subjects.

**Results:** In study 1, mean estradiol maximum serum concentrations after one, two, or three sprays were 36, 57, and 54 pg/mL on Day 14, respectively. Estradiol area under the serum concentration-time curve over 24 hours (AUC<sub>0–24h</sub>) was 471, 736 and 742 pg·h/mL for the one-, two-, or three-spray groups, respectively. In study 2, the 90% confidence intervals for the AUC<sub>0–24h</sub> GMRs were within the 0.80–1.25 range for post/pre skin-to-skin contact, unwashed/washed site and sunscreen applied 1 h before spray/no sunscreen and was 0.76–1.06 for sunscreen applied 1 h after spray/no sunscreen.

**Conclusions:** Lenzetto delivered therapeutic estradiol levels with a favorable safety profile. There was no significant skin-to-skin estradiol transfer after Lenzetto application. Estradiol exposure was lower when sunscreen was applied after Lenzetto application. However, Lenzetto PK was not altered by washing or use of sunscreen before Lenzetto application.

### ***P145: Ten cases from different aspects of menopause in Anwer Khan Modern Medical College and Hospital***

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Here we presents 10 cases from different aspects of menopause.

Case 1: Hot flushes, sweating and insomnia: it occurs in 15% women. Some feels and burning sensation. Managed by psychotherapy, lifestyle modification – avoid hot beverage, spicy food, warm air, stress etc. diet modification (soya and phytoestrogen), gabapentin, clonidin, fluoxetine, vit E and C, hypnotics, anxiolytic.

Case 2: Vaginal dryness, dysperunia, loss of libido: chronic vulvovaginitis also common. Lubricants, estrogen cream, psychotherapy for regular sexual stimulation which can help by maintainng elasticity.

Case 3: Mood swings and depression. They have fluctuation erratic attitude. Mood swings means laughing in one minute the another minute crying. Regular yoga, counselling, antidepressant, SSRIs as treatment gave to them.

Case 4: Memory and concentration loss. Some have dementia and cognitive problem. Counseling, psychotherapy, the idea is challenge the brain with new thoughts in new way.

Case 5: Recurrent UTI. Some suffers from recurrent UTI. Decreased estrogen may be the cause. Treatment includes fluid intake, antibiotic, alkali mixture.

Case 6: Urinary incontinence. We gave them bladder training, elimination of beverage such as coffee, tea and alcohol, kegels exercise. Estrogen cream, some medications and sometimes need surgery.

Case 7: Low back pain and joint pain. In our country it is more common. We suggest xray lumbosacral region, BMD and vit D analysis. We advised them for exercise, life style modification, Ca and vit-D supplementation, bisphosphanate therapy, HRT, raloxifene.

Case 8: Concern about HRT. Some women came for consult about importance of HRT. Some asked questions about the controversy of HRT.

Case 9: Postmenopausal bleeding. TVS usually prescribed. Managed by progesterone therapy, tranexamic acid, Levonorgesterol containing IUCD, D&C, hysterectomy.

Case 10: Palpitation, hair loss, dry skin, wrinkles, headache.

### ***P146: Relationship between menopausal symptom severity and exercise avoidance***

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Victoria University

Menopausal symptoms can reduce quality of life. HRT is effective in ameliorating symptoms; however, reporting side effects

resulted in alternative treatment options. One such option is exercise. It may alleviate psychological, vasomotor, somatic and sexual menopausal symptoms. Maintaining an active lifestyle can delay the onset of menopause associated conditions and ageing.

**Objectives:** To identify the meaning to exercise during menopause, and whether this is affected by the severity of their symptoms and examine the association between symptom severity and self-reported physical activity and active living habits.

**Methods:** 220 women (mean age 52.2 y) mainly Caucasian participated in the study. The survey included Greene Climacteric Scale for menopausal symptoms, Perceived Stress Scale measuring stress; and Kaiser Physical Activity Scale assessing household duties, active living activities and exercise behaviour. Items surveying activity avoidance due to menopause symptoms were also used. Data was assessed for normality and descriptive statistics analysed according to menopausal status. Stepwise linear regressions were used to assess differences in activity based on the severity of symptoms and controlling for menopausal status, age and stress.

**Results:** Severities of symptoms for each category strongly correlated with each other and with perceived stress. Regression analyses revealed menopausal symptoms were associated with reduced participation in moderate intensity exercise ( $p=0.032$ ) and reduced household duties engagement ( $p=0.002$ ). Activities avoided included household chores, gardening and structured exercise classes due to tiredness, sweating, weight gain and lack of motivation.

**Conclusions:** Severity of menopausal symptoms can have a significant influence on the amount of self-reported activity women engage in and is associated with avoidance of physical activities.

### **P147: Effectiveness and safety of using Amberen supplementation in perimenopausal and postmenopausal women**

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**Objective:** To evaluate the effectiveness and safety of using dietary supplement Amberen to relieve vasomotor and psychosomatic symptoms in perimenopausal and postmenopausal women.

**Methods:** Randomized, double-blind, placebo-controlled trial was conducted among women 42–60 years of age with vasomotor and psychosomatic menopausal symptoms. The treatment lasted 3 months. The study included medical evaluations, questionnaires using the Greene Climacteric Scale and the Spielberger-Hanin test, evaluation of plasma levels of gonadotropins, estradiol, leptin, and apolipoproteins.

**Results:** We enrolled 104 women and randomly assigned them in two groups. Treatment group received Amberen and control group received placebo for 3 months. Analysis of the Greene Climacteric Scale results showed a statistically significant ( $p<0.05$ ) improvement in 13 out of 21 menopausal symptoms in patients who took Amberen. During the course of the Amberen treatment and by the end of the study the patients showed significant changes in the levels of estradiol and gonadotropins, decrease in the average body weight and waist circumference. The Spielberger-Hanin test showed that Amberen supplementation allows for stabilization of patients' psychological status with reliable reduction in anxiety, increased resistance to stress, and

improved adaptability. Comparative analysis of vital signs, blood and urine tests did not show any negative effects of Amberen.

**Conclusions:** Using Amberen during menopausal transition and postmenopause can be considered a method to relieve vasomotor and psychosomatic menopausal symptoms for women who have a high risk of complications associated with hormone therapy (HT) or do not wish to undergo HT.

### **P148: Hormonal status of premenopausal women with non-functioning pituitary macroadenomas undergoing surgery in a single Australian centre**

Anna Watts (AU)

Western Health

**Objective:** To describe the disruption to the gonadal axis pre and post operation in cases with non functioning pituitary macroadenoma.

**Methods:** We reviewed the notes of 177 consecutive non functioning pituitary macroadenoma cases operated on between 1995 and 2013. Secondary hypogonadism was diagnosed in premenopausal women with a reported history of oligomenorrhoea or amenorrhoea associated with low oestradiol. Post operatively, gonadotrophin deficiency included premenopausal women in whom menses had not returned by 6 months post operation.

**Results:** There were 32 premenopausal women in the cohort, mean age at presentation was 41.9 years, range 27–42. The majority 83% (25/30) of premenopausal women (with intact uterus) had either oligo or amenorrhoea at presentation. Almost one third (10/32) of premenopausal women reported galactorrhea. One case was detected in pregnancy and was not included in the analysis. 31.8% 7/22 had pre operative gonadal dysfunction of whom 4 had postoperative recovery. One had ongoing gonadal dysfunction post operation. Post operative gonadal status was unknown in the remaining two cases. 18.8% (6/32) of premenopausal women had new gonadal deficiency post operation. Hormone replacement therapy (HRT) was discussed with all cases, of whom two chose to commence treatment post operation. One case was able to cease HRT post operation.

**Conclusions:** Hormonal dysfunction is common in patients with functioning pituitary macroadenoma. Premature menopause is a common presenting complaint in younger women. Surgery may result in de novo gonadotrophin dysfunction or resolution of pre-existing hormonal disturbance. Predicting individual patient outcomes prior to surgery remains difficult.

### **P149: Effect of transcranial direct current stimulation on menopausal symptoms: parallel blind randomized clinical trial controlled with placebo-sham**

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and Wolnei Caumo (BR)

UFRGS

**Objective:** To assess the effect of transcranial direct current stimulation (tDCS) compared with tDCS-sham on vasomotor symptoms of postmenopausal women.

**Methods:** Postmenopausal women, with at least five episodes of vasomotor symptoms per day, were recruited from a specialized outpatient clinic at a tertiary hospital in the south of Brazil and through a media call after inclusion and exclusion criteria were ensured. tDCS was administered for ten consecutive days, except for weekends. Active stimulation with tDCS x placebo-sham. The number of hot flashes was evaluated and questionnaires were validated to assess quality of life and depressive symptoms.

**Results:** The mean of hot flashes/day behaved in a similar way in both groups, and there was a reduction in hot flashes in the first three weeks following the intervention with return to baseline starting in the fourth week after the administration. In the tDCS group, a trend towards a conversion of intensive hot flashes into mild ones was noted, which suggested a clinical improvement.

**Discussion:** Our results, despite not showing statistical significance, supported the idea of extending the investigation with a larger number of patients and longer duration, in addition to the innovating nature of the research. The described technique showed minimum undesired effects, which makes its use plausible in daily clinical medicine.

Clinical Trial Registration: NCT01896791

### **P150: Determinants of hormone therapy uptake and decision making in surgically menopausal women**

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University of Alberta

**Objective:** Early surgical menopause ( $\leq 45$  years) is associated with short and long-term health consequences. In women with early menopause and without contraindications, hormone therapy (HT) is often recommended. However, HT is underutilized in this population. Our objective was to identify and describe determinants of HT uptake and decision making in women with early surgical menopause.

**Methods:** We searched Medline, EMBASE and CINAHL, from inception to February of 2015. Inclusion criteria included studies that assessed factors affecting the uptake and decision-making about HT in surgically menopausal women. Studies involving both natural and surgically menopause were also included. Search terms were derived from 3 concepts: surgical menopause, hormone therapy, and decision-making. Only English articles were included.

**Results:** Of the 1,952 articles identified, 20 were included. Studies were mostly published before the WHI (65%), and had a quantitative cross-sectional study design. Only 15% focused strictly on surgical menopause. Among studies that included both surgical and natural menopausal women the proportion of surgical menopausal women was 22% (1.4-44). The mean age at time of surgical menopause was 41.9 years (range 29-68). HT uptake was associated with younger age, higher education, higher income and adopting positive health related behaviours. Factors affecting decision-making included woman related factors such as knowledge and beliefs on HT, attitudes towards menopause, knowledge, value system and personal life experiences. External factors included interaction with health care system and influence of information sources.

**Conclusions:** This review identified a number of modifiable determinants of decision making that tailored interventions, such as evidence based decision aids can target to help women make an informed value-based therapy decision.

## **Metabolic/obesity**

### **P151: Endometriosis in an obese postmenopausal lady**

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**Introduction:** Endometriosis means implantation of endometrial tissue outside the uterus. This is actually occur in reproductive age. Incidence about 10%. But in 2%-3% cases it can occur in postmenopausal period. It is rare due to absence of estrogen hormone. But when a patient is obese and has a source of estrogen from skin and adipose tissue then endometriosis should kept in mind. We report a case of endometriosis in an obese postmenopausal lady with no past history or family history of endometriosis.

**Case:** A 54 years obese para3 (NVD) patient came to our clinic with abdominal pain; she was menopausal for 3 years. On clinical examination all the vitals were normal. BMI – 40. Per abdominal examination showed tenderness in right sided iliac region. TVS report showed right sided ovarian mass about 5.7 × 4.9 cm. In color Doppler RI was normal. CA-125 showed 556.7 U/ml and others tumour markers were normal. She was in our follow up. After 2 months size of tumour increase in size about 10.8 × 9.9 cm and CA-125 level also 667.98 U/ml. We decided for laparoscopic evaluation. During operation chocolate colour fluid was observed from right sided cystic mass and right sided salpingo-oophorectomy with adhesiolysis was done. Histopathology report showed it was endometrioma.

**Discussion:** Postmenopausal endometriosis is rare. Endometriosis is estrogen dependent tumour. Our patient was obese and her source of estrogen was skin and adipose tissue. HRT may cause endometriosis but our patient was not on HRT. Chance of malignant transformation is very less. But we should follow up the patient.

**Conclusions:** We should open our thinking plot when we deal with obese postmenopausal lady with chronic pelvic pain. Though endometrioma is rare during menopause but it should be in mind. Early diagnosis can help to prevent complications and malignant transformation.

### **P152: Prevention of menopausal metabolic syndrome and treatment of sleep disorders with melatonin in patients with polycystic ovary syndrome**

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**Context:** Polycystic ovary syndrome (PCOS) is an endocrine disorder, complicated by menopausal metabolic syndrome, which includes insulin resistance, diabetes, cardiovascular disease, dyslipidemia, obesity in the late reproductive and premenopausal age. Preventing these conditions is a key problem of management of patients with PCOS. Administration of melatonin as an antioxidant and a drug for sleep disorders can improve metabolic parameters and prevent metabolic syndrome and ovulatory dysfunction in women with PCOS.

**Objective:** To study the severity of metabolic and sleep disorders in patients with PCOS and the possibility of using melatonin in preventing and treating this disease.

**Methods:** The survey through questionnaires scoring subjective sleep characteristics; examination of glucose and insulin blood levels; calculation of HOMA-IR index.

