INV1

Protective anti-inflammatory properties of estrogens in neurodegenerative diseases

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Brain injury results in a loss of neurons in the epicenter of the lesion. These initial responses are followed by sustained deficiency in nutrition, oxygenation, excessive expanding of ROS and lipid peroxidation and edema formation. Secondary pathological processes mainly depend on escalating neuroinflammation involving brain-extrinsic and intrinsic immune cells. In contrast, slowly progressing neurodegenerative diseases such as amyotrophic lateral sclerosis (ALS) follow other mechanisms of molecular pathology with slowly advancing impairment. New insights into the sequence of inflammatory cascades have broadened the knowledge about brain inflammation and included the inflammasome concept. Inflammasomes are cytosolic protein complexes, act as intracellular sensors of toxic signals and activate pro-inflammatory caspases which cleave the precursors of pro-inflammatory cytokines into their active forms. Inflammasomes show a large degree of structural heterogeneity due to their protein composition and assembly. Using the transient middle cerebral artery occlusion (tMCAO) stroke model, we show the induction of the inflammasomes NLRP1, NLRP3 and AIM2 and of IL1β in microglia and neurons. Estradiol (E2) given immediately after the insult reduced the infarct volume. E2 attenuated the expression of the inflammasomes and cytokines. For studying ALS, we used a mouse carrying a mutant form of the human superoxide dismutase 1 (hSOD1G93A) with progressive symptoms of spinal cord motoneuron death. E2 administration before the onset of clinical symptoms improved motor performance, supported survival of motoneurons and reduced spinal neuroinflammation by preventing the activation of NLRP3, caspase 1 and IL1β.

We show that inflammasomes are a critical intracellular platform of neuroinflammation in acute brain damage and chronic neurodegeneration. E2 effectively dampened inflammatory processes and inflammasome activation in both models.

INV2

Microencapsulated GDNF for the treatment of Parkinson’s disease

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Glial Derived Neurotrophic Factor (GDNF) is a therapeutic protein with tremendous potential for the treatment of Parkinson’s disease (PD), a debilitating disorder, for which there is no cure. However, the administration of GDNF is not an easy task due to its short in vivo half-life and its physical and chemical instability. Since GDNF brain delivery remains an important issue, its microencapsulation in bioresorbable microparticles (MP) represents a valuable therapeutic approach. Indeed, the clinical application of GDNF for PD treatment has been hampered by safety and efficacy concerns, many related to the brain delivery strategies attempted to date.

In this talk a translational study that demonstrates the efficacy and safety of GDNF delivered via MPs in a clinically relevant non-human primate model of PD will be discussed. Notably, a single administration of microencapsulated GDNF within the putamen achieved long-term improvement of motor function in animals with restoration of dopaminergic function. In addition, the treatment with GDNF-MPs did not elicit adverse effects such as immunogenicity, cerebellar degeneration or weight loss, providing preclinical validation of this approach. This study provides support for the advancement of this strategy from preclinical studies to clinical trials in advanced PD patients.

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0378-5122/
Cognitive frailty

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The burden imposed by the decline of cognitive function during ageing has increased the interest on cognitive frailty (CF). Frailty is a status of diminished resilience that puts the individual at increased risk for an adverse outcome. CF has emerged as a new construct that aims at accommodating frailty in the field of cognitive decline. CF originates because the brain, as other organs in the body, may also experience frailty. Although there are other risk factors, ageing is crucial for the advent of frailty. The pathophysiological basis includes disintegration of the neuronal network, which may be influenced by the worsening of integrated systems, like for example the vascular tree. CF predisposes to different variants of cognitive deficit, where mild cognitive impairment (MCI) is often an initial form. MCI corresponds in cognitive decline to the mild forms of physical frailty, or to the subclinical states of the noncommunicable chronic diseases. Also as for the other forms of frailty, one main feature of CF is malleability, which opens the door to implementation prevention. Early diagnosis is the key to define strategies to achieve reversal, which is an option mainly in the early phases of the process evolution. The discovery on new biomarkers, which in the case of CF include imaging techniques, is the basis of early diagnosis. There is a gender profile in frailty, but it is unknown whether this replicates in the case of CF.

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Impact of gestational diabetes and other metabolic diseases on later life of mother and child

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Pregnancy is a unique period of a women life time, unique from many points of view of the human body capacity of adaptation to sustain the development of the embryo and fetus. From the point of view of carbohydrate metabolism, it is a unique time when, in an apparently normal person, risks of further impairments of glucose metabolism may be seen and identified.

Taking into consideration that diagnosing GDM and treating even “mild GDM cases” will increase costs, but these costs are related to the real incidence of the glycemic disturbances and diabetes mellitus incidence in general population, in a time when we are facing a real worldwide epidemic of diabetes.

The follow up trails demonstrated that identifying and treating mild GDM with diet is largely effective: only 8% and 20% women required insulin. Group patient education may be helpful, and there is increased evidence that less frequent glucose monitoring – every second or third day, rather than daily – may be feasible.

Diabetes Prevention Program study found a 58% reduced incidence of diabetes in the lifestyle intervention arm. In the lifestyle intervention arm, women with a history of GDM presented a risk reduction of diabetes risk similar to the risk reduction in the group of women without a history of GDM, with a better response to metformin. ADA clinical practice recommendation indicates that lifestyle interventions (medical nutrition therapy and individualized exercise program) or metformin should be prescribed for women with a history of GDM who are identified with prediabetes.

Nowadays, it is clear that identifying of gestational diabetes mellitus (GDM) overpasses the medical discussion of utility, both for the mother and child, both for the short term and long term possible complications. It is a fact that diagnosis can be done only in pregnancy and it is a problem of medical ethics to do this.

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The consequences of stopping MHT: Cardiometabolic perspectives

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Menopausal hormone therapy (MHT) provides benefits to symptomatic women. Stopping treatment may have a negative impact on their quality of life due to the return of menopausal symptoms, sleep and mood problems, vulvovaginal atrophy and body weight changes. As women age body weight increases. After the menopause, estrogen deficiency may also have a role in weight increase; however, evidence supporting their direct role is controversial. Increased weight enhances cardiovascular risk factors: dislipidemia, hypertension and insulin resistance, which seem to be improved by estrogens. Experimental data also suggest their antiatherosclerotic and pro-thrombotic properties. Future research
should focus on finding ideal MHT candidates that will take advantage of estrogen’s benefits over cardiometabolic aspects.

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Parallel Session: Gender differences in midlife and beyond

INV7

Headache, gender and aging

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What is headache and what type of headache are we talking about? If we discuss the different types of headache, are there differences between men and women? Do these headaches change over the years? This lecture will cover the different types of headache, their prevalence, pathophysiological backgrounds and therapeutic challenges, in the perspective of gender and aging.