Patients with PCOS aged 17-35 years old: 27 patients with a body mass index (BMI) >25 kg/m<sup>2</sup> and 32 patients with BMI <25 kg/m<sup>2</sup>. PCOS was diagnosed on the basis of ESHRE/ASR criteria. Control group: 45 healthy women without menstrual disorders.

**Interventions:** Administration of a synthetic analogue of melatonin 3 mg for 3 months to patients with sleep disorders.

**Results:** HOMA-IR index was higher than normal level in PCOS group with BMI <25 kg/m<sup>2</sup> in 14.8% of patients. Insulin resistance was detected in 63.6% of patients with BMI >25 kg/m<sup>2</sup>. 20 women with PCOS and sleep disorders observed an improved sleep quality while taking melatonin, reducing the number of nighttime awakenings, while 12 patients with BMI >27 kg/m<sup>2</sup> reduced the weight by 6.25 ± 0.76 kg (p < 0.05) after treatment.

**Conclusions:** Patients with PCOS and BMI >25 kg/m<sup>2</sup> are at high risk of metabolic syndrome. Sleep disorders lead to changes in feeding behavior, increasing metabolic risk later in life. Treatment with melatonin can be used as a preventive measure for these disorders.

### **P153: Evaluation of metabolic parameters in women with polycystic ovary syndrome following treatment with metformin**

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University of Campinas

**Objective:** To evaluate the influence of metformin therapy over metabolic manifestations of women with polycystic ovary syndrome (PCOS).

**Methods:** A retrospective study was performed to evaluate the metabolic parameters of women with PCOS after 6 months of treatment with metformin. Sixty two medical records were evaluated of women of reproductive age diagnosed with PCOS according to the Rotterdam criteria in the University of Campinas. We used a statement made especially for this research contains information on age, parity, marital status, color, education and clinical and metabolic parameters (triglycerides, total cholesterol, LDL, HDL, fasting glucose, fasting insulin, homeostasis model assessment for insulin resistance (HOMA-IR), weight, body mass index (BMI), blood pressure).

**Results:** The mean age of women was 28.69 ± 8.52 years, 70.97% were nulligravida, 67.74% were obese and 84.62% had medium education. There was a significant improvement in HOMA-IR (initial HOMA-IR 4:48 ± 2.95, 3.70 ± 2.70 end; p = 0.006). The lipid profile and blood glucose and insulin values although there has been an improvement was not significant (initial total cholesterol 188.79 ± 43.36 and final 182.84 ± 36.49, p = 0.14, initial LDL 112.59 ± 37.54 and final 107.68 ± 33.53, p = 0.27, triglycerides initial 164.27 ± 89.52 and final 155.05 ± 77.37, p = 0.30; initial glucose 98.20 ± 38.80 and final 95.51 ± 36.47, p = 0.35; insulin initial 18.73 ± 5.13 and final 16.65 ± 12.42, p = 0.10). The blood pressure, BMI and HDL remained stable (p = 0.61, p = 0.21 and 0.85 respectively).

**Conclusions:** Metformin reduces insulin resistance in polycystic ovary syndrome; however returned no influence on metabolic parameters or BMI.

### **P154: Polycystic ovary syndrome and its metabolic impact on postmenopausal women**

Pablo Carpintero (AR), Maria Franchina (AR), Gustavo Litterio (AR) and David Fusaro (AR)

IGBA

**Objective:** To determine the number of postmenopausal women (PMW) enrolled between 10/1/14 and 9/30/15 and establish a correlation between their lipid profile, glycemia and body mass index (BMI) with their premenopausal history of polycystic ovary syndrome (PCO).

**Methods:** Retrospective, cross sectional, correlation study.

**Population:** Consecutive review of 350 PMW that attended IGBA between 1/10/14 and 30/9/15. 220 cases were selected.

**Exclusion criteria:** Patients that had not completed the requested laboratory.

**Variables:** Age, menopause, history of PCO, cholesterol, triglycerides, glycemia, BMI.

**Statistics:** Percentage, range, standard deviation (SD). Descriptive and correlation statistics were used according to the variable scale and correlation model. Confidence intervals (CI) of 95% were calculated. Pearson's linear correlation coefficient and logistic regression method was used for data analysis. It was considered an  $\alpha$  error = 0,05 and  $\beta$  error = 0,10.

**Results:** n = 267 PMW. Menopause: Mean: 48,2. SD: ± 9,2. Range: 43-65. Cholesterol >200 mg%: 170 PMW (63,6%); Triglycerides >140 mg%: 98 PMW (36,7%); Glycemia >110 mg%: 48 PMW (17,9%); BMI >25: 168 PMW (62,9%); History of PCO: 31 PMW (11,6%). Coefficient correlation analysis: Cholesterol (n:267; r:0,070; CI:-0,26-0,12; p:0,46; RR:0,0049); Triglycerides (n:267; r:0,190; CI: -0,0034-0,3700; p:0,05; RR:0,036); Glycemia (n:267; r:0,419; CI: 0,241-0,570; p:0,000; RR:0,1755); BMI (n: 267; r: 0,067; CI: -0,20-0,14; p: 0,40; RR: 0,0044).

**Conclusions:** We found statistically significant correlation between hypertriglyceridemia and hyperglycemia with history of PCO. We did not find any statistically significant correlation between history of PCO and hypercholesterolemia, and obesity in our population of postmenopausal women. Further investigations will be needed in order to determine its negative and late impact on postmenopausal women's health.

### **P155: Prevalence of obesity rather than the metabolic syndrome increases by menopausal status in mid-aged women**

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**Background:** The prevalence of metabolic syndrome (METS), and its components, increases after the menopause and as women age; however, most research focuses on the METS after the menopause.

**Objective:** To determine the prevalence of the METS (Modified ATP III criteria) and its components in mid-aged women and compare results in each menopausal stage.

**Methods:** This was a cross-sectional study in which 195 pre-, peri, and postmenopausal women aged 40 to 65 were screened for the METS. Weight (kg), height (m), body mass index (BMI, kg/m<sup>2</sup>), waist circumference (cm) and blood pressure were registered. In addition, fasting HDL-C, triglyceride and glucose levels were assayed.

**Results:** For the whole sample median [IQR] age was 50 [9.5]. Overall, prevalence of the METS 16.9% and 6.1% used hormone therapy. A 20.5% were pre-, 23.0% peri-, and 56.4% postmenopausal. Abdominal obesity and hypertension were the two main components of the METS among all participants and only in those with the METS. Prevalence of the METS and four of its components did not differ when menopausal stages were compared; nevertheless, abdominal obesity showed a significant increasing trend through the different stages pre-, peri- and postmenopausal (27.5, 44.4 and 59.0% respectively,  $p=0.002$ ).

**Conclusions:** Prevalence of the METS did not differ according to menopausal stage in this mid-aged female sample; nevertheless, obesity an important feature of the syndrome increased throughout the stages.

### ***P156: Is lactose intolerance related to some metabolic syndrome parameters in obese patients – our experience***

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**Objective:** Aim of the paper was to reveal possible relationship between lactose intolerance (LI) and metabolic parameters such are blood glucose (BG) level, cholesterol (CH), HDL, LDL, and triglycerides (TR). Also, possible link between LI and gluten intolerance was tested.

**Methods:** Obese subjects were subjected to Chrono-nutrition program Dr Gifing® (CNPDrG®) in order to reduce body weight and to balance impaired metabolic parameters. CNPDrG® is completely personally tailored nutrition and means taking meals of certain food which body well tolerate at proper day-time accompanied with supplementation. Food tolerance test was done on MORA nova touch machine. Basic methods of descriptive statistics were applied, as well as, Chi-Square test.

**Results and discussion:** Of 164 examinees, there were 44 males (M) and 120 females (F). No statistically significant difference in mean values of age between these two groups was found. LI was found in 56 examinees (34,15%). LI was statistically significant related to increased level of CH ( $p=0.03$ ) and decreased level of HDL ( $p=0,001$ ) in whole group of subjects examined. This trend was the same when groups were analyzed separately - M ( $p=0,000$ ), and F ( $p=0,007$ ). Also, LI was statistically significant related with high BG level in F ( $p=0,047$ ), which was not true for M (may be explained by low number of examinees). At last, LI was found to be statistically highly significant related to gluten intolerance when both sexes are considered ( $p=0,000$ ); this was also true when analysis was done for M ( $p=0,02$ ) and F ( $p=0,000$ ) separately. No significant link was found between LI and TR, and LI and LDL level.

**Conclusions:** Should patients have metabolic parameters changed, medical professionals are advised to consider LI as possible co-

existing condition and to suggest proper nutrition to their patients (i.e. elimination of lactose).

### ***P157: Serum thyroid stimulating hormone levels are associated with the presence of coronary atherosclerosis in healthy postmenopausal women***

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**Objective:** The aim of this study was to assess the association between increased thyroid-stimulating hormone (TSH) levels and coronary atherosclerosis in healthy postmenopausal women.

**Methods:** We performed a retrospective review of 247 postmenopausal women who visited the health promotion center for a routine checkup. Subjects who were not euthyroid were excluded. Coronary atherosclerosis was assessed by 64-row multi-detector computed tomography.

**Results:** Using a multiple linear regression analysis, TSH levels were significantly associated with age ( $p=0.020$ ), high density lipoprotein (HDL)-cholesterol ( $p=0.023$ ), and triglyceride ( $p=0.008$ ). A higher overall risk for coronary atherosclerosis emerges with increased TSH levels after removing bias for age and cardiovascular risk factors.

**Conclusions:** We demonstrated that elevated TSH levels and coronary atherosclerosis were closely linked in euthyroid postmenopausal women. Therefore, more attention should be focused on postmenopausal women with elevated TSH levels in the management of coronary heart disease.

### ***P158: Weight gain in the perimenopausal period***

Assaad Kesrouani (LB), Habib Atallah (LB) and Enaam Hatoum (LB)

Saint Joseph University

**Objective:** To assess weight gain in the perimenopausal period.

**Methods:** A case series of 50 consecutive Lebanese patients with irregular cycles and elevated FSH that were followed at one year for weight changes. Weight gain was assessed by using self-reported body weight gain. We also evaluated eating patterns and the impact of this weight gain on the patients. Diabetes, recent abdominal surgery, psychiatric history or antidepressants use were exclusion criteria.

**Results:** Median age is 46 years [43-50]. Initial BMI is 26.7 [23.2-31.3]. Weight increase was noted in 22/50 (44%) of the patients. This was estimated at less than 3 kg in 28%, between 3 and 5 kg in 12% and more than 5 kg in 4%. Among these 22 patients, 16 considered this increase as a major complaint and 12 stated that it had an impact on their self-esteem. Only 13 patients reported increased caloric intake and 5 patients noted a qualitative change in their diet. Six patients described a recent night-eating pattern.

**Conclusions:** Weight gain in the perimenopause is common and should be checked, aiming to an early management by diet restriction or increasing activity.

### **P159: Association between osteocalcin and metabolic syndrome in Korean postmenopausal women**

Suk Woo Lee (KR)

Hallym University College of Medicine

**Objective:** Undercarboxylated osteocalcin (ucOC) has been proved as a regulator of glucose and fat mass in an animal model. This study examined the association between osteocalcin and metabolic syndrome (MetS) in postmenopausal women.

**Methods:** We selected 135 postmenopausal women and determined anthropometric values [waist-hip ratio (WHR), visceral fat area (VFA), body fat mass (BFM), and skeletal muscle mass (SMM)], the lipid profile, fasting plasma glucose (FPG), insulin, high-sensitivity C-reactive protein (hs-CRP), homeostasis model assessment of insulin resistance (HOMA-IR), serum leptin and adiponectin level, and serum tOC and ucOC level.

**Results:** There were 52 postmenopausal women in the MetS group. After adjusting for age and years since menopause, ucOC was negatively correlated with WHR, VFA, BFM, triglyceride, fasting insulin, HOMA-IR, and serum leptin and was positively correlated with serum adiponectin. The odd-ratio for MetS was significantly lower in the highest quartile than the lowest quartile after adjusting for age, years since menopause, and BMI. In multiple regression analysis, serum leptin and HOMA-IR were the most important predictors of the independent variables that affect serum ucOC.

**Conclusions:** ucOC showed an inverse correlation with markers of insulin resistance, central obesity, and the presence of MetS in postmenopausal women and appears to protect against MetS. Further large-scale clinical and experimental studies are needed to clarify the potential of ucOC as a predictor of MetS in postmenopausal women.

### **P160: Association between metabolic risks and bone mineral density in postmenopausal women**

Suk Woo Lee (KR)

Hallym University College of Medicine

**Objective:** Menopause is associated with osteoporosis and an increased risk of metabolic disorders, including obesity, abdominal adiposity, hyperlipidemia, hypertension, and insulin resistance, which may increase the risk of cardiovascular disease (CVD). Recent studies have demonstrated a correlation between fat, glucose, and bone metabolism which could contribute to CVD and osteoporosis. This study examined the association between metabolic risk factors and bone mineral density (BMD) in postmenopausal women.

**Methods:** We determined the anthropometric values [waist-hip ratio (WHR), visceral fat area (VFA), body fat mass (BFM), and skeletal muscle mass (SMM)], lipid profile, fasting plasma glucose levels, high-sensitivity C-reactive protein levels, homeostasis model assessment of insulin resistance (HOMA-IR) scores, serum leptin and adiponectin levels, serum osteocalcin level [total osteocalcin (tOC) and undercarboxylated osteocalcin (ucOC)], and BMDs of the lumbar spine and femoral neck in 137 postmenopausal women.

**Results:** There was a positive correlation between BFM, HOMA-IR score, and serum leptin level and BMD of the lumbar spine, and a negative correlation between BFM, total cholesterol, and serum adiponectin and BMD of the lumbar spine after adjusting for age,

years since menopause, current alcohol consumption, and current smoking status. In a multiple regression analysis, serum adiponectin level and SMM were the most important predictors of the BMD of the lumbar spine.

**Conclusions:** There were several metabolic risk variables that had a harmful effect on the BMD of the lumbar spine, but not the femoral neck. However, higher serum adiponectin levels were negatively correlated with BMD of the lumbar spine as adiposity decreased.

### **P161: Evaluation of the body composition of women with polycystic ovary syndrome**

Carolina Macruz (BR), Sonia Maria Lima (BR), João Eduardo Salles (BR), Gustavo Silva (BR) and Nilza Scalissi (BR)

Irmandade Santa Casa de Misericórdia de São Paulo

**Objective:** To compare the body composition of women with polycystic ovary syndrome (PCOS) to those of women with ovulatory menstrual cycles depending on body mass index (BMI) of  $\geq 18,5$  to  $<30 \text{ kg/m}^2$ , waist circumference (WC) and fat distribution using total-body dual x-ray absorptiometry (DXA).

**Methods:** A case-control study was conducted on 37 women with PCOS and 20 control women, aged 14 to 39 years with a body mass index of  $18,5$  to  $29,9 \text{ kg/m}^2$ . Anthropometric measurements, biochemical hyperandrogenism, metabolic pattern and to evaluation of body composition based on DXA were obtained these women.

**Results:** Luteinizing hormone ( $p=0,026$ ) levels, as also were the 17-hydroxyprogesterone ( $p=0,005$ ), testosterone ( $p=0,003$ ), glycemia ( $p=0,045$ ), HOMA -IR ( $p=0,034$ ) and trunk fat ( $p=0,002$ ) were higher in the PCOS Group than in the Control Group. The sex hormone-binding globulin ( $p=0,004$ ) level was lower in the PCOS Group than in the Control Group.

**Conclusions:** In our study shows that non-obese women with PCOS had an increase in truncal fat. This supports the hypothesis that central fat deposition is either a very early effect of, or possibly cause of, insulin resistance in this population. It also implies that reducing central fat should reduce insulin resistance, which accounts for the observation that lifestyle modifications have beneficial effects on both the short-term and long-term sequelae of metabolic dysfunction in these women.

### **P162: Prevalance of increased abdominal girth and hypercholesterolemia in perimenopausal women living in urban area of a developing country**

Lakshmi Marakani (IN) and Asna (IN)

Nice Hospital for Women, Newborn and Children

**Objective:** To study the prevalence of high lipid levels and increased abdominal girth in perimenopausal women with sedentary lifestyle between 45 to 55 yrs from urban areas of Hyderabad, India. The secondary outcomes will be co-morbid conditions like hypertension, diabetes mellitus, hypothyroidism and morbid obesity.

**Materials and methods:** Apparently healthy women staying in urban areas were physically examined and abdominal girth

measured by same medical worker, co-morbid conditions and the investigation results were noted.

**Results:** Lipid levels in 200 women from the urban areas between 45 to 55 yrs were assessed. Among them 52% had hypercholesterolemia, 92% had waist circumference more than 80 cm, 46% were hypertensive, 22% were diabetic, 30% were hypothyroid, 6% had some form of arthritis, 20% had other co-morbid conditions like migraine, asthma, CCF. Based on BMI, 16% were morbidly obese (BMI >35), 36% were obese, 24% were overweight, 24% were normal. Only 12% were on statins for increased levels of cholesterol.

**Conclusions:** In a developing country like India, women even in urban areas are not aware of the risks of hypercholesterolemia with morbid obesity which can lead to atherosclerosis and various cardio-vascular accidents. In our study, all the women were leading sedentary lifestyle. Only 24 out of 104 with hypercholesterolemia were on treatment. Only 16 women have abdominal girth of 80 cm. Absolute risk for cardiovascular disease increases substantially in mid life during perimenopause. Abdominal girth and lipid levels can be taken as markers to identify these women who should be targeted for intervention. We menopausal practitioners must increase the awareness about the adverse outcomes of increased abdominal girth and its association with metabolic syndrome which ultimately lead to cardio-vascular accidents with increased morbidity and mortality.

### ***P163: A phase 1, open-label, parallel-group study of the single-dose pharmacokinetics of conjugated estrogens/bazedoxifene (CE/BZA) in non-obese and obese postmenopausal women***

William Mckeand (US), Anna Plotka (US), Kelly Ryan (US), Joanne Salageanu (US) and Carol Cronenberger (US)

Pfizer Inc

**Objective:** CE/BZA is approved for treating moderate/severe vasomotor symptoms and preventing osteoporosis in postmenopausal women. BZA, an estrogen antagonist in the endometrium, decreases endometrial hyperplasia risk when administered with CE. A US FDA population pharmacokinetic (PK) analysis predicted that BZA's oral clearance would increase as body mass index (BMI) increases, potentially raising endometrial hyperplasia risk. However, the analysis did not include CE; therefore, the relationship between CE and BZA with respect to BMI was not studied. This study evaluated the impact of BMI on the PK of BZA and CE following CE/BZA administration.

**Design:** In this open-label, parallel-group study, generally healthy obese (BMI  $\geq 30$  kg/m<sup>2</sup>) and non-obese (BMI <30 kg/m<sup>2</sup>) postmenopausal women received a single dose of CE 0.45 mg/BZA 20 mg. Blood samples were drawn during a 5-day, 4-night inpatient stay. Natural log transformed AUCinf, AUC0-72, and Cmax for BZA, total estrone and equilin, unconjugated estrone and equilin, total estrone adjusted for baseline, and unconjugated estrone adjusted for baseline were analyzed using a mixed effect model with treatment, BMI, and treatment by BMI interaction as fixed effects and subject as a random effect.

**Results:** The study included 24 women (mean age 54.8 y; 96% white). Mean (range) BMI was 32.7 (30.0–36.7) kg/m<sup>2</sup> in obese (n=12) and 25.3 (20.9–28.6) kg/m<sup>2</sup> in non-obese women (n=12). Obesity was associated with decreased systemic exposures to BZA (AUCinf: 13%), total equilin (Cmax: 25%, AUCinf: 32%), baseline-adjusted total estrone (Cmax: 31%), and baseline-

adjusted unconjugated estrone (Cmax: 33%, AUC0-72: 34%). There were no adverse events.

**Conclusions:** Obese women had decreased systemic exposures to BZA and CE, but their relative systemic exposures were not altered in a manner that would be expected to compromise endometrial protection.

### ***P164: Neck circumference correlation to metabolic syndrome during menopausal transition***

Hephzibah Navamani (IN)

Saveetha Medical College, Saveetha University

**Objective:** Prevalence of obesity and metabolic syndrome known to increase in midlife of a woman. Neck circumference with metabolic syndrome correlated better among females. Aim of this study was to investigate whether NC independently contributes to the prediction of cardio-metabolic risks beyond body mass index (BMI), waist circumference (WC) and waist to hip ratio.

**Methods:** Cross sectional, observational prospective study conducted at Saveetha Medical college Obstetrics & Gynaecology Outpatient Department. Neck Circumference (NC) in 150 women from 35 years to 65 years without medical disorders were taken. Women were divided into 4 groups: premenopausal 35–45 years, perimenopausal 46–50 years, early postmenopausal 51–55 years and late postmenopausal 56–65 years. After informed consent after eliciting Gynaec history, after physical examination, all cardio metabolic risk factor, were assessed. NC was measured with head erect and eyes facing forward, horizontally at the upper margin of the laryngeal prominence (Adam's apple). BMI, waist circumference, hip circumference, waist circumference (WC) were measured.

**Results:** Premenopausal women 29%, perimenopausal 34%, early menopausal 24%, late menopausal 12%. NC >34 cms in 62% and all of them had metabolic syndrome (MS). NC <34 cms in 2% had MS. Increased NC seen in 18% of pre, 24% perimenopausal, 12% early, 10% late postmenopausal women. NC is more strongly associated with cardio metabolic risk factor. NC had best correlation with waist circumference, hip circumference, W/H ratio, BMI.

**Conclusions:** NC is a simple, easy, screening tool. Our study points that NC increased and its association with metabolic syndrome in midlife transition, hence preventive measure can be taken during this period.

### ***P165: Neck circumference as biomarkers for identifying survival prognosis after exercise stress test in menopausal status: a preliminary study***

Pornpip Nimkuntod (TH) and Pattama Tongdee (TH)

Institute of Medicine

**Background:** During the menopausal transition, when many are not only be gaining weight, but are also experiencing changes in body composition and fat distribution. Neck circumference (NC) may represent a better cardio-metabolic risk parameters, when compared to fat stored in the visceral region.

**Objective:** The aim of this study was to investigate whether NC independently contributes to the prediction of survival prognosis

of exercise stress test (EST) and anthropometric parameters in perimenopausal/menopausal women.

**Methods:** The cross-sectional study of 76 perimenopausal/menopausal women. Main indicators included anthropometric indices NC, body mass index (BMI), waist circumferences (WC) and waist to hip ratio (WHR), biochemical and clinical parameters were measured. Statistical analysis was done by using Student's T-test and Pearson correlation. The p-value was taken as significant at 5 percent confidence level ( $p < 0.05$ ).

**Patients:** Perimenopausal/menopausal women.

**Intervention:** Exercise stress test.

**Results:** Total 76 perimenopausal/menopausal women, with average age of  $50.26 \pm 8.36$  years, mean NC  $33.51 \pm 3.14$  cm. Correlations of NC with 5 year survival ( $p = 0.04$ ) and inverse correlation with average annual mortality ( $p = 0.04$ ) but no correlation with other anthropometric parameters body mass, BMI and WHR were observed. Exercise functional capacity  $7.77 \pm 0.99$  METS and not difference EST values when compared with abnormal NC group ( $> 35$ cm).

**Conclusions:** High NC was associated with an increased identifying survival and average annual mortality that prognostic parameters in EST and contributed to the prediction beyond the classical anthropometric indices.

### **P166: Effect of aging and menopausal hormone therapy on waist circumference and weight along 10 years of follow-up**

Karen Oppermann (BR)<sup>a</sup>, Mariana Sgnaolin (BR)<sup>a</sup>, Giovanni Zin (BR)<sup>a</sup> and Bernardo Lisboa (BR)<sup>b</sup>

<sup>a</sup>University of Passo Fundo; <sup>b</sup>Universidade do Rio Grande do Sul

**Introduction:** Menopausal hormone therapy (MHT) has shown diverse effects on weight and waist circumference (WC) in women.

**Objective:** To assess WC, weight and metabolic syndrome (MS) over 10 years among women who initiated MHT for climacteric complaints.

**Methods:** Design: prospective longitudinal study. A subsample of 23 out of 56 women with vasomotor symptoms who consulted at the Clinic for Menopause at the São Vicente de Paulo Hospital (Passo Fundo, Brazil) and completed 10 years of follow up were enrolled in the study. Main outcomes measures: primary outcome, WC, was measured between the lower rib margin and the iliac crest. Others outcomes: weight, body mass index (BMI), blood pressure, lipids, glucose, metabolic syndrome. The patients received either estrogen or estrogen with progesterone to treat the menopausal complaints and were examined every six months. The baseline values were compared with those at 10-year follow-up. At a significance level of 0.05, the sample of 23 women had a power of 90%, 78% and 62% for detecting an increase of 5 cm, 4 cm, and 3 cm, respectively, in abdominal waist circumference over the 10-year follow-up period.

**Results:** The mean of age was  $47.6 \pm 4.7$  years and the majority was in perimenopause. Although there was no change in weight ( $68.2 \pm 11.1$  versus  $68.2 \pm 12.5$  kg;  $P = 1.0$ ), there was a tendency toward decreased WC ( $89.9 \pm 9.8$  versus  $88.2 \pm 9.6$  cm;  $P = 0.076$ ). There was a statistically significant decrease in central adiposity, which was measured by the National Cholesterol Education Program (NCEP;  $P = 0.017$ ) and International Diabetes Federation (IDF;  $P = 0.012$ ) WC cut-offs. There was no change in the prevalence of MS during the follow-up.

**Conclusions:** In this subsample of young climacteric women the MHT could have had a beneficial effect on fat distribution along

10 years of follow-up. Future studies must confirm with larger sample.

### **P167: Graves disease across ages: observational study in a tertiary referral center in Romania**

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<sup>a</sup>"Dr. I. Cantacuzino" Hospital, "Carol Davila" University of Medicine and Pharmacy; <sup>b</sup>"C. I. Parhon" National Institute of Endocrinology; <sup>c</sup>"C. I. Parhon" National Institute of Endocrinology, "Carol Davila" University of Medicine and Pharmacy

**Background:** Graves' ophthalmopathy (GO) is a condition associated with Graves' disease that occurs when cells from the immune system attack the muscles and other tissues around the eyes. The disease can affect adolescents and is most often diagnosed among women under 40 years old, but can also be found in pre- and postmenopausal women.

**Objective:** To identify the incidence of Graves' disease in postmenopausal women and the risk factors and comorbidities for this patients.

**Methods:** We performed the analysis of a retrospective cohort performed in "C.I.Parhon" National Institute of Endocrinology between 2011-2015. We included 850 women patients admitted for hyperthyroidism and ophthalmopathy caused by Graves' diseases. Clinical assessment was performed at baseline and at the follow-up visits after the restoring of euthyroid state.