Headache classification: In the field of headache care and research we are using since 1988 the International Headache Society (IHS) classification system to define all the different types of headache in an interchangeable way, understandable and the same all over the world. In its last version, ICHD-3beta, there are 14 different types of headaches classified. The most important or first separation we make is division in primary and secondary types.

Gender: Are there sex differences in headache? Migraine is two to three times more prevalent in women than men, and women report a longer attack duration, increased risk of headache recurrence, greater disability, and a longer period of time required to recover. Whereas in cluster headache (Horton’s neuralgia) this is the opposite.

Aging: Are there age-differences in headache? The ratio of migraine prevalence between men and women is not consistent across all age ranges. Boys and girls have a similar 1-year prevalence of migraine until puberty, after which prevalence rises in both sexes, but with a greater rise in women than men. The prevalence of headache in men and women after the age of 40 decline. After menopause, in 2/3 of women migraine disappears.

Finally, what is the burden due to headache disorders? Not only is headache painful, but it is also disabling. In the 2013 Global Burden of Disease Study (WHO), migraine on its own was found to be worldwide the sixth highest cause of years lost due to disability. Headache disorders collectively were third highest.

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INV8

Is testosterone important for women as they age?

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In women, is testosterone an obligatory precursor for extragonadal estradiol production after menopause, and has important direct androgenic genomic and nongenomic effects. Testosterone levels in women decline with age from the 4th decade, reaching a nadir in the 7th decade of life. Testosterone levels are positively associated with sexual function in women, and multiple randomised placebo-controlled trials have shown that testosterone therapy can be effective for the treatment of female sexual dysfunction in postmenopausal women. However, low testosterone in ageing women has multiple potential undesirable consequences that have been somewhat ignored. In the brain, testosterone exhibits neuroprotection against oxidative stress, serum deprivation-induced apoptosis and soluble amyloid beta toxicity, and clinical trials suggest exogenous testosterone enhances cognitive performance in postmenopausal women. Lower free testosterone in older women is associated with a decline in bone mineral density and a greater risk of hip fracture. Observational studies implicate testosterone as having favourable cardiovascular effects measured by surrogate outcomes, however associations between endogenous testosterone and CVD risk, and total mortality, particularly in older women are yet to be established.

Quality clinical trials evaluating the effects of testosterone on CVD risk, cognitive performance, musculoskeletal health and fragility fracture risk are needed.

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Parallel Session: PCOS and the menopause

INV9

PCOS a multifaceted disease in need of a multidisciplinary approach

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At an early age the most common reason of women diagnosed with PCOS to consult a doctor is irregular bleeding and infertility. Bleeding problems can often be addressed adequately by hormonal interventions. Prognosis for infertility is usually excellent with high cumulative (singleton) pregnancy rates. However, pregnancies complications are clearly increased and perinatal outcomes are compromised. Obstetricians are currently focusing on gestational diabetes in these women and aim to develop preventive strategies.

When women with PCOS get older, menstrual cycle patterns often normalize, but metabolic abnormalities aggravate and type 2 diabetes or hypertension occurs. Many studies confirm the presence of subclinical cardiovascular disease (i.e. abnormal intima media thickness and flow mediated dilatation) in women with PCOS between 40 and 50 years of age. However, despite overwhelming evidence suggesting increased risk for cardiovascular disease in these women, most studies so far failed to demonstrate in increased incidence of cardiovascular events such as myocardial infarction, stroke or death. These studies are often in postmenopausal women, cross section or retrospective in nature. It remains surprising that many increased risk factor in PCOS for developing cardiovascular disease do not seem directly linked to actual disease. The presence of – as yet unknown – protective factors may be hypothesized.

PCOS has become a disease condition broadly recognized as having major implications for quality of life throughout the life cycle. In the past, gynecologists focused only on reproductive dysfunction in these women, but at present many other specialties are getting involved. We need multi-disciplinary approaches for proper care of women with PCOS at different phases of life.

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Hormone therapy and breast cancer: Is adding progesterone an issue?

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Menopause hormone therapy is associated with an increased risk in luminal breast cancers in some conditions: the combined treatment with estrogen and progestins, increased duration, increased breast density. This risk appears lower in women treated by progestins but a small increase is still seen in cohort of lean women such as the ‘Nurses’. The only trial to show a decrease in the risk with estrogen only treatment is the WHI randomized trial in hysterectomized women. But obesity was highly prevalent in this population. Among the use of progestins, progesterone and hydrogesterone have less deleterious effects as shown in two French studies and a Finish study. Difference in pharmacology may explain the different impact on breast cancer risk.

Some lifestyle factors can however possibly help to control the risk of breast cancer.

The current knowledge will be presented.

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Parallel Session: PCOS and the menopause

INV11

PCOS and cardiovascular disease

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Polycystic ovary syndrome (PCOS) is a prevalent pathological entity in young women. The phenotype of PCOS shares common characteristics with cardiovascular disease (CVD), especially coronary heart disease (CHD). These characteristics are insulin resistance, impaired glucose tolerance, obesity, and dyslipidemia. Therefore, the main clinical question is if women diagnosed with PCOS are at an increased risk of developing CHD later in their lives.

A first piece of evidence derives from the presence of CVD markers in women with PCOS. A recent meta-analysis demonstrated significantly elevated C-reactive protein (CRP), homocysteine (Hcy), plasminogen activator inhibitor-1 (PAI-1) antigen, PAI-1 activity, vascular endothelial growth factor (VEGF), asymmetric dimethylarginine (ADMA), advanced glycation end-products (AGEs) and lipoprotein (a) [Lp(a)] concentrations in women with PCOS compared with controls.

A second piece of evidence derives from endothelial function and imaging studies. Data on endothelial function in women with PCOS are conflicting, with some studies reporting such a dysfunction in women with PCOS. Carotid artery intima-media thickness (IMT) is higher in women with PCOS. Computed tomography studies revealed more prevalent aortic calcification and coronary artery calcium (CAC) in premenopausal women with PCOS, compared with age- and weight-matched controls. Finally, women with PCOS have more extensive coronary disease on angiography.

Nevertheless, the definitive answer has to come from long-term, prospective studies. Up to now, data on long-term morbidity and mortality by CHD in women with PCOS are inconclusive. The Nurses’ Health Study provided data of a positive association between personal history of menstrual cycle disturbances and risk of CHD.

In conclusion, despite the evidence that women with PCOS have risk factors for CVD and imaging features of CHD, an excess morbidity attributed to CHD in women with PCOS is not well established.