**Results:** The mean age was 49.2, with 10 cases (1.2%) 8-18 years old, 238 (28%) – 19-40, 285 (33.5%) – 41-55 and 317 (37.3%) – 55-90; 14 cases had severe thyrotoxicosis. Cardiac hypertrophy, atrial fibrillation, high blood pressure and osteoporosis were the most common associated disorders in the postmenopausal women group. The frequency of cardiovascular complications was significantly reduced as compared before and after the antithyroid therapy. The presence of hyperthyroidism could mask dyslipidemia, while after restoration, the lipid profile restore to basal levels, often in the dyslipidemic range. Associated severe ophthalmopathy required steroid treatment, while this represents a risk factor for osteoporosis, which required additional follow-up visits.

**Conclusions:** Graves' disease appears in more than one third of cases, in postmenopausal women. Its presence at this age requires additional measures of treatment and more follow-up visits.

### **P168: Metabolic patterns during the menopausal transit in Chinese women**

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<sup>a</sup>Beijing Obstetrics & Gynecology Hospital, Capital Medical University; <sup>b</sup>Department for Women's Health, Tuebingen, Germany  
**Objective:** During menopausal transit from perimenopause to postmenopause, the changes in the patterns of lipids and lipoproteins including Lp(a), body fat, resting energy expenditure (REE), Fasting plasma glucose (FPG) for the first time have been investigated as primary study endpoints in Chinese women.

**Methods:** 1,015 menopausal women from 20 provinces of China without HRT aged 34–76 years. Menopausal status was defined by “2011 Stages of Reproductive Aging Workshop criteria”. Besides REE, body fat and FPG, the lipids including total cholesterol (TC), triglyceride (TG), high density lipoprotein-cholesterol (HDL-C), low density lipoprotein-cholesterol (LDL-C), lipoprotein(a) (Lp(a)), apolipoprotein A 1 (Apo A1), apolipoprotein B (Apo B), fasting plasma glucose (FPG), and hormones including estradiol (E2), and follicle-stimulating hormone (FSH) were assessed.

**Results:** Comparing postmenopausal with perimenopausal women ( $n = 279/736$ ), TC, TG, LDL-C, FPG, body fat increased significantly, and HDL-C and REE decreased significantly. LDL-C was correlated to increasing age and decreasing E2; HDL-C was correlated to decrease of FSH, TC was correlated to increase of FSH and to increasing age (all  $p < 0.05$ ).

**Conclusions:** Metabolic patterns are significantly changed during the transit, some can be related to menopausal status, some to increasing age, some to both; especially triglycerides and apolipoprotein A1 were found also to be related to BMI. Surprisingly lipoprotein(a) did not change either with increasing age or during the transition despite known possible interference with estrogenic status.

### **P169: The complex immunological network and inflammatory response activated in obesity**

Lily Stojanovska (AU) and Vasso Apostolopoulos (AU)

Victoria University

Obesity is a medical condition whereby excess body fat may have a negative effect on health. Today, obesity is the 6th most important risk factor contributing to overall burden of disease and is the leading preventable cause of death. Obesity increases the likelihood of metabolic syndrome, osteoarthritis, cancer, gallbladder disease and autoimmunity, thus contributing to decreased life expectancy. In fact, obesity contributes to approximately 70% of cases of diabetes. Obesity involves a complex pathological process which is reflected by environmental and genetic interactions, although a few cases are caused primarily by medical disorders.

A number of approaches have been utilized in the prevention and management and treatment of obesity, including, surgery, medication, diet, exercise and overall lifestyle changes. Despite these interventions, the prevalence of obesity and the various disorders related to it is growing. In obesity there is a constant state of chronic low-grade inflammation which is characterized by activation and infiltration of pro-inflammatory immune cells and a dysregulated production of high levels of pro-inflammatory cytokines. This pro-inflammatory milieu contributes to insulin resistance, type-2 diabetes, cardiovascular disease and other related co-morbidities. The roles of the innate (macrophages, neutrophils, eosinophils, mast cells, NK cells, MAIT cells) and the adaptive (CD4+, CD8+ T cells, regulatory T cells and B cells) immune responses and the roles of cytokines in adipose tissue inflammation and obesity are discussed. An understanding of the crosstalk between the immune system and adipocytes may shed light in better treatment modalities for obesity and obesity-related diseases.

### **P170: Metabolically unhealthy phenotype as a marker of subclinical atherosclerotic risk in perimenopausal/menopausal women using lipid accumulation product**

Pattama Tongdee (TH) and Porntip Nimkuntod (TH)

Institute of Medicine

**Background:** Obesity produces the most profound metabolic abnormalities and is associated with an increased risk of atherosclerotic cardiovascular diseases (CVD). Lipid accumulation product (LAP) were used waist circumference (WC) and fasting triglycerides (TG).

**Objective:** To investigate whether LAP is related to subclinical atherosclerosis risk in metabolically unhealthy perimenopausal/menopausal women.

**Material and method:** A cross-sectional study was conducted on 130 perimenopausal/menopausal women, aged 40 to 70 years from January 2015 to December 2015. The following variables of interest were recorded on a protocol form: demographic data, systolic blood pressure, diastolic blood pressure, weight, body mass index (BMI), WC and hip circumferences, waist to hip ratio (WHR), serum levels of fasting glucose lipid and LAP was calculated. High resolution B-mode ultrasonography was performed to measure carotid intima media thickness (CIMT).

**Patients:** Perimenopausal/menopausal women.

**Intervention:** Carotid intima media thickness (CIMT).

**Results:** Metabolically unhealthy normal weight and overweight/obese 16.15%, 83.84% respectively. Cardiovascular risk parameters: systolic blood pressure, diastolic blood pressure, BMI, WHR and lipid ratio, were associated in women with abnormal LAP index ( $LAP \geq 34.5$ ) ( $p < 0.01$ ). Pearson correlation analyses revealed that metabolic unhealthy normal weight and overweight/obese were significantly associated with LAP index but was negatively correlated with subclinical atherosclerosis.

**Conclusions:** The lipid accumulation product seems to be sufficient to differentiate metabolically unhealthy normal weight to metabolically unhealthy overweight/obesity in perimenopausal/menopausal women.

### **P171: Asymptomatic metabolic syndrome in urban Indian women aged 40 years and above**

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Jehangir Hospital, Pune

**Context:** Cardiovascular disease (CVD) in Indian women has increased significantly. Metabolic syndrome has an overall negative impact on cardiovascular health and mortality and has a worse prognosis in women. Studying the presence of asymptomatic metabolic syndrome is important to modify future risks before menopause.

**Objective:** To determine the prevalence of asymptomatic metabolic syndrome in women aged 40 yrs and above and to study the possible risk factors.

**Methods:** Women who presented voluntarily for screening from 01 September 2015 to 01 April 2016 to Jehangir Hospital, Pune, India were included. Those with history of diabetes, hypertension, dyslipidemia or a cardiac event were excluded. A detailed history was taken and a thorough clinical examination was performed. Fasting and postprandial sugars and lipid profile was done and data evaluated.

**Results:** 98 women were enrolled. There were a similar number of pre- and postmenopausal women. The mean age of menopause was 46.9 years. Majority of the women were overweight (53.1%). The prevalence of metabolic syndrome was 34.5% and this was significantly higher in those who had attained menarche after 14 years ( $p=0.001$ ). Menopause did not make a significant difference to the prevalence of metabolic syndrome ( $p=0.26$ ). More than half the women in the 40-44 (62.5%) and 45% of the women in the 45-49 age group had metabolic syndrome. There was a higher incidence of metabolic syndrome among women with menopausal symptoms. However this did not achieve statistical significance ( $p=0.56$ ).

**Conclusions:** This study highlights that there is a higher risk for women to develop metabolic syndrome in the perimenopause. Women should be screened, so that lifestyle modification can be advocated to reduce morbidity.

### **P172: Proper nutrition and supplementation in relation to fertility – case report**

Dusan Vesovic (RS)<sup>a</sup>, Ana Gifing (RS)<sup>b</sup> and Jelena Mihailovic (RS)<sup>b</sup>

<sup>a</sup>Visan - Sanitary Medical School of Applied Sciences, Center for Preventive Medicine and Chrono Nutrition Dr Gifing; <sup>b</sup>Center for Preventive Medicine and Chrono Nutrition Dr Gifing

**Objective:** Aim of the paper was to present case-report showing possible relationship between proper nutrition and female's fertility.

**Methods:** 42,5 year old lady having no children, went to gynecological clinic to try in vitro fertilization. Since she was obese, gynecologist referred her to Center for preventive medicine and chrono-nutrition Dr Gifing®, Belgrade, Serbia in order to first reduce body mass. When her body mass is optimal, she was told that she would commence with in vitro fertilization. All of the biochemical parameters followed were disturbed – C-reactive protein – 7,1 mg/l, blood sugar level – 18,5 mmol/l, HbA1c – 10,2%, cholesterol – 8,1 mmol/l, HDL – 1,6 mmol/l, LDL – 5,36 mmol/l, triglycerides – 2,5 mmol/l, ALT – 57 IU/l, AST – 30 IU/l, gamma-GT – 159 IU/l, vitamin D – 12,7 nmol/l, and antibodies towards thyroid gland were elevated. Her body mass was 111,5 kg; excess of fat mass was 33,7 kg. She was subjected to Chrono-nutrition program Dr Gifing® (CNPDrG®) in order to reduce body weight and to balance impaired metabolic parameters. CNPDrG® is completely personally tailored nutrition and means taking meals of certain food which body well tolerate at proper day-time accompanied with supplementation. Food tolerance test was done on MORA nova touch machine. CNPDrG® started during August of 2014.

**Results and discussion:** After the first month of CNPDrG®, majority of her blood biochemical parameters were within physiological ranges. Following 4,5 months, her HbA1c was normal. During whole follow-up time she has been successfully losing her fat. Her gynecologist planned to start with in vitro during summer time of coming year (2015). However, she became pregnant naturally during April 2015 and gave a birth to daughter later.

**Conclusions:** This is an example how proper nutrition, accompanied with good supplementation, is important for restoring balance into human body.

### **P173: Chrono Nutrition Program Dr Gifing® regulates both body weight and impaired metabolic parameters**

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**Objective:** Aim of the paper is to reveal at what extent Chrono-nutrition program Dr Gifing® (CNPDrG®) influences metabolic parameters (blood sugar, cholesterol, and triglycerides) in obese patients of both sexes.

**Methods:** Data was obtained from medical records. Each patient had blood analysis prior commencing CNPDrG® and one month after being on the program. CNPDrG® is personally tailored and means taking meals of certain food which body well tolerate at proper day-time. Each patient received personally tailored supplementation and nutrition plan, which was based on lab analysis, current medical condition of the person, and results of food tolerance test done on MORA nova touch machine. Basic methods of descriptive statistics were applied, as well as Student's t-test for paired samples.

**Results and discussion:** Of 265 examinees included in the study, 96 of them were males and 169 were females. After one month of CNPDrG®, cholesterol and triglycerides mean value were significantly reduced –  $p=0,000$  reaching physiological values within this period (cholesterol - 6,46+-1,08 vs. 5,09+-0,83 and triglycerides - 2,37+-1,9 vs. 1,32+-0,62). The same trend was seen in LDL level - 4,04+-0,94 vs. 2,92+-0,75; this reduction was high significant –  $p=0,000$ . This can be explained by proper, individually adjusted nutrition and supplementation, and body mass reduction. Mean value of HDL showed trend of rise (1,27+-0,35 vs. 1,28+-0,33), but it was not statistically significant –  $p=0,771$ . Further follow up of these patients should be done to clarify this issue. Blood sugar mean level showed decrease (5,92+-1,00 vs. 5,25+-0,76), which was high statistically significant –  $p=0,000$ .

**Conclusions:** Beside reducing body mass in obese patients, CNPDrG® proved to be efficient approach in solving impaired metabolic parameters, thus preventing further development of various diseases.

## **Primary ovarian insufficiency**

### **P174: Different aspects of primary ovarian insufficiency**

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**Introduction:** Primary ovarian insufficiency also known as premature ovarian failure that means loss of normal function of both ovaries before the age of 40. The triad for the diagnosis are - amenorrhoea, hypergonadotropism and hypoestrogenism. POI affects 1% of the female population. Here we report three cases of primary ovarian insufficiency from three different point of views. **Case 1:** A 27 years old unmarried lady had amenorrhoea for 16 months. Her secondary sexual characteristics were normal and had no mental impairment or cognitive deficient. USG of whole abdomen showed normal size uterus with small size ovaries. FSH: 68.31 mIU/L, LH: 29.46 mIU, estradiol: 5pg/ml. Karyotyping

analysis showed: 45,X(44%)/46,X,rea(X)(56%) mosaicism which is compatible with the Turner like condition.

*Case 2:* A 24 years old married regularly menstruating woman came with secondary amenorrhoea with primary subfertility. She had hot flushes, dyspareunia, and loss of libido. FSH: 125.69 mIU/ml and LH: 38.69 mIU/ml, estradiol level was less than 10 pg/mL. Karyotype was 46XX. TVS report showed normal sized uterus with thin endometrium and small ovaries. Progesterone withdrawal test was negative. HRT given. After 3 years of treatment during routine analysis of FSH and LH we got FSH: 9.67 mIU/ml and LH: 4.62 mIU/ml. We again repeated the tests and found FSH: 8.01 mIU/ml, 6.32 mIU/ml and LH level: 4.01 mIU/ml, 3.03 mIU/ml. After these results we gave her ovulation induction and after 3 cycles she conceived.