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Parallel Session: Andropause

INV12

Low testosterone in the aging man: A normal process or an endocrine disease

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The aging process has only a marginal effect on circulating testosterone (T). In fact, the increasing prevalence of T deficiency as a factor of age is mainly explained by the greater prevalence of chronic morbidities, in particular of metabolic disturbances such as type 2 diabetes mellitus, obesity and metabolic syndrome. The latter conditions are associated with both primary and secondary hypogonadism (HG), while an age-related effect on T levels is evident only for primary hypogonadism. Considering that secondary HG is the most common form of T deficiency in the aged man, it is derived that the independent contribution of aging to T deficiency is negligible. Hence, a true “andropause” does not exist. A FDA position and some recent guideline suggest that only “organic” form of HG should be treated, whereas T deficiency associated to obesity and other comorbidities should be left untreated and the underlying conditions removed. In the Florence experience this is tantamount to say that 85% of HG subjects complaining for sexual dysfunction should not receive T therapy (TTh) because they are not satisfying criteria for “organic” HG. However, meta-analysis of randomized controlled trials (RCTs) – enrolling, for the large majority, patients without an “organic” form of HG – indicates that TTh is able to significantly increase sexual desire and improve erectile dysfunction and orgasm. In addition, TTh is associated with a reduction of fat mass and an increase in lean mass, with an overall improvement in glucose metabolism. Nonetheless, effect of TTh is more apparent in trails of longer duration and in those enrolling subjects without diabetes or obesity at baseline.

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Parallel Session: Brain aging

INV13

Memory and menopause

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Longitudinal studies demonstrate that women’s performance on tests of memory and attention decreases during the menopause transition even after controlling for advancing age and psychological symptoms such as depression and anxiety. Preliminary data indicate that memory problems are related to vasomotor symptoms, the primary symptoms of menopause, but only when...
vasomotor symptoms are measured objectively using ambulatory skin conductance monitors. Objective vasomotor symptoms also relate to alterations in brain structure and function. The "critical window hypothesis" states that use of hormone therapy during the perimenopausal or early postmenopausal period confers favorable cognitive effects whereas later use confers negative effects. For memory endpoints, there is some support for this hypothesis for estrogen alone but less support for combined hormone therapy. Recent randomized clinical trials of combined hormone therapy in younger postmenopausal women show neutral cognitive effects. Notably, those trials were not conducted in women with bothersome vasomotor symptoms, so it is unclear whether hormone therapy improves cognition in symptomatic women. Whether hormone therapy alters the risk for Alzheimer's disease is a critical public health question because the prevalence of Alzheimer's is increasing, more women than men will die of the disease, and there is no cure. A randomized clinical trial of the critical window hypothesis for prevention of Alzheimer's disease is not feasible so insights must come from observational studies and biomarker studies. Three of four observational studies support the critical window hypothesis, and preliminary neuroimaging data from a randomized clinical trial show less Alzheimer's pathology following midlife use of transdermal estradiol compared to placebo. Currently there are no data to support the use of hormone therapy for the treatment or prevention of cognitive decline.

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Parallel Session: Lessons to be learned from cross-sex hormonal therapy

INV14

Androgens and cardiovascular risk in female-to-male gender dysphoric subjects

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The mainstay of medical treatment for gender dysphoria in female-to-male subjects (FtM) is testosterone (T). The overall goal of T administration is to suppress female functional and phenotypic characteristics and to induce masculinization. These changes typically lead to an improvement in well-being and quality of life and a relief of gender dysphoria. The general, although not evidence based, recommendation is to maintain serum T levels within the range of natal adult men. Short acting intramuscular T esters, such as enanthate or cypionate or mix, and long acting T undecanoate (TU) or T gels are the most used formulations.

The cardiovascular effects of T in this population are still not known. Available data are mainly extrapolated form cohorts of hypogonadal natal men or natal women treated with T or with polycystic ovary syndrome. However, these data should be applied with caution for the differences in the T duration and dosages used and in the genetic background.

Available retrospective studies do not report any evidence of increased cardiovascular (CV) events such as myocardial infarction or stroke in the FtM population in a 10 year follow up.

In our series of 70 FtM treated with T (T enanthate or TU or T gel), after a mean follow up of 15 years, HDL cholesterol levels were significantly decreased in all subjects, while glucose and insulin levels did not significantly change. No significant changes of systolic or diastolic blood pressure were detected during treatment. However, these subjects had a mean age of 30 years at the beginning of treatment and longer follow-up may be needed to fully evaluate their CV risk.

In conclusion, the data available in the literature and our own data do not suggest any increased CV risk in FtM subjects treated with T after 15 years of follow-up.

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Society Symposium: The consequences of stopping MHT (IMS)

INV15

The consequences of stopping MHT: Why, when and how? (IMS symposium)

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Women taking menopause hormone therapy (MHT) may decide, at some stage, to discontinue their treatment or their healthcare practitioner may advise them to do so. The decision to discontinue may be influenced by the media, findings of recent studies, recommendations, efficacy of treatment and adverse effects. When a woman wishes to continue, there should be a discussion about the benefits and risks for that individual woman and what she could expect if she stops treatment. In recent years, many women were advised to stop MHT within 5 years of use or before the age of 60; the evidence for this advice is uncertain and IMS believe that treatment duration should be individualized.

Options for discontinuation are either to stop treatment immediately or to gradually wean off by decreasing the dose or number of days per week. Most of the data pertaining to immediate cessation or tapering are from low quality randomised controlled trials (RCTs). Some data from RCTs suggest that tapering MHT until discontinuation made no difference to a woman’s experience of total menopausal symptoms in the shorter term (2–4 weeks after stopping MHT abruptly) and longer term (6 months) compared with abrupt discontinuation. However, specifically for VMS, there may be some improvement in the relief of menopausal symptoms in the shorter term (2–4 weeks after stopping MHT abruptly) and longer term (6 months) associated with tapering compared with the abrupt HRT discontinuation method.

Given that strong evidence does not exist to indicate differential outcomes for tapering or abruptly stopping, both methods can be used and this decision should be based on the woman’s preference. Recent data suggesting that discontinuation of MHT may lead to increased cardiovascular morbidity and mortality, do not yet indicate whether the risks can be mitigated through tapering the dosage. This clearly warrants further investigation.

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Society Symposium: European Society for Sexual Medicine Testosterone and Healthy Aging

INV16

Testosterone and sexual function

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Testosterone is not the only fuel for a man’s sex drive and performance. But low testosterone can reduce the ability to have satisfying sex. Lack of sex drive and erectile dysfunction are sexual problems that can result from low testosterone. Testosterone modulates nearly every component involved in erectile function. It also regulates the timing of the erectile process as a function of
Sexuality is influenced by bio-psycho-social factors and is for many an essential part of quality of life. Sexual expression occurs throughout life and there are no age limits for sexuality, sexual needs and sexual wishes.

With increasing age changes in sexuality are inevitable, the prevalence of sexual dysfunctions increase with increasing age and can cause suffering and deterioration of quality of life and relationships. These dysfunctions can have both physical and psychological causes. Dysfunctions are harrowing, it may be a signal of other diseases, it can affect other diseases, and other issues may be exposed. As the bother decrease with age, the sexual dysfunctions do not always need to affect the quality of life or sexual satisfaction. Physicians should be aware of these issues, offer coping strategies and keep in mind that not addressing sexuality in older population is always need to affect the quality of life or sexual satisfaction. Physiologically, decreases in testosterone levels may also help improve bone density, muscle mass and even cognitive function in women who have very low levels of free testosterone. The FDA did not approve testosterone treatment for women because they were concerned about increase the risk of CVD while trials seem to indicate that non-systemic testosterone (creams, ointments) do not affect lipids or blood markers for CVD.

Although there are no direct studies that show that testosterone therapy increases risk for breast cancer, no one can make a definitive statement about its breast safety. In case of high level of testosterone is prescribed, it can result in virilization effects such as acne, abnormal hair growth, enlargement of the clitoris and even voice changes.

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Parallel Session: Andropause

INV17

Sexuality and aging

Yacov Reisman

Amstelland Hospital, Amstelveen, Netherlands

Sexuality is influenced by bio-psycho-social factors and is for many an essential part of quality of life. Sexual expression occurs throughout life and there are no age limits for sexuality, sexual needs and sexual wishes.

With increasing age changes in sexuality are inevitable, the prevalence of sexual dysfunctions increase with increasing age and can cause suffering and deterioration of quality of life and relationships. These dysfunctions can have both physical and psychological causes. Dysfunctions are harrowing, it may be a signal of other diseases, it can affect other diseases, and other issues may be exposed. As the bother decrease with age, the sexual dysfunctions do not always need to affect the quality of life or sexual satisfaction. Physicians should be aware of these issues, offer coping strategies and keep in mind that not addressing sexuality in older population is always need to affect the quality of life or sexual satisfaction. Physiologically, decreases in testosterone levels may also help improve bone density, muscle mass and even cognitive function in women who have very low levels of free testosterone. The FDA did not approve testosterone treatment for women because they were concerned about increase the risk of CVD while trials seem to indicate that non-systemic testosterone (creams, ointments) do not affect lipids or blood markers for CVD.

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Parallel Session: In utero predictors of disease in later life

INV18

Prenatal nutrition and health in later life

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Animal experiments have shown that restriction fetal nutrition indeed induces adaptations that lead to altered structure and function of organs, increased rates of disease and shortened lifespan. While famine is sadly not uncommon in many parts of the world, studying effects of undernutrition during pregnancy in humans is hampered by the fact that undernutrition is usually not restricted to pregnancy alone, and effects of chronic undernutrition and accompanying problems of infection complicate the situation. The tragic circumstances of the Dutch famine of 1944–45 created a unique opportunity to assess the effects of prenatal famine exposure on health in later life.

Studies of men and women born around the time of the Dutch famine have show that effects depended on its timing during gestation, and the organs and tissues undergoing critical periods of development at that time. Early gestation appeared to be the most vulnerable period which may not be surprising considering the fact that all organs are laid down during the first 12 weeks after fertilisation. The effects of famine were widespread and affected structure and function of organs and tissues, resulted in altered behaviour and increased disease risks, which in turn led to reduced participation in the labour market and increased mortality. The effects of famine exposure were apparent in the absence of any effects on size at birth, and were independent of size of the baby at birth. Also, there is preliminary evidence to suggest that the effects of famine may not to be limited to those affected directly, but were passed on to the next generation, both through the maternal and paternal line. This is likely to involve epigenetic regulation mechanisms. Adequately feeding women before and during pregnancy will allow future generations to reach their potential and lead healthier lives.

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INV19

Preeclampsia and future health risks to the mother and child

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Preeclampsia affects approximately 3–7% of all pregnancies and is the third leading cause of maternal mortality globally. In the United States, preeclampsia has increased over the past two decades, complicating 6% of all pregnancies, and accounting for 15% of all preterm deliveries, and 17% of maternal deaths. Until recently, preeclampsia was considered a disorder limited to pregnancy, which fully resolved with the delivery of the placenta; however, it is now clear that women with a history of preeclampsia have approximately double the risk of future cardiovascular events compared to women with normotensive pregnancies. Preterm preeclampsia is associated with a seven- to eight-fold increased risk of CVD mortality. Furthermore, recent epidemiological data has shown that adult offspring of mothers with preeclampsia have long-term risk for hypertension and CVD compared to normal pregnancies. Vascular dysfunction has been implicated in the pathogenesis of both preeclampsia and CVD, and a shared pathway
may explain the association of preeclampsia with CVD events decades later. We and others have begun to study the relationship to whether women enter pregnancy with normal vascular function or if vascular dysfunction predates a preeclamptic pregnancy. This talk will focus on the hemodynamic and vascular changes that occur in preeclamptic pregnancies and discuss future CVD risk to both offspring and mothers with a history of preeclampsia.

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Parallel Session: Andropause

INV20

Endogenous testosterone and the male cardiovascular system

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Some studies have found that men with CHD have lower levels of testosterone than matched controls. Not only are low testosterone levels associated with the presence of CHD, there is also evidence that the coronary artery disease is more severe. There is also evidence that low testosterone levels are associated with an increased risk and severity of heart failure.

Lower testosterone levels are associated with various risk factors for CHD, including increased central fat distribution, lower HDL cholesterol concentrations, higher triglycerides, increased insulin resistance, and an increased incidence of hypertension and diabetes mellitus. Some studies have shown that low testosterone levels are inversely associated with carotid artery intima-media thickness, incident cardiac events and all-cause mortality including cardiac death. Overall it would appear that low testosterone levels are associated with an increased risk of cardiovascular disease, including CHD and heart failure. However, it has to be considered that cardiovascular disease itself may cause the lower testosterone levels.

Testosterone replacement therapy has been shown to improve the metabolic abnormalities and to have beneficial cardiovascular effects. Improvements in myocardial ischaemia have been demonstrated as have improvements in heart failure. However, the latter might reflect improvements in skeletal muscle as ventricular ejection fractions do not appear to change with the therapy. It is still not established whether testosterone therapy has beneficial or adverse effects for CHD, and as such testosterone cannot be currently recommended for its prevention. One problem is that different types of testosterone preparations and route of administration can have different metabolic effects, and this may influence cardiovascular outcomes.

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Plenary Session: Active and healthy menopause

INV21

The menopause and its consequences: Lessons from the SWAN study

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The Study of Women’s Health Across the Nation (SWAN) is one of the largest and most comprehensive prospective cohort studies of the menopause transition in the United States (US). Study aims include

(1) characterizing the natural history of the menopause transition in a racially/ethnically diverse sample of women; and
(2) investigating the relative contribution of menopause (ovarian aging) and chronologic aging to a range of major health outcomes.