*Case 3:* A 14 years young girl came to our clinic for HPV vaccine. After 2 months of vaccination patient complained of secondary amenorrhoea with hot flushes. FSH, LH showed POI.

*Conclusions:* The early detection and identification of POI would provide a better opportunity for early intervention and also provide for potential targets for therapeutic intervention.

### P175: Premature menopause – another view

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*Context:* The menopause and premature ovarian failure (POF) can have similar symptoms. Therefore, the POF is often referred to as premature menopause. However, menopause, in contrast to POF, is the result of natural aging of women. The causes of premature ovarian failure are unknown. It is mostly idiopathic, so there is no prevention. Modern Western Medicine (MWM) uses models to understand biological systems.

A system model helps us see the complex relationships, to simplify, to determine the links between system components. A model is an approximation of reality. None of them is sufficiently accurate, but most of them are useful. One of the principles of modeling is to use the existing model whenever possible. The modeling is also known in the Traditional Chinese Medicine (TCM). It uses symbols – general signs with deeper meaning, such as Water, Fire, Kidney, Qi or Blood.

Natural menopause is understood as the result of Kidney Essence deficiency. Premature menopause relates to the stagnation of Qi Energy and resultant Blood Stagnation. This manifests in clinical signs of Fullness, Excess.

Energy (Qi) and Blood are essential components to allow vital activities of the body. In the modern physiology, the basic properties of blood include viscosity and suspension stability. Their disruptions, such as hyperviscosity, leads to microcirculatory disturbances.

*Objective:* To illustrate the nature of premature menopause using schematic and photo documentation of tongue, with emphasis on the TCM etiology. To show the analogy between the TCM Blood Stagnation and blood pathophysiology in MWM.

*Methods:* Biological systems modeling.

*Results:* Many causes may act through one pathophysiological mechanism.

*Conclusions:* The integration of traditional Chinese medicine model and modern Western medicine knowledge could lead to opening up new prevention and POF treatment possibilities.

### P176: Bone mineral density in women with premature ovarian insufficiency with and without the use of standard dose hormone therapy

Cristina Benetti-Pinto (BR), Helena Giraldo (BR), Valeska Ferreira (BR) and Daniela Yela (BR)

University of Campinas

Women with premature ovarian insufficiency (POI) should be treated with estrogen replacement in order to reduce hypoestrogenism symptoms and preserve bone mineral density (BMD).

*Objective:* To assess whether hormone therapy (HT) with standard estrogen dose is sufficient to avoid bone mass loss in women with POI.

*Methods:* Cross-sectional study. Women with POI with secondary amenorrhoea seen 2000-2012 in the Gynecological Endocrinology outpatient Clinic at the State University of Campinas were included. Two hundred and thirty nine women were evaluated: 132 using standard dose HT (1 mg 17-Beta-Oestradiol or 0.625 mg conjugated estrogen) and 107 women without HT. Detailed history was obtained and these women were subjected to evaluation of bone mineral density (BMD) in the lumbar spine (LS), femoral neck (FN) and total femur (TF) through DEXA technique.

*Results:* The mean age, age at last menstrual period and BMI for the untreated group and the group with HT were  $38.1 \pm 6.1$  and  $36.8 \pm 7.3$  years;  $31.4 \pm 7.3$  and  $30.7 \pm 7.2$  years;  $26.6 \pm 7.1$  and  $25.8 \pm 4.6$  respectively ( $p = NS$ ). The mean LS BMD was  $1.06 \pm 0.15$ ,  $1.00 \pm 0.17$  g/cm<sup>2</sup> ( $p = 0.003$ ), FN  $0.92 \pm 0.15$ ,  $0.89 \pm 0.14$  ( $p = 0.0479$ ) and TF  $0.92 \pm 0.19$ ,  $0.91 \pm 0.13$  g/cm<sup>2</sup> ( $p = 0.039$ ) respectively. BMD at LS was compromised in 45% for women without treatment and 60% standard dose HT ( $p = 0.01$ ). For the FN 25% of women without treatment and 29% for standard dose HT, were compromised ( $p = 0.38$ ). For TF compromise was found in 32% of the untreated women and 36% for standard dose HT ( $p = 0.34$ ).

*Conclusions:* The standard dose HT seems to be inefficient to reduce bone loss in the lumbar spine and femur of women with POI.

### P177: A double-blind randomized controlled trial of vaginal misoprostol before outpatient hysteroscopy in postmenopausal women

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*Objective:* To evaluate the efficacy of vaginal misoprostol for cervical ripening in postmenopausal women before diagnostic outpatient hysteroscopy without anesthesia. *Methods:* A double-blind randomized clinical study was performed. One hundred and fifty-eight patients were included in the study and randomly allocated into two groups (79 patients used 200 µg of misoprostol by the vaginal route and 79 used placebo). The following variables were studied: age, parity, time since menopause, associated diseases, indication for the exam, duration of the procedure, frequency and severity of pain during exam, need for additional cervical dilatation, adverse effects and complications. For statistical analysis, the chi-square tests of association were used. Fisher's exact test and the Mann-Whitney tests were used for the comparison

between groups, considering an alpha error lower than 5%. SAS version 9.02 was the software used to perform these procedures. **Results:** Women from both groups displayed similar characteristics. The duration of hysteroscopy was similar in both groups:  $2.5 \pm 2.7$  minutes for the misoprostol group and  $2.1 \pm 1.6$  minutes for the placebo group ( $p=0.43$ ). Pain during grasping of the uterine cervix was rated as  $3.29 \pm 3.09$  for the misoprostol group and  $3.52 \pm 3.06$  for the placebo group. During exam, pain was categorized as  $5.27 \pm 3.52$  for the misoprostol group and  $5.53 \pm 3.36$  for the placebo group. During biopsy, pain was classified as  $4.08 \pm 3.46$  for the misoprostol group and  $3.83 \pm 3.34$  for the placebo group. In both groups there was no significant difference in pain severity ( $p=0.52$ ,  $p=0.69$  and  $p=0.68$ , respectively). **Conclusions:** Previous use of misoprostol does not prepare the uterine cervix and fails to decrease pain during the performance of diagnostic hysteroscopy without anesthesia in postmenopausal women.

### **P178: GAPO syndrome: a new syndromic cause of premature ovarian insufficiency**

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Premature ovarian insufficiency has the following causes: genetic, autoimmune, metabolic, infectious, and iatrogenic dysfunctions (including radiotherapy, chemotherapy and surgery). However, premature ovarian insufficiency remains without a definite cause in a substantial number of cases. This article describes GAPO syndrome in association with premature ovarian insufficiency, as well as a novel ANTXR1 gene mutation. Histopathological study of the ovaries of a woman with hypergonadotrophic hypogonadism revealed extensive deposition of hyaline extracellular material, with bilateral parenchymal atrophy and follicular depletion. Molecular study revealed a novel ANTXR1 gene mutation. The homozygous  $c.378 + 3A > G$  transition at position at the consensus donor splice site of intron 4 was identified.

**Conclusions:** Our results support the involvement of ANTXR1 gene mutations in deregulated extracellular matrix. In addition, our study identified a novel ANTXR1 mutation causing GAPO syndrome indicating it as a new cause of early loss of ovarian function.

### **P179: Epidemiological observation of patients with premature ovarian failure (POI). Preliminary results**

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**Objective:** Since 2014 the Spanish consortium for the study of premature ovarian failure has set up a Registry of new cases of

primary or secondary ovarian failure. This communication updates the information lend by the first 92 cases registered.

**Methods:** High gonadotropin and low oestrogen levels before age 39 where the basic inclusion criteria. Basal evaluation included: hormonal determinations (FSH, LH, E2, PRL and TSH) and biochemical profile. A completed Immunological study was performed including antithyroid, antiphospholipid and antinuclear (ANA) antibodies. Karyotyping was complemented with a determination of FMRI premutations to detect molecular changes related to X-Fragile Syndrome. Bone mineral density (BMD) was measured by dual energy X-ray (DEXA).

**Results:** We included 92 women in the age range 18-39 years. In 27 cases (29.3%) a family history (mother sister/s or both) of POF was recorded. Evidences of an active autoimmune disease was detected in 10 (10.8%) and 12 (13.04%) had positive antibodies non related to a clinically active disease. Thirteen patients (15.3%) presented with previous oncological pathology. From them 10 (11%) received chemotherapy, 3 (3.6%) radiotherapy and 5 (5.43%) underwent a bilateral anexectomy. The genetic evaluation disclosed 3 (3.3%) cases of chromosomal alteration and 6 (6.5%) cases of abnormal count of Fragile X pre-mutations. In 52 cases none of the aforementioned studies detected any potential cause of POF and were considered as "idiopathic".

**Conclusions:** As in the literature the cause of the majority of POF remains undetected. The prevalence of familial association suggest undetected genetic causes in cases without family history. Previous oncologic treatments remains the best known and frequent cause of POF.

Code protocol IIBSP health - IOP - 2012-109 . Clinical Trials.gov ID: NCT02068976

### **P180: A study of dyslipidemia, arteriosclerosis and osteoporosis in the primary ovarian insufficiency**

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**Objective:** Primary ovarian insufficiency is a risk factor for coronary artery disease, stroke and osteoporosis. To improve health care for primary ovarian insufficiency patients, we aimed to retrospectively verify the presence/absence of carotid lesions and reduced bone density in them.

**Methods:** Seventy patients with primary ovarian insufficiency were investigated by carotid ultrasonography for the presence/absence of arteriosclerotic plaques, given a plaque score, and assayed for various lipid values. Bone density was measured by lumbar spine dual energy X-ray absorptiometry (DXA), and osteoporosis was diagnosed if bone mineral density was  $\leq 70\%$  of the young adult mean (YAM). Testing for significance used the t-test and Kruskal-Wallis test. The study was approved by the ethics committee of our hospital.

**Main outcome measures:** The mean age of the 70 patients was  $42.8 \pm 5.0$  years. Carotid ultrasonography found arteriosclerotic plaques in 13 patients. The median plaque score was 1.5. Stratified by age, 2 of these 13 patients were in their 30s, 10 were in their 40s and one was in her 50s. Only one patient was diagnosed as having osteoporosis. Stratification on the basis of presence/absence of carotid plaques indicated no significant differences with regard to any of the lipid values or YAM.

**Results:** The present study of patients with primary ovarian insufficiency found high incidences of carotid artery lesions of more than 20% in women in both the 4th and 5th decades of life. However, it was difficult to predict carotid artery lesions based

on the assayed lipid values. Additionally, the prevalence of osteoporosis was low, suggesting that hormone replacement therapy might be contributing to its prevention.

**Conclusions:** The incidence of carotid artery lesions is high in women with primary ovarian insufficiency, whereas the prevalence of osteoporosis may be low.

### ***P181: Gonadotropin-releasing hormone agonist therapy as ovarian protectants for prevention of chemotherapy induced ovarian failure in patient with cervical cancer***

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**Objective:** To assess the efficacy of a gonadotropin-releasing hormone agonist (GnRH-a) depot (leuprolide acetate) in women with cervical cancer receiving chemotherapy while taking a continuous add-back on the prevention of premature ovarian failure.

**Methods:** Twenty eight premenopausal patients with cervical cancer stage who had undergone conservation of ovaries surgery received a GnRH-a depot plus add-back until chemotherapy was completed. Four weeks thereafter, a hormonal profile (follicle stimulating hormone) was measured.

**Results:** The mean of follicle stimulating hormone level was 18.3 IU/L. Among 28 women who received GnRH, ovarian function was preserved in 25 (92.9%) and 2 (7.3%) had premature ovarian failure.

**Conclusions:** GnRH-agonist appears to protect ovarian function following chemotherapy during short-term follow-up. A large randomized controlled trial with longer period of follow-up is needed.

### ***P182: The effectiveness of vaginal estriol and plazmolifting in women with vulvovaginal atrophy***

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**Objective:** To investigate the impact of Plazmolifting and vaginal estriol in women with symptomatic vulvovaginal atrophy (VVA): kraurosis and leukoplakia. Prospective study. The criteria for inclusion in the study were: symptoms of VVA; menopausal age; absence of menstruation for  $\geq 12$  months; dissatisfaction with hormonal therapy. The exclusion criteria: use of hormonal therapies; prolapse staged  $\geq II$ ; urinary tract infection; previous reconstructive pelvic surgery. Plazmolifting<sup>TM</sup> is the commercial name of the injectable form containing platelets autoplasm applied for the purpose of tissue regeneration. Women were treated with autoplasm injections per visit. The procedure was performed in the outpatient clinic, not requiring any specific preparation, analgesia or anesthesia. We administered estriol vaginal gel 1 application/day during the first week (maximum of 4 weeks), more maintenance dose (1 applique 2 times a week) for 1 month. We evaluated the result of two months from the first visit. The study included 30 patients. The average age of 57.8 years. At baseline,

18 women (60.0%) were sexually active while 12 (40.0%) did not have sexual intercourses due to the severity of VVA. After the treatment, 11 patients (91.7%) have resumed sexual activity. We observed complete disappearance of itching, dryness, cracking of the external genitalia and the vulva in 28 (93.3%) of women. Symptoms of dysuria, frequent and painful urination ( $n=24$ ) stopped in 21% (87.5%) of women. In 8 (26.7%) of the patients had complaints of frequent exacerbations of hemorrhoids. These patients complained of discomfort and pain in the perianal region at the time of the first contact. As a result of the treatment of hemorrhoids symptoms were stopped in all patients. We have seen a good effect improved the color, turgor, hydration of the skin and mucous vulvar labia 26 (86.7%) of women.