Conducted at seven sites across the United States, the study included a cross sectional phase including 16,605 women 3302 of whom have been followed longitudinally. These women span five different racial/ethnic groups in the US (non-Hispanic Caucasian, African American, Japanese, Chinese, Hispanic). Participants have been assessed approximately yearly for over 15 years on a range of key indices spanning psychosocial factors, menopausal symptoms, biological indices, and health outcomes. This ongoing study has yielded critical insights into the menopause transition. This talk will report on select key findings from SWAN, highlighting new findings including on the natural history of menopausal symptoms, menopause-associated changes in women’s cardiovascular health, and the inter-relation between relation of menopausal symptoms and women’s health. New and ongoing directions of scientific inquiry will be emphasized.

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Parallel Session: Lessons to be learned from cross-sex hormonal therapy

INV22

Obesity and cross-sex hormones

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Sex hormones are important modulators of food consumption and interaction with neurotransmitters and gastrointestinal system to change energy intake and expenditure. Adipose tissue has a central role in a homeostasis interplay of lipids, glucose and gonadal steroids. Visceral fat increases 400% in women between 3 and 7 decade reaching the peak of adipose tissue mass between 40 and 50 years of age. In a study from 15 European and American centers on more than 2000 participants morbid obesity was detected in 2.5% male to female transsexuals (MF) and 2.5% female to male transsexuals (FM). Decreased insulin sensitivity and type 2 diabetes were seen in both groups. Ten studies examining 171 MF and 354 FM shown changes in body weight, fat and lean body mass. MF receiving ethynilestradiol and cyproterone acetate: +1.8 kg for body weight, +3.0 kg for body fat, and −2.4 kg for lean body mass having beneficial effects (increase of HDL and decrease of LDL)
and detrimental effects (increases of triglycerides, subcutaneous fat, visceral fat and decrease of insulin sensitivity). In our study following body weight during 15 years therapy increase of body mass index were found (23.59–26.08 kg/m). Testosterone therapy decreases HDL, LDL subcutaneous fat and increases triglycerides, visceral fat inducing increase in weight of +1.5 kg, −2.6 kg body fat and −3.9 kg lean body mass increasing risks for cardiovascular disease. Blood pressure, total and LDL cholesterol, LPL activity and insulin sensitivity are unaffected.

Conclusion: The complete endocrine milieu must be taken into account in order to achieve appropriate individual cross-sex hormone therapy doses and ways of application improving quality of life in transgender persons.

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Parallel Session: Premature ovarian dysfunction
INV23

Fertility and egg quality in survivors of childhood cancer
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The hugely increased rate of survival following childhood cancer is one of the major advances in modern medicine. However this comes at a cost in long-term health consequences for many survivors, prominent amongst which is the loss of fertility. The US-based childhood cancer survivor study has for many years provided authoritative analyses of the effects of cancer and its treatment on female fertility. These, with other studies, have highlighted the high risk from abdominopelvic radiotherapy, impacting uterine as well as ovarian function. A recent analysis has examined the effect of chemotherapy without radiotherapy on subsequent chance of live birth. This has shown largely reassuring results except for those exposed to some specific agents, but the impact was greater in those delaying childbirth till after age 30. Additionally, another analysis from the same group has highlighted that some childhood cancer survivors show subfertility, despite preserved ovarian function as reflected in normal menstrual cyclicity; the aetiology of this is as yet unclear but may indicate a loss of oocyte quality. Reassuringly, cancer therapies do not carry risks to the next generation. A population-based analysis of pregnancy after childhood cancer has shown that the risks of loss of fertility are markedly reduced in girls diagnosed more recently than 20 years ago for some diseases such as Hodgkin lymphoma, but have changed little for those with leukaemia. There is a pressing need to identify those at risk of loss of fertility to offer ovarian tissue cryopreservation where appropriate, as this is the only option for prepubertal girls.

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Parallel Session: Body composition and cardiometabolic health after menopause
INV24

Sarcopenic obesity in the elderly
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Human aging involves many changes, such as a variation in body composition. Different factors work together leading to an increase in fat mass, decreased muscle mass and reduced bone mass among seniors. These characteristic changes among elderly people may lead to suffer several diseases such as obesity, sarcopenia and osteoporosis and may result in decreased quality of life, increased dependence and increased risk of mortality in this population. In the late 90s, “sarcopenic obesity” (SO) was a concept that emerged in order to define those people who simultaneously have an excess of body fat and a significant loss of muscle mass. Evidence suggests that older adults with both sarcopenia and obesity have worse physical functioning than those with only one of these disorders; thus, sarcopenia and obesity may act synergistically, and together increase the risk of disability (1). In spite of the importance of SO, nowadays there is no consensus on its definition. Recently, for the first time in Spain (the elderly EXERNET multi-centre study) (2), it has been shown that the prevalence of SO in a representative sample of non-institutionalized seniors reaches values of 15%. Moreover, these figures can reach values higher than 20% when subject are older than 75 yrs. A strong relationship between both physically active and sedentary lifestyles and the level of adiposity is present. Thus, it is important to establish the relationship between physical activity and more importantly physical fitness of the elderly with SO. Higher levels of physical fitness are associated with a reduced risk of suffering SO and better-perceived health among elderly. Elderly people with SO have lower physical functional levels than healthy counterparts do (3). Among the most used physical fitness tests, those that better predicted the risk of SO are leg strength, arm strength, agility, walking speed and balance in men and balance test and agility in women.

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Parallel Session: Vitamin D
INV25

Vitamin D and bone health
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Circulating vitamin D predominantly originates from cutaneous synthesis and therefore it should be considered as a hormone rather than a vitamin. Vitamin D deficiency (<50 nmol/L) is a worldwide epidemic with multiple implications on human health, due to its role in various physiological systems. Challenges and controversies are still ongoing regarding the best method of measuring vitamin D levels in the circulation. In spite of this, various studies have shown that with higher serum 25 hydroxyvitamin D levels, there is a decrease in the incidence of non-vertebral and hip fractures. There is limited research data on the management of vitamin D deficiency using therapeutic doses. The majority of studies focus on lower physiological doses rather than high pharmacological doses. In order to reach serum levels of 75 nmol/L from a deficiency
state, higher doses than 800–1000 IU/day are required. Future focus should be on the implications of a rise in systemic 25(OH)D3 levels from a deficiency state to 75 nmol/L on bone density and fracture risk, and the use of high doses in cases of vitamin D deficiency. Vitamin D treatment and supplementation need to be re-evaluated in the light of new evidence suggesting that high pharmacological doses need to be used in order to obtain the desired effect in the prevention of osteoporosis and recurrence of osteoporotic fractures.

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Parallel Session: Men’s health

INV26

Obesity and the metabolic syndrome in older men

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Metabolic syndrome (MetS) is a relatively new medical phenomenon which was established as a clinical syndrome only in 2001. It comprises insulin resistance, hyperinsulinism, high triglycerides, decreased HDL, hypertension and overweight (obesity). The consequences of this syndrome are obvious: higher cardiovascular risks and diabetes. However, a number of urological diseases and abnormalities became directly related to MetS as well. The first is low testosterone which results in a number of symptoms such as loss of vitality, depression, muscle weakness, loss of libido, erectile and sexual dysfunction and in the long run osteoporosis. Over the age of 50 MetS is hence often associated with hypogonadal hypogonadism and/or LOH (Late Onset Hypogonadism). But LUTS (Lower Urinary Tract Symptoms) and BPH (Benign Prostatic Hyperplasia) are also directly linked to obesity as is the onset and progression of PCa (Prostate Cancer). In the presentation casual relationships between MetS in older men and urological symptoms will be elucidated and ways of treatments will be discussed.

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Parallel Session: The aging pelvic floor

INV27

Laser treatment for stress urinary incontinence

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Stress urinary incontinence (SUI) is defined as involuntary leakage of urine with increased intra-abdominal pressure. SUI is due to the progressive herniation of bladder, bladder neck and urethra from the anterior vaginal wall defect. Main defect in the anterior vagina is due to deficient collagen content of the endopelvic fascia.

On the other hand laser energy increases the temperature in the tissue. Cross links between the collagen helix are broken by increasing temperature. Finally laser can improve collagen structure and initiate neocollagenesis. Nowadays, there are increasing numbers of studies suggesting the beneficial effect of laser treatment on SUI, whereas in contrary. My goal is to evaluate and discuss the role of laser treatment on SUI in the light of current data.

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Society Symposium: Dutch Menopause Society

INV28

The impact of menopause on work ability in symptomatic women with severe menopausal symptoms

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Objective: To measure the impact of menopause on work ability in women with severe menopausal symptoms.

Study design: This cross-sectional study compared the work ability of a sample of otherwise healthy employed Dutch women (n = 205) to a sample of first-time attendees of a menopause clinic (n = 60); both aged 44 and 60 years. Self-reported questionnaire data assessing work ability (Work Ability Index; WAI) and menopausal symptoms (Greene Climacteric Scale; GCS) were used.

Main outcome measures: Logistic regression analyses were used to examine whether women with severe menopausal symptoms were more likely to have low work ability (<37.0 points) versus women in the reference group, after adjustment for individual and lifestyle factors.

Results: Symptomatic women had significantly higher total GCS scores (mean 26.7 vs 14.2, t = 10.8, P < 0.001) and significantly lower WAI scores (median 32.0 vs 40.0, U = 2380, P < 0.001) compared to the reference group. They were 8.4 times more likely to report low work ability than their healthy counterparts, 76.7% versus 30.2% (OR 8.4, 95% CI 4.1–17.2).

Conclusions: Over three-quarters of symptomatic menopausal women report serious problems dealing with the physical and mental demands of their work indicated by low work ability, hence these women might be at risk for developing future sickness absence.

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Parallel Session: Perimenopausal health

INV29

Menopause hormone treatment after gynecological cancers

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Some gynecological cancers can occur in relatively young women and part of their treatment consist is an oophorectomy. Some others can be cured by conservative treatment and thus women will undergo a natural menopause. In both situations but predominantly the first one, the question of a hormonal substitution is opened. The available literature abundantly demonstrates that premature ovarian insufficiency is associated with higher mortality from all causes, higher cardio-vascular events mostly coronary heart diseases and bone osteoporotic fractures. It is thus important to know how and to who prescribe an hormonal
treatment. The endometrial cancer is often hormone dependent. Estrogens should be contraindicated in women with stages over 1A. However progesterone and progestins can help to alleviate climacteric symptoms without harm in these patients. Ovarian cancer is a severe disease associated with a high rate of mortality. Three randomized studies have shown that mostly estrogen treatment (in these hysterectomised women) is associated with a better survival. It is likely that low grade serous ovarian cancers however should still constitute a contraindication because of the presence of hormone receptors. Cervical squamous cancers are not hormone dependent and do not constitute a contraindication to an estrogen therapy. Adenocarcinoma of the cervix is however classified as an estrogen dependent carcinoma. The evidence from the literature will be presented.

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Parallel Session: Men’s health

INV30

Fertility in older male

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Late parenthood has declined over the 20th century, to increase again since 1980. Women have been increasingly delaying the start of motherhood and the same trend is also seen for men. A wide spectrum of economical and sociological factors has tried to explain this phenomenon. The unfavorable influence of paternal age on fertility, pregnancy complications and offspring outcome has been thoroughly investigated. These studies provided evidence for the implementation of clinical strategies, such as pre-gestational counseling. On the other hand, advanced paternal age and reproductive outcome has gained considerably less attention.

Male age has been linked to a series of reproductive function and reproductive outcome parameters. Reproductive function parameters include decrease in androgen concentrations, decrease in sexual activity, alterations of testicular morphology (reduced numbers of Sertoli, Leydig and germ cells) and decrease in semen parameters (volume, motility and normal morphology). In addition, advanced paternal age appears to increase sperm DNA fragmentation, a phenomenon suggested to have epigenetic effects. Reproductive outcome parameters include decrease in fertility, increase in pregnancy-associated complications (miscarriage, fetal death, pre-eclampsia, risk of operative delivery) and increase in adverse outcomes in the offspring.

Although there is not enough evidence to support the implementation of specific clinical procedures for late fatherhood, further studies are needed in order to elucidate the complex association between advanced male age and reproduction.

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Parallel Session: Vitamin D

INV31

Vitamin D and sarcopenia

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The world population is aging rapidly due to increasing life expectancy. With aging, a progressive and generalized loss of muscle mass and muscle function, termed sarcopenia, takes hold. In women, this entity is highly prevalent in the postmenopausal period. Sarcopenia is related to many adverse clinical outcomes such as functional disability, increased risk of falls and fractures, poor quality of life, and premature mortality.

Vitamin D deficiency is considered a public health problem, affecting almost half of the population worldwide. Vitamin D is essential for the optimal functioning of the musculoskeletal system. Adverse consequences of vitamin D deficiency on bone mineral density are widely known, and both direct and indirect detrimental effects of vitamin D deficiency have been recognized in muscle structure and functionality. Older adults are at high risk of developing vitamin D deficiency because of aging, and this deficit has been associated with sarcopenia independent of several covariates such as body composition, serum parathyroid hormone levels, dietary intake, or hormone replacement therapy.