### ***P183: The prevalence and psychological impact of sexual dysfunctions following bone marrow transplantation in young women survivors***

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**Objective:** Bone marrow transplantation (BMT) has been successfully used to treat hematological malignancies such as leukemia, lymphoma. The transplant causes both direct injury to gonads and indirect irreversible damage to the hypothalamic-pituitary-gonadal axis leading often to premature ovarian failure, sexual dysfunctions and low quality of life. Sexuality is defined as a dynamic multidimensional construct involving physiological, psychological and social processes, by which personality is expressed, love is communicated and emotions are experienced.

**Methods:** This study is a part of an ongoing clinical research started in 2014 and held within the Obstetrics and Gynecology Department of "Nicolae Malaxa" Clinical Hospital, Bucharest, Romania. It included 14 women diagnosed with premature ovarian failure and subsequent sexual dysfunctions. Patients completed a questionnaire and the aim of the study was to determine the prevalence of sexual dysfunctions among women survivors, and the additional impact on quality of life.

**Results:** The analysis of the data showed significantly changes in sexual behavior. The desire level was found to be low or moderate, with an arousal degree of 2 or 3 of a maximum 6 level. Most reported to become sometimes lubricated, the difficulty level 2 and 3 out of a maximum 6, and difficulties in maintaining it during intercourse. Two women reported no sexual activity, and for the rest achieving orgasm was mostly very difficult or difficult. The satisfaction level was reported low or moderate, while the pain experienced during intercourse was present most of the times and at a moderate or high level. All women showed significant decrease in sexual and emotional related quality of life.

**Conclusions:** Cancer diagnosis and its treatment are usually followed by profound and irreversible changes in sexual behavior and emotional closeness.

### **P184: The characteristics of premature ovarian insufficiency in a Romanian cohort**

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**Context:** Natural menopause occurs at a median age of 51.4 years and results from ovarian follicle depletion. Premature ovarian insufficiency (POI) is defined as a heterogeneous disorder leading to amenorrhea and ovarian failure before the age of 40 years. The elevated level of follicle stimulating hormone (FSH)  $\geq 40$  UI/L is a routine diagnosis for the disease.

**Objective:** The assessment of the occurrence of POI, the age-specific incidence rates, the heritability, the ultrasound appearance and the natural history of the disease.

**Methods:** Observational study including a cohort of 980 women between 25-40 years old which have been annually evaluated clinically and by ultrasound during a 15 years period. **Results:** We found 22 women with loss of menstrual regularity and postmenopausal range of FSH, having symptoms related to estrogen deficiency significant correlated with the decrease of follicular reserve. Few antral follicles  $\geq 3$  mm have been detected by transvaginal ultrasound examination in 45.45% of women, having only 1 case of large luteinized follicle cyst. The incidence of POI was three times higher in the age interval 35-40 compare with the younger group and 90.9% of cases had a first relative degree with a positive history for premature ovarian failure; 4 patients returned for a short period to regular menses but no woman conceived during the follow-up period.

**Conclusions:** Young women with menstrual irregularity for three or more consecutive months have to be evaluated at their first visit in order to increase the rate of POI early diagnosis. The age of mother's menopause accompanying the decrease of follicular reserve seems to be a valuable prognostic factor.

### **P185: Effects of conventional HRT and oral contraceptive pills in women with premature ovarian insufficiency**

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**Objective:** Women with premature ovarian insufficiency (POI) should be advised to take HRT for bone protection and for prevention of cardiovascular diseases. Some women with POI prefer the oral contraceptive pills (OCs) to avoid pregnancy even if it is low possibility. The aim of this study was to compare the effect of conventional HRT and OCs on bone mass density (BMD), lipid profile and liver enzyme in women with POI.

**Methods:** One hundred twenty five women with POI were recruited in this study (age range 13-40). One hundred five women took estradiol valerate (2 mg/day) with cyclic progestins (Provera® 10 mg), and 20 women took OCs contained ethinylestradiol 0.02 mg and drospirenone 3 mg for 12 months. Serum cholesterol, LDL, HDL, triglyceride, SGOT and SGPT were

measured. BMD was measured by DEXA at study entry and 12 months later.

**Results:** Among POI women, only 2.9% of women with primary amenorrhea chose OCs; however, 21.1% of women with secondary amenorrhea chose OCs. Mean age of HRT group was younger than that of OCs group ( $26.12 \pm 7.97$ ,  $30.85 \pm 7.39$  respectively). Body weight, height, blood pressures were not different between two groups. Serum FSH, LH, TSH, AMH were not different either. Pretreatment lumbar spine BMD z-score was  $-1.51 \pm 1.04$ , increased to  $-1.35 \pm 0.92$  after HRT. BMD of femur was increased from  $-1.17 \pm 0.74$  to  $-0.95 \pm 0.59$  after HRT. In OCs group, lumbar spine and femur BMD were also increased after treatment. Changes in BMD in response to HRT and OCs were not significantly different. After treatment, serum cholesterol, LDL, HDL, triglyceride, SGOT and SGPT were not deteriorated in each group. Those parameters were comparable between two groups.

**Conclusions:** Conventional HRT in women with POI has the beneficial effect on BMD without changes of lipid profile or liver enzyme. OCs has similar effects and might be offered as patients' preference at least 12 months.

### **P186: Serum anti-Müllerian hormone levels as diagnostic marker for premature ovarian insufficiency in young women with amenorrhea**

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**Objective:** Serum AMH levels follow the reduction in follicular number over time in healthy women and fall to very low levels prior to menopause. The aim of this study was to investigate serum AMH levels in women with amenorrhea and to determine the predictive value for differential diagnosis of premature ovarian insufficiency (POI) in young women complained amenorrhea.

**Materials and methods:** One hundred twenty women with primary and secondary amenorrhea were recruited in this study (age range 13-29). Women with hypergonadotropic amenorrhea (POI,  $n=18$ ), hypogonadotropic amenorrhea (HA,  $n=21$ ), polycystic ovary syndrome (PCOS,  $n=68$ ), normogonadotropic amenorrhea with other cause such as MRKH, hypothyroidism or hyperprolactinemia (NA,  $n=13$ ), and were compared with normogonadotropic regularly menstruating women ( $n=57$ ). Sera were collected for determining the levels of AMH, basal FSH, LH, E2, T, DHEA-s, TSH, and prolactin.

**Results:** The AMH serum levels of each group were  $0.20 \pm 0.15$  ng/mL in POI,  $6.40 \pm 3.53$  ng/mL in HA,  $12.73 \pm 4.91$  ng/mL in PCOS,  $6.08 \pm 3.67$  ng/mL in NA and  $4.73 \pm 2.18$  ng/mL in control group. AMH was well correlated with FSH, LH, E2, and T, however, not correlated with TSH, prolactin or DHEA-s. The AMH serum levels of POI were significantly lower than HA, PCOS, NA, and control group ( $p$ -value  $< 0.01$ ). The cut-off value for predicting POI was 0.72 ng/mL with sensitivity of 100%, and specificity of 100%. The AMH serum levels of PCOS were significantly higher than POI, HA, NA, and control group ( $p$ -value  $< 0.01$ ). No significant differences were observed between FHA, NA, and control group.

**Conclusions:** The measurement of AMH, in addition to FSH, LH, and E2 might give more detailed information for diagnosis about the ovarian status, and avoid the excessive serial test. Serum AMH could be a useful marker of differential diagnosis for POI in young women with amenorrhea.

### **P187: Effects of a short-term Tamoxifen treatment on menopausal symptoms of perimenopausal breast cancer patients**

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**Objective:** Tamoxifen treatment for breast cancer is effective before and around menopause, but lower estrogen levels may cause variety of unidentified complaints. To investigate effects of short-term tamoxifen treatment on mental and physical health conditions.

**Methods:** Perimenopausal breast cancer women who were prescribed tamoxifen were asked to answer the total condition by VAS (Visual Analogue Scale) and the HADS (Hospital Anxiety and Depression Scale) for investigating anxiety and depression at the first and the second prescription. The subjects were 57 Japanese women (mean age $\pm$ SD; 45.3 $\pm$ 6.9 years), and the treatment range was 4.7 $\pm$ 1.5 weeks. We also evaluated changes in the intensity and nature of complaints with Keio modified menopause index with 41 headings.

**Results:** VAS score was slightly increased after about one month's tamoxifen treatment, but no significant change. There was also no change in all the total HADS score, the anxiety and the depression score; from 8.7 $\pm$ 6.5 to 8.7 $\pm$ 7.4, 4.8 $\pm$ 3.3 to 4.7 $\pm$ 3.7, 3.9 $\pm$ 3.7 to 4.0 $\pm$ 4.0, respectively. The number of doubtful or definitive cases in anxiety and depression was 12 and 9 at the initial check, and 7 and 9 at the second check. According to the analysis with Keio modified menopause index, the overall rates of improvement, remain unchanged, and worsening were almost the same. About 35% of women with hot flash had sign of worsening. However, other reputed typical side effects of tamoxifen, such as sense of numbness, were not changed apparently during this period.

**Conclusions:** Tamoxifen treatment on perimenopausal women with short term had an insignificant effect on so-called climacteric symptoms. Other causes than hormonal factors may be considered during this period. Further investigation with long and periodical checks will be needed.

### **P188: Determinant factors in mammographic breast density in women with premature ovarian insufficiency**

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University of Campinas

To minimize the consequences of premature ovarian insufficiency (POI), the main treatment is hormone therapy (HT). There is a lack in knowledge about the influence of HT in the breast composition of these women. The percentage of mammographic density (PMD), an independent risk factor for breast cancer, it is also understudied in POI. **Objective:** To evaluate the PMD of women with POI.

**Methods:** Cross-sectional study of 163 women with secondary amenorrhea due to POI who underwent mammograms. PDM was evaluated by digitalization on the left medial-lateral incidence. Areas corresponding to fibroglandular and fatty tissue were

marked and scanned. The percentage of glandular tissue in relation to the total volume of the breast was calculated, and was analyzed by age at menarche, age at onset of POI, length of POI, age at onset of mammogram, body mass index (BMI), parity and HT time, dose and regimen.

**Results:** The mean age of woman were 41.3 $\pm$ 5.4 years, PMD 24.3 $\pm$ 18.5. The POI was at 32.3 $\pm$ 5.9 years. There was no significant difference in the PMD by age group (29-39, 40-49, 50-55 years,  $p=0.23$ ) or when comparing no use of HT with low, high dose or other HT, 24.7 $\pm$ 16.7, 19.6 $\pm$ 23 and 25.9 $\pm$ 16.9 and 24.6 $\pm$ 16.2 respectively, ( $p=0.82$ ) used for 5.57 $\pm$ 4.7 years. Comparing cyclical or continuous HT, there was no difference in PMD ( $p=0.49$ ). The nulliparous had higher PMD than multiparous women ( $p=0.0016$ ), however POI occurred earlier in nulliparous women ( $p<0.0001$ ). Among the variables studied were determinants of PMD the presence or absence of pregnancy and BMI.

**Conclusions:** In POI woman, only parity and BMI are consistently associated with the determination of PMD, with higher density of the breast in nulliparous women with lower BMI. Age at menarche, age at POI and at the time of mammography, besides the use of HT, regardless of the duration of use, dose and regimen, had no influence on PMD.

### **P189: Clinical profile of a group of outpatients with premature ovarian failure in a Gynecologic Clinic from a University Hospital in the South of Brazil**

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**Introduction:** Premature ovarian failure (POF) is defined as the development of hypogonadism hypergonadotropic in women 40 years old or younger. The etiology may vary from idiopathic, post-surgical, post radiotherapy and/or chemotherapy, and even due to autoimmune and genetic causes.

**Objective:** To assess the clinical profile of patients with POF treated in a Gynecologic Clinic from a University Hospital in the South of Brazil.

**Materials and methods:** Retrospective study with review of medical records of 38 patients with POF attending a gynecologic service referral from a hospital in the South of Brazil.

**Results:** The average age was 40.50 years old (yo) (19 yo - 63 yo). The average age of the occurrence of POF was 29.58 yo. The average period of menopause (current age - age of POF) at the time the records were reviewed was 11.26 yo. The average body mass index (BMI) was 28.34 ( $\pm$  7.33). The most prevalent cause was post-surgical cases (36.8%), followed by idiopathic cases (21.1%). Autoimmune causes, genetic and gonadal dysgenesis accounted for 5.3% of the total each. Twelve (31.6%) of the 38 patients had a personal history of cancer, 8 (21.1%) were smokers and 3 (7.9%) had diabetes mellitus. The Kuppermann Index average score was 28.05, ranging from 2 to 46. There was a weak and direct but statistically significant correlation between the period of menopause and the Kuppermann index, showing an increase of this score as the length of the period of menopause increased, although both did not increase at the same rate.

**Conclusions:** Different from the revised literature, in which POF's predominant cause is idiopathic, our review revealed a predominance of post-surgical cases. This result is probably due to the fact

that our service is located in a University hospital and it is a reference for the follow-up of patients with cancer treatment.