The complex etiology of sarcopenia requires integrated interventions. Combined strategies that include an appropriate intake of vitamin D and other related nutrients, together with physical exercise and healthy lifestyle habits, may help in both prevention and treatment of sarcopenia and its related comorbidities.

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Parallel Session: Body composition and cardiometabolic health after menopause

INV32

Menopause and its metabolic implications

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Menopause, through both estrogen decline and aging, has a negative influence on many metabolic pathways. Body fat distribution changes to the android pattern, characterized by visceral fat accumulation and central obesity. Dyslipidemia manifests by increased LDL-cholesterol and triglycerides and decreased HDL-cholesterol. Furthermore, menopause is associated with increased prevalence of hypertension and impaired glucose metabolism. Physical inactivity, mood instability and sarcopenia may also worsen the metabolic profile of the postmenopausal women. Prompt identification and treatment of these conditions can dramatically reduce the incidence of diabetes, ischemic heart disease and stroke in the postmenopausal population.

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Parallel Session: A personalized approach to care at the perimenopause

INV33

Menopause: Time for a new paradigm?

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Menopause is defined as the permanent cessation of ovulation and hence menstruation due to ovarian failure. The median age of menopause is 51 years. However, early menopause might occur at 40 years of age whereas late menopause might happen as late as 62 years of age. Menopause is also a highly heritable condition. Genetic variants are known to contribute to about 50% of the variation in age at menopause.

Several genetic studies have tried to unravel this genetic background making use of different genetic techniques in population studies as well as in animal models. Genome wide linkage studies have only identified a limited amount of genetic variants that seem to be associated with menopause. Population based studies as well as animal research into the genetic background of menopause have identified several genetic variants that are associated with primary ovarian insufficiency. However, a lot of these studies suffer from methodological flaws since results are generally not replicated in different independent samples and most of these studies are underpowered. Hence results are conflicting.

Recent genome wide association studies (GWAS) have identified several genetic variants that are associated with menopause. Genes involved seem to be involved in DNA repair and maintenance as well as in immune function. Biological as well as epidemiological data seem to indicate that reproductive performance, age at menopause and longevity are interlinked through common genetic factors involved in DNA repair and DNA maintenance. In case these systems fail cell death and accelerated ageing occurs. Consequently it seems that the ageing of the soma as a results of dysfunctional DNA repair is responsible for failure to reproduce and the subsequent occurrence of menopause. Hence, reproductive performance constitutes a good predictor for general health in later life.

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Parallel Session: Cardiovascular disease and the aging woman

INV34

Osteoporosis and cardiovascular disease

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Osteoporosis (OP) and cardiovascular diseases (CVD) are very important conditions associated with an increased risk of mortality and morbidity in postmenopausal women. Various studies have showed a significant correlation between bone loss and cardiovascular disease. The link between OP and CVD could be firstly explained by various common risk factors: age, smoking, alcohol consumption, physical activity and menopause status. However, also other theories are proposed to clarify this link. Bone morphogenetic proteins, osteoprotegerin, receptor activator of nuclear factor kB ligand (RANKL), parathyroid hormone, phosphate, oxidized lipids and vitamins D and K seemed to be involved in OP and CVD, suggesting potential common mechanisms. Further studies are warranted to better explain the association between OP and CVD.

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Parallel Session: Perimenopausal health

**INV36**

**Migraine in the transition period**

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Migraine is a paroxysmal disorder of a neurovascular origin, with great adverse effects on the quality of life. According to the Global Burden of Disease Survey 2010 conducted by the World Health Organization, migraine is ranked as seventh highest cause of disability in the world when both genders are considered, and as third when women are considered separately. The distinctive pulsating headaches manifest as attacks that can last from 4 up to 72 h and are located unilaterally. The headaches worsen with physical activity and/or are associated with photophobia and phonophobia. The prevalence of migraine is according to the recently published American Migraine Prevalence and Prevention study 17% in women and 6% in men. Especially hormonal milestones accompanied by fluctuations in estrogen levels such as menarche, pregnancy and menopause seem to have vast effects on migraine prevalence and frequency. Indeed, during the perimenopausal period, 8–13% of women with migraine report the onset of their migraine during this period. However, the pathogenic mechanism behind this association remains to be clarified.

During the lecture, recent advancements in the research of migraine, including the development of novel antimigraine drugs, will be discussed in relation to perimenopausal migraine. A better understanding of these mechanisms will lead to a better treatment of patients suffering from this debilitating disorder.

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Parallel Session: Women and mental health

**INV38**

**WHO claims “Estrogens are carcinogenic” – Is this true?**

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The WHO has classified estrogens and estrogen/progestogen combinations as ‘carcinogenic’, because they may increase the risk of breast cancer. There are two main pathways:

1) increased proliferation and/or
2) development of carcinogenic estrogen metabolites, leading to DNA strand breaks and to mutations.

Addition of progestogen may further increase the risk. Ligand-bound receptors can work in the classical genomic pathway with binding to the DNA estrogen responsive element and activation of the transcription machinery. The non-genomic pathway includes cross-reactions of the ER-alpha with intracellular signal molecules such as the tyrosine kinase domain of growth factor receptors or directly with the mitogenic kinase PI3K. In addition the ER-complex can bind to DNA elements such as AP1 or cyclin D1. We could demonstrate that synthetic progestogens can increase the proliferation by reaction with certain membrane-bound receptors which we have found to be increased in tissue of breast cancer patients, especially if prognosis is poor. We also have been able to assess the biological potency of various metabolites and that their pattern during HRT can be influenced by administration route and the type of added progestogen. In addition, life-style factors as well as genetic polymorphisms of the enzymes involved in the E2-metabolism may have a crucial impact. However, we also found carcinoprotective estrogen metabolites which can add to other protective estrogen-dependent (e.g. apoptosis) or independent (e.g. immunoprotection) mechanisms. Because during estrogen-only the proliferation rate is very low, those protective effects can even lead in a statistical analysis to a decrease of breast cancer risk, if more patients with carcinoprotection compared to carcinoproliferation are in the study population. This can explain the decrease of breast cancer risk with estrogen-only but increase with estrogen/progestogen-combination in the WHI-study.