**P190: Does menopause affect the response to complex decongestive physiotherapy in breast cancer related lymph edema?: A pilot study**  
Nesrin Yagci (TR), Orcin Telli Atalay (TR), Nilgun Simsir Atalay (TR)  
**Objective:** Complex decongestive physiotherapy (CDP) is the only treatment option in most cases of lymph edema; its effectiveness has not been well established. Clinical response to CDP is difficult to predict and factors influencing the response to treatment are unknown. In this study it was aimed to compare the response to CDP between pre and postmenopausal women with breast cancer related lymph edema.

**Methods:** Complex decongestive physiotherapy was applied to fifteen women with breast cancer related lymph edema. The decrease in circumference of affected extremity was measured, depression levels (Beck Depression Inventory) and quality of life (Nottingham Health Profile) was assessed before and after treatment. The results of 7 premenopausal women (mean age:  $43.78 \pm 7.98$  year) were compared with the results of 8 postmenopausal women (mean age:  $44.66 \pm 9.92$  year).

**Results:** The depression scores of premenopausal women decreased  $12.67 \pm 3.44$  averagely and the total scores quality of life decreased  $42.14 \pm 4.16$  whereas the depression scores of postmenopausal women decreased  $8.46 \pm 4.27$  averagely and the total scores quality of life decreased  $34.31 \pm 6.28$ . There were significant differences in terms of depression levels and quality of life between pre and postmenopausal women ( $p < 0.05$ ). The mean reduction in the lymph edema was 7.42% in premenopausal women and 8.12% in postmenopausal women respectively. Any significant difference was not found in the comparison of reduction in circumference measurement of affected extremity ( $p > 0.05$ ).

**Conclusions:** In the results of this pilot study, menopause was not found to be a factor that affects the response to CDP in breast cancer related lymph edema in terms of decrease in edema however it can be effective on depression levels and quality of life. Further studies with higher population are needed.

### **P191: Promoter mutation in the XIST gene is not related to X-chromosome inactivation patterns in patients with idiopathic primary ovarian insufficiency**

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**Objective:** There were reports that incidence of skewed X-chromosome inactivation (XCI) was significantly higher in the primary ovarian insufficiency (POI) patients and a promoter C43G mutation in the X-inactive specific transcript (XIST) gene was associated with skewed XCI. This study was performed to investigate whether the XIST gene promoter mutation is associated with idiopathic POI which shows skewed XCI in a Korean population.

**Methods:** The subjects consisted of 126 idiopathic POI patients ( $35.3 \pm 13.9$  years old, mean  $\pm$  SD) and 126 healthy controls ( $35.2 \pm 13.9$  years) that had normal menstrual cycles. The women recruited as control were age-matched. The XCI status was evaluated by the methylation assay of androgen receptor locus in cases and controls. For the promoter C43G mutation in the XIST gene, genotyping was identified using PCR-RFLP analysis.

**Results:** The incidence of skewed XCI on all three levels ( $\geq 90\%$ ,  $\geq 80\%$  and  $\geq 70\%$ ) was similar between POI patients and controls, and showed random pattern. Within POI population, the patterns of skewed XCI were not associated with age at the time

of POI and LH, FSH, estradiol levels. There was no C43G mutation in the XIST gene, on the contrary to our expectation, in both idiopathic POI patients and controls. Result of no mutation was confirmed by sequence analysis. Small deletions or mutations in X-linked genes do not appear to be a common feature of POI.

**Conclusions:** The C43G mutation in the XIST gene was not associated with idiopathic POI and also not XCI patterns in a Korean population, implying that the role of X-inactivation pathway in the pathogenesis of POI is not clear yet. This is the first report regarding the association between the XIST gene variations and XCI patterns in idiopathic POI.

## **Sexual health**

### **P192: Intravaginal testosterone provides efficacy and safety for postmenopausal vaginal atrophy treatment: a randomized controlled trial**

Tatiane Fernandes (BR), Adriana Pedro (BR), Luiz Baccaro (BR), Lucia Costa-Paiva (BR) and Aarao Pinto-Neto (BR)

State University of Campinas - UNICAMP

**Context:** Vaginal atrophy is a chronic condition common in women in postmenopause that causes changes on quality of life. There are currently few therapeutic options adequately assessed.

**Objective:** To evaluate the metabolic, hormonal and endometrial safety after the use of estrogen, testosterone and polyacrylic acid used for the treatment of vaginal atrophy in postmenopausal women and compared to a control group.

**Methods:** A randomized controlled clinical trial on 80 postmenopausal women between 40 and 70 years of age with follow-up at the Menopause Clinic of State University of Campinas. The women were randomized to treatment with topical vaginal estrogen, testosterone, polyacrylic acid, or water lubricant alone, three times a week for a period of 12 weeks from November 2011 to January 2013. In all four groups, data were collected at baseline and after 6 and 12 weeks of use of the respective medication. To examine the hormonal and metabolic safety, it was measured the endogenous levels of FSH, LH, 17 estradiol, estrone, androstenedione, DHEA, DHEA sulphate, SHBG and metabolites: total cholesterol, HDL, LDL, triglycerides, AST, ALT, GGT. Transvaginal sonography was performed to evaluate endometrial thickness at baseline and after 12 weeks.

**Results:** Topical estrogen, testosterone and polyacrylic acid in comparison with lubricant after 12 weeks of treatment showed no significant laboratory and endometrial alteration. Treatment with vaginal estrogen presented with elevation of serum estradiol values after 12 weeks in only 3 women. There were no statistically significant differences in endometrial thickness between the four groups at baseline and after 6 and 12 weeks of treatment.

**Conclusions:** The vaginal use of testosterone and estrogen for treatment of postmenopause vaginal atrophy demonstrated hormonal, metabolic and endometrial safety when compared to the lubricant.

### P193: Menstrual cyclicity change in ovarian aging in Chinese women

Rong Chen (CN)

Peking Union Medical College Hospital

**Objective:** To observe the alterations of menstrual factors in ovarian aging in Chinese women.

**Methods:** The data were obtained from one-year observation of a prospective cohort involving 323 healthy women in the age of 30-54 years in a community in Beijing. Menstrual diary was kept and serum level of follicle-stimulating hormone (FSH) was tested. The participants were divided into groups based on age, FSH level, and stages of reproductive aging. Alterations of length of menstrual cycle (LMC), length of menstrual period, and menstrual volume were analyzed in each group.

**Results:** (1) Age: the mean LMC extended after the age of 40 years, obviously after 48, and peaked in 50-year-old group. The menstrual volume scores were approximately stable between 38 to 46 years old, with a  $(45.06 \pm 93.54)$  peak in 48-year-old group, and a minimum of  $(15.87 \pm 13.81)$  in 52-year-old group. (2) FSH level: LMC increase with elevation of FSH levels. There was no significant difference on the mean length of menstrual period among each FSH level group, but the variation of length of menstrual period was maximum in  $20 < \text{FSH} \leq 40$  U/L group. The maximum mean menstrual volume scores was  $(30.69 \pm 31.84)$  observed in  $10 < \text{FSH} \leq 15$  U/L group, while the minimum was  $(17.38 \pm 24.38)$  in  $\text{FSH} > 40$  group. (3) Stages of reproductive aging: the length of menstrual period and menstrual volume scores among each stage showed no statistical significant difference ( $P > 0.05$ ).

**Conclusions:** The LMC altered significantly in ovarian aging, which could be used as staging criteria of reproductive aging. The length of menstrual period and menstrual volume are also showing some characteristic changes, possibly of some clinical values.

### P194: Female sexual function index (FSFI) in Brazilian postmenopausal women with metabolic syndrome

Gustavo Dutra Da Silva (BR)<sup>a</sup>, Sonia Lima (BR)<sup>b</sup>, Benedito Reis (BR)<sup>b</sup>, Carolina Macruz (BR)<sup>b</sup> and Sóstenes Postigo (BR)<sup>b</sup>

<sup>a</sup>São Francisco University; <sup>b</sup>Santa Casa de São Paulo School of Medical Sciences

**Objective:** To compare the application of questionnaire FSFI in Latin-American women used the traditional and adapted score.

**Methods:** The group consisted of postmenopausal women that usually seek treatment at the Endocrine Gynecology Clinic at the Santa Casa de São Paulo Medical School of Sciences, in the period between February 2011 and February 2013. The women considered as being postmenopausal were those with amenorrhea  $\geq 1$  year and  $\text{FSH} \geq 30$  mIU/mL. The MetS diagnosis was determined by the ATP III. The assessment of their sexual function was performed by using the FSFI. We used the cutoff value  $\leq 23$ , and we also calculated the SD rates while considering a cutoff value of  $\text{FSFI} \leq 26.5$ .

**Results:** When we used a cutoff value of 23 for determining the presence of SD, we observed that 18.4% of the patients in the Control Group and 57.4% in the MetS Group showed that disorder. When we used a cutoff value of 26.5, 48.2% of the patients

in the Control Group and 83.3% in the MetS Group were diagnosed with SD.

**Conclusions:** We chose to employ an instrument validated to Portuguese, the FSFI, whose outcome is a set of predominantly qualitative results, which represents a validated method for assessing sexual function. As proposed in previous studies, we believe that a less rigorous cutoff value is more appropriate for the Brazilian population, considering that the percentage of the population affected by SD is very high and incompatible with what we observed during the interviews. We also believe that new studies are needed in order to demonstrate the reason why the total FSFI score obtained from our sample was lower than expected, similarly to what was observed in the studies aforementioned. An important hypothesis would be the existence of socio-cultural and religious variables, which are difficult to measure statistically.

### P195: Sexual function after Vaginal Erbium Laser: a multicentric observational study on Genitourinary Syndrome of Menopause

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The estrogen deficiency associated with menopause leads to the genitourinary syndrome of menopause (GSM), that may jeopardize sexual function and quality of life in up to 50% of postmenopausal women (PMW). The aim of this study is to evaluate the effects of a second generation, non-ablative photothermal therapy, the Vaginal Erbium Laser, (VEL®), on sexual function in PMW with GSM. The Female Sexual Function Index (FSFI) and the Female Sexual Distress Scale-Revised (FSDS-R) were administered to 47 sexually active PMW before and after 2 treatments with VEL, using a non-ablative solid state Erbium in yttrium aluminum-garnet crystal (Er:YAG) Laser (Fotona Smooth™ XS, Fotona, Ljubljana, Slovenia) with a wavelength of 2940 nm. After introducing a patented vaginal speculum, the probe is inserted into the speculum, and full beam circular irradiation of vaginal walls is performed till the vestibulum. Then the vestibule is irradiated with a fractionated beam. The procedures were performed on an outpatient basis without anesthesia or drug use before or after the intervention. No adverse events were recorded during the study.

**Results:** The FSFI from basal values of  $16.5 \pm 4.2$  reached  $20.0 \pm 2.5$  and  $27.5 \pm 3.2$  after the first and the second VEL treatment, respectively ( $p < 0.001$ ). We observed a significant ( $p < 0.001$ ) improvement in each specific domain FSFI scores at the end of treatment compared to baseline. The FSDS-R from basal values of  $19.5 \pm 1.5$  dropped to  $15.0 \pm 1.6$ ,  $9.7 \pm 2.0$ ,  $10.5 \pm 1.5$  after the 2 first and the second VEL treatment, respectively ( $p < 0.001$ ).

**Conclusions:** Albeit not randomized, this prospective study shows that VEL treatment may induce a significant decrease the distress associated with impaired sexual function with an improvement of satisfaction with sexual life in PMW suffering from GSM

### **P196: Obstructive sleep apnea and female sexual dysfunction**

Glaury Coelho (BR), Cristina Frange (BR), Lia Bittencourt (BR), Monica Andersen (BR), Sergio Tufik (BR) and Helena Hachul (BR)  
Universidade Federal de São Paulo

**Objective:** Many studies have shown that patients with obstructive sleep apnea have impairments that may suggest a risk factor for the development of sexual dysfunction. Unlike men, few studies have investigated sexual dysfunction among women with obstructive sleep apnea. The aim of this review is to investigate the existence of an association between obstructive sleep apnea and female sexual dysfunction in different reproductive life stages (pre- and postmenopause).

**Methods:** A PubMed and LILACS database were searched using the keywords obstructive sleep apnea intersected with female sexual dysfunction. The search used an end date of March 2015.

**Results:** Thirty-two articles were found and from these, 7 were selected for this review, 4 cohort studies and 3 control studies. We found an association between obstructive sleep apnea and female sexual dysfunction in both pre- and postmenopausal women. All studies included polysomnography to diagnose obstructive sleep apnea. Different definitions of obstructive sleep apnea as well as different cut off of respiratory disturbance index were used by the investigations analyzed by these review. Patients reproductive life stage (pre- and postmenopause) and female sexual dysfunction were also classified distinctively. We also point out to the risk factors and the different methodologies to evaluate each sexual disorder.

**Conclusions:** Few studies have investigated female sexual dysfunction among people with obstructive sleep apnea. The climacteric symptomatology appears to be a confounding factor that some studies have explored. Obstructive sleep apnea is associated with female sexual dysfunction in pre- and postmenopausal women.

### **P197: Addressing sexual problems in the climacteric: how common is common**

Assaad Kesrouani (LB)  
Saint Joseph University, Obstetrics and Gynecology Department

**Objective:** To assess the prevalence and type of sexual problems in the climacteric.

**Material and methods:** Climacteric patients attending a consultation clinic in Lebanon were asked about sexual problems or complaints. Inclusion criteria were: perimenopausal patient, consultation for a regular check-up, patient married or having a partner, Exclusion criteria included medical problems or medication for the patient or her partner. Oral consent was obtained, a brief questionnaire was then filled by the physician. It evaluated by a 1 to 5 Likert scale (1 is the least, 5 the most) the following items: Global satisfaction, fatigue, depressive symptoms, partner's attention, libido, orgasm satisfaction, vaginal dryness, erectile problems for the partner.

**Results:** 50 women were included in the study. Mean age is 46 years [43-50]. All patients accepted to participate in this study. Overall 26% had some complaint about sexual issues. Evaluation by Likert scale for the studied items showed a score of 3.8 for global satisfaction, 2.2 for fatigue, 3.1 for depressive symptoms, 2.5 for partner's attention, 2.8 for libido, 2.3 for orgasm satisfaction, 4.2 for vaginal dryness, 1.7 for erectile problems for the partner.

**Conclusions:** Many sexual problems are present in the climacteric period and they should be present in the history taking of the patients during regular consultation.

### **P198: Quality of life and psychosomatic symptoms of menopause – national multicenter study**

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<sup>a</sup>Carol Davila University of Medicine and Pharmacy Bucharest; <sup>b</sup>Nicolae Malaxa Clinical Hospital Bucharest; <sup>c</sup>University of Medicine and Pharmacy Craiova

**Objective:** To determine the impact of physiological and surgical induced menopause upon quality of life, comparing to a control group.

**Methods:** We have accomplished a national, multicenter, retrospective study, between February 2015 and January 2016 concerning quality of life and psychosomatic symptoms in surgical induced menopause and physiological menopause comparing to a control group. In all the groups have been included a similar patients number with an approximate average age. Greene Scale has been used in order to quantify the signs and symptoms.

**Results:** Psychosomatic changes have been reported increased in the menopause group comparing to the control group. Affective disorders (anxiety and depression) are more frequently among women with physiologic menopause comparing to the surgical induced group. Anxiety was reported to be 76,92% in the physiological menopause group, 45.5% in the surgical induced menopause group and 2% in the control group, while depression was found to be 53.9%, 45.5% and 1%. Sexual dysfunctions are more frequently in both menopause groups comparing to the control group, respectively 61.53%, 36.36% and 20%.

**Conclusions:** Surgical induced menopause is considered an accident in endocrine and psychic status, the psychosomatic disorders taking place in an organism with highly compensatory reactions (including the psychological level). The Greene Scale highlighted both qualities and limits, which can be overcome when applying on a considerable number of patients and correlated to other psychological tests. The study of menopause psychological disorders requires a good medical training in the psychosomatic field, as well as overcoming the comfortableness of hormonal replacement therapy.

### **P199: Sexual disorder and anxiety disorder in menopausal women**

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Faculty of Medicine Sebelas Maret University

**Objective:** To understanding sexual disorder and anxiety disorder in menopausal women and investigating many factors such as age, the long of menopause period, occupation, income, domicile demographics, that influence it significantly.

**Methods:** Dependent variable of our study are sexual disorder and anxiety disorder that measure with Hamilton Rating Scale (HARS) Modification Questionnaire as tools to establish sexual

disorder and anxiety disorder. Independent variable of our study is age, occupation, income, domicile demographics. The samples are 100 menopausal women that agree to participate in this study. We observed 22 menopausal women with <5 years long of menopause period as control, and compare to 78 menopausal woman with  $\geq$  than 5 years long of menopause period then perform bivariate and also multivariate analysis to determine all factors that significantly influence sexual and anxiety disorder in menopausal women.

**Results:** From this study, we found 27% menopausal women had sexual disorder. Occupation, income, domicile demographics statistically had no significant influence both of sexual disorder and also anxiety disorder in menopausal women ( $p > 0.05$ ) but we found that age had significant impact ( $p = 0.001$ ). From multivariate analysis we found that sexual disorder had significant impact to anxiety disorder in menopausal women ( $p = 0.001$ ), with OR = 1,266.

**Conclusions:** Menopausal women had sexual disorder. Occupation, income, domicile demographics statistically had no significant influence both of sexual disorder and also anxiety disorder in menopausal women. Sexual disorder statistically had significant impact to anxiety disorder in menopausal women.

### P200: Menopause and sexuality

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Menopause women suffer from psychosexual dysfunction, such as loss of libido, vaginal dryness, lack of orgasm dyspareunia, lack of interest in husband, feeling of forced sex with husband or partner, which results poor quality of life and low self esteem. These symptoms are not only because of menopause but depend on some other complex factors like physical distress, personal attitude, emotional, cultural, social and religious belief, economic condition and the health of the partner. Women are oblivious about the sexuality. Among the biggest misconception of society is that women lose libido whereas men never lose their lust and capability. This is incorrect as evidence says that menopausal women may remain quite sexually healthy. However, because female do undergo more dramatic biological changes than their counterparts, sexual problems becomes challenging. Most women never report to doctors and suffer with extreme mental agony. Unfortunately this area is less investigated. There is no national or international guideline to address. 500 million women will enter in menopause within next 5 -10 years. So it is our duty to find out the ways to combat the sexual problems. Self reporting is rare so health provider has greater responsibilities to find the problems, they should ask and do a comprehensive assessment which might reveal the problems and many interrelating factors. That might help to construct the treatment strategy to ameliorate the problem. The management needs to be in holistic approach. Not the menopause there are many other factors that need to be considered. An integrated approach involving, physician with MRT (estrogen, androgen, ospemefene), sex therapy, cognitive therapy, couple therapy and psychotherapy all are required. Future studies should take more cognizances of women attitude and interrelated factors along with newer hormone therapy.

### P201: Female sexual function in mid-aged Hispanic women: report of a multicentric study

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**Background:** Sexuality is a multidimensional phenomena related to many bio-psycho and social aspects; the menopausal transition being an important one.

**Objective:** To assess sexual function and related factors in mid-aged Hispanic women.

**Methods:** This was a cross-sectional multicentric study in which women aged 40 to 65 from various Latin American sites ( $n = 857$ ): Cartagena, Colombia ( $n = 215$ , Afro-Colombian), Guayaquil, Ecuador ( $n = 195$ , Mestizo), Cusco, Perú ( $n = 231$ , Quechua and high altitude) and Asunción, Paraguay ( $n = 216$ , Mestizo) were surveyed with the short six item Female Sexual Function Index (FSFI-6) and a questionnaire containing personal and partner data.

**Results:** The median age of the whole sample was 48 years. Postmenopausal women were evenly distributed among studied sites. Median total FSFI-6 score for surveyed women was 14.0. Lower scores (indicating worse sexual function) were significantly correlated to postmenopausal status and ethnics. In this regard, Afro-Colombian and Paraguayan displayed better sexual function; whereas lowest scores were observed for indigenous women living in high altitude.

**Conclusions:** In this mid-aged Hispanic female sample, sexual function as measured with the FSFI-6 was related to menopausal status and ethnics.

### P202: Correlation between depression and sexuality in mid-aged Paraguayan women

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**Background:** Reports indicate that depressive symptoms may affect sexuality of mid-aged women and vice versa sexual problems tend to aggravate depression. Despite this, information from mid-aged Paraguayan women is scarce.

**Objective:** To establish a correlation between depressive symptoms and sexual function in mid-aged women.

**Methods:** This was a cross-sectional study in which 216 women aged 40 to 65 were surveyed with the FSFI-6, CESD-10 and a questionnaire containing personal and partner data. Spearman correlation coefficients were calculated between FSFI-6 and CESD-10 total scores.

**Results:** Median age of the sample was 48 years, 48.1% were postmenopausal, 8.8% used hormone therapy, 39.3% used psychotropic drugs, 43.5% had hypertension, 6.5% diabetes, 44.9% abdominal obesity. An 89.3% (n=193/213) had a partner and 93.3% (n=180/193) sexual activity. Among sexually active ones median total FSFI-6 score was 24.0, with a 23.9% obtaining a total score of 19 or less, suggestive of sexual dysfunction (lower sexual function). Median score for the CESD-10 among these women was 3.5, higher scores indicate more depressed mood. There was an inverse correlation between total FSFI-6 and CESD-10 scores ( $\rho = -0.54$ ), indicating that women with lower sexual function are more depressed.

**Conclusions:** In this mid-aged female sample from Paraguay, sexuality was inversely correlated to depressive symptoms.

### **P203: The prevalence of sexual dysfunction in perimenopausal women, a survey of women in Gujarat, India**

Jignesh Shah (IN)

Dr. Shah Institute for Women's Health

**Introduction:** The loss of estrogen and testosterone during the phase of menopause can lead to changes in a woman's body and sexual drive. Perimenopausal and postmenopausal women may notice the change in their sexual activities. Various studies have investigated the prevalence of sexual dysfunction in perimenopausal women around the world, especially in US and Europe. However, community-based studies investigating women's sexual dysfunction during menopausal transit are very few in Indian women.

**Objective:** Our study was aimed at reporting the incidence of sexual dysfunction as well as characterizing the type of sexual dysfunction in perimenopausal women of Ahmadabad, Gujarat.

**Materials and methods:** Participants included all patients diagnosed with perimenopausal symptoms in our medical center at Dr. Shah Institute For Women's Health and who were willing to participate in the study. The study was conducted over a period of one year. A validated Female Sexual Function Index (FSFI) was used to assess the female sexual function.

**Results:** The median age of menopause in this study population was 46.2 years. The prevalence for sexual dysfunction was high (42%). The most affected sexual domains were: lack of sexual desire (30%), lack of arousal (46%) unable to achieve orgasm (42%), decreased lubrication (50%), pain during sex (34%) and lack of overall sexual pleasure (40%). Women with naturally occurring menopause were found to be slightly more likely to have sexual dysfunction.

**Conclusions:** The prevalence of sexual dysfunction was significant among perimenopausal women. The most affected domains were satisfaction, desire and arousal.

### **P204: Sexual function and general sensation after abdominal hysterectomy**

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University Hospital of Obstetrics and Gynecology

**Background:** Our study tries to evaluate the sexual outcomes and the patient satisfaction after the total abdominal hysterectomy.

**Methods:** We selected the patients who met the following criteria: were between 39-49 years old; lived in reachable areas, in order to fill the questionnaires; had a total hysterectomy without the ovaries; were sexually active. In the recent 3 years (2012, 2013, 2014), we have performed 277 hysterectomies without ovaries, and 89 of these met our criteria. 65 of these patients accepted to fill our questionnaires. Patients who met criteria for participation were sent a two page confidential, anonymous questionnaire to assess sexual function and the overall satisfaction experienced postoperatively. We made generally closed questions, but we used also open questions as well.

**Results:** The sense of general health was reported better in 69% of patients (45). 86% of patients (56) reported that their sexual lives was affected by pain, bleeding or depression before the surgery, and the symptoms has affected their relationship in couple. 61% (40) reported that their expectations were lower before surgery, as regarding to their sexual life. The sexual interest and ease of arousal was increased in 53% of patients (35), compared to before hysterectomy. Dyspareunia was reported as present in 46% of patients in the first year after the surgery. 30% (20) reported serious signs of depression and anxiety before and after hysterectomy.

**Conclusions:** Patients undergoing total hysterectomy without ovaries, for benign indications, experience a sense of general health better than before. Most of them have an increased sexual interest and ease of arousal, but pain during intercourse is a great barrier especially during the first year. Depression and anxiety before the hysterectomy are associated mostly with dyspareunia and loss of sexual interest after the surgery.

### **P205: Sexual function assessment in middle-aged Chinese women**

Hong Zang (CN) and Caiyun Zhang (CN)

The First Affiliated Hospital of Dalian Medical University

**Objective:** To assess sexual activities, sexual function and its association with vaginal maturation status in mid-aged Chinese women.

**Methods:** 120 women were divided into three age groups: 45-50 (A group), 51-55 (B group) and 56-60 years old (C group). Sexual activities were obtained with self-administered questionnaire. Sexual function was assessed by FSFI. Vaginal maturation status was determined by vaginal maturation index (VMI) and the vaginal PH value.

**Results:** Low sexual frequency was presented in 48.7% women in C group, while 12.5% in A, 12.2% in B group ( $p = 0.001$ ). Sexual distress was reported in 17.5% women of A group, while 9.8% in B, 2.6% in C group ( $p = 0.086$ ). The total FSFI score was significantly lower in women of C group ( $21.52 \pm 2.85$ ) than that in women of A ( $24.80 \pm 4.01$ ), B ( $23.45 \pm 4.35$ ) group ( $p = 0.001$ ). The prevalence of female sexual dysfunction (FSD) was increased with age, 42.5%, 61%, 92.3% respectively ( $p < 0.001$ ) according to the cutoff point of FSFI score  $< 25$ . The mean domain score of sexual lubrication, desire, pain and sexual arousal was significantly decreased with age in women. Regarding VMI, the high degree

of estrogen effect (EE) was exhibited in 80.8% women, the mild degree EE only in 7.7% women in the A group; in opposite, the mild degree EE was presented in 38.1% women, whereas high degree EE in 28.6% women in the C group ( $p = 0.001$ ). Moreover VMI was positively related to the sexual domain score of lubrication ( $p < 0.01$ ). Vaginal PH value was gradually increased with the

age ( $p < 0.01$ ). It was inversely associated with the domain pain score ( $p < 0.01$ ).

*Conclusions:* Sexual frequency is decreased, the prevalence of FSD increased with age in mid-aged Chinese women. Main changes in sexual function with age are decreased vaginal lubrication, sexual desire, pain and sexual arousal. Vaginal maturation status is associated with sexual function.