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Parallel Session: Women and mental health

**INV39**

**The functions of estrogen receptor beta in the female brain: A systematic review**

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Females have unique and additional risk factors for neurological disorders. Among classical estrogen receptors, estrogen receptor beta (ERβ) has been suggested as a therapeutic target. However, little is known about the role of ERβ in the female brain. Six electronic databases were searched for articles evaluating the role of ERβ in the female brain and the influence of age and menopause on ERβ function. After screening 3186 titles and abstracts, 49 articles were included in the review, all of which were animal studies. Of these, 19 focused on cellular signaling, 7 on neuroendocrine pathways, 8 on neurological disorders, 4 on neuroprotection and 19 on psychological and psychiatric outcomes (6 studies evaluated two or more outcomes). Our findings showed that ERβ phosphorylated and activated intracellular second messenger proteins and regulated protein expression of genes involved in neurological functions. It also promoted neurogenesis, modulated the neuroendocrine regulation of stress response, conferred neuroprotection against ischemia and inflammation, and reduced anxiety- and depression-like behaviors. Targeting ERβ may constitute a novel treatment for menopausal symptoms, including anxiety, depression, and neurological diseases. However, to establish potential therapeutic and preventive strategies targeting ERβ, future studies should be conducted in humans to further our understanding of the importance of ERβ in women's mental and cognitive health.

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**INV40**

**Vitamin D and response to major illness**

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Vitamin D deficiency and insufficiency is a major health concern worldwide. Vitamin D status varies with skin type, latitude, foods fortified with vitamin D, use of supplements, sunshine exposure, and habitual clothing style. Vitamin D insufficiency is prevalent among older adults and may be associated with higher risk for cardiovascular (CV) disease, mortality, depression, and cognitive deficits. Although, the Women’s Health Initiative Randomized Trial did not find a benefit of vitamin D supplementation on blood pressure, myocardial infarction, or mortality in postmenopausal women. The benefits of vitamin D treatment are still under evaluation.

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Parallel Session: Perimenopausal health

**INV41**

**The management of premenstrual syndrome in late reproductive years and perimenopause (perimenopausal health)**

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Many women experience mild physical and emotional PMS symptoms which are not particularly troublesome. However, when severe these symptoms can lead to a breakdown in interpersonal relationships and interference with normal activities. These symptoms can be particularly troublesome in the late reproductive and perimenopause years due to increasing hormonal fluctuations which can trigger symptoms in genetically predisposed, hormonally vulnerable, women. The International Society for Premenstrual Disorders (ISPMD) has made recommendations for a new classification with core (typical, pure or reference disorders associated with spontaneous ovulatory menstrual cycles) and variant premenstrual disorders (such as symptoms of an underlying psychological or somatic disorder significantly worsening premenstrually). PMS/PMDD continues to be poorly understood and in many cases inadequately managed. It can be the cause of considerable morbidity and at time even mortality. It is imperative that a consensus on definition is reached globally and that properly conducted research continues to be funded.

Progestogens should not be used as they are good at reproducing the symptoms of PMS/PMDD! The more established therapies for which randomized controlled data exist are the combined “fourth” generation pills (e.g. the 24/4 or flexible regimen 20 mcg ethinylestradiol/3 mg drospirenone), transdermal estradiol, selective serotonin re-uptake inhibitors and the GnRH analogues with add back HRT. Hysterectomy with BSO and adequate HRT remains an important option for severely afflicted women whose family is complete and have not responded to other therapies. The presentation will follow the recently updated 2016 UK RCOG Green Top Guideline No 48 on the Management of Premenstrual Syndrome available from the National Association for Premenstrual Syndrome www.pms.org.uk.

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Parallel Session: A personalized approach to care at the perimenopause

**INV42**

**Diet and lifestyle in the management of hot flushes**

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Obesity has been linked to higher levels of menopausal symptoms such as hot flushes. While weight loss interventions including bariatric surgery have been associated with an improvement in hot flushes, the Women’s Health Initiative Dietary Modification (DM) trial has given more complex insights. Thus women who lost weight reported a reduction or elimination of vasomotor symptoms (VMS) over one year. However, women in the intervention who gained >10 lbs also had reduced VMS suggesting that the beneficial impact of a healthy diet was not restricted to those who lost weight. Different diets appear to have health benefits. The Mediterranean type of diet has consistently been found to be compatible with healthier aging and longevity in observational studies. Regular physical activity reduces the risk of coronary heart disease, type 2 diabetes, osteoporotic fracture and breast and endometrial cancer. A 2014 Cochrane review concluded that evidence was insufficient to show whether exercise is an effective treatment for vasomotor menopausal symptoms. Subsequently a randomised trial found that exercise is not an effective treatment for hot flushes/night sweats. However another study found that in sedentary women, aerobic training for 6 months may decrease the typical menopausal symptoms, especially night sweats, mood swings, and irritability, but not vaginal dryness. Furthermore exercise participation may result in lower perception of symptom severity. Thus while exercise and maintaining a healthy weight have general benefits their effect on hot flushes is modest. Neither intervention improves vaginal dryness.

http://dx.doi.org/10.1016/j.maturitas.2017.03.047

Society Symposium: German and Swiss Menopause Society – Endometrial cancer and breast cancer

**INV43**

**Progestogens and breast cancer – Importance of membrane receptors**

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**Objective:** In an Editorial of the journal “Menopause”, discussing our research on mechanisms of breast cancer development during menopausal hormone therapy (MHT), it has been suggested that the observed increase in breast cancer risk using hormone therapy in the combined arm of the Women’s Health Initiative study could probably be explained by overexpression of a special...
receptor, i.e. the progesterone receptor membrane component-1 (PGRMC1) (Editorial Stanczyk F. Menopause 2011).

**Methods:** MCF7 cells were stably transfected with PGRMC1 expression plasmid or empty vector. Various MHT regimens were in vitro tested. Nude mice were used for animal models transfected with breast cancer cells. The experiments were repeated also with T47D cells.

**Results:** Regarding the expression of PGRMC1 in the malignant tissue of breast cancer patients we have been able to show that this is significantly higher compared to their normal mammary glands. We could demonstrate that certain synthetic progestins can increase the proliferation of PGRMC1-overexpressing breast cancer cells in vitro and also in animal models and may thus be involved in tumorigenesis, while progesterone and certain synthetic progestins derived from progesterone react more neutral. Especially strong proliferation we have seen adding norethisterone or medroxyprogesterone acetate to cells during estradiol-induced proliferation, in vitro and in vivo (animal model). Moreover, in our experimental models, continuous combined estrogen/progestogen act stronger on proliferation compared to sequential combined estrogen/progestogen treatment of breast cancer cells, especially if transfected with PGRMC1.

**Conclusion:** Activation of PGRMC1 may explain the increased breast cancer risk observed during treatment with certain progestogens. In the future screening for PGRMC1 might be a predictor of breast cancer risk during hormone therapy including using COC.

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**INV44**

**Membrane-bound progesterone receptor to predict the prognosis of breast cancer**

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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 and if present, may increase the risk of breast cancer in women getting menopausal hormone therapy (MHT). This has been discussed within two Editorials on our recent research in the journal “Menopause” (Editorial Stanczyk F. Menopause 2011; 18: 833–834; Price T. Menopause 2013; 20: 486–487). Aim of our clinical study in patients with breast cancer was to investigate if this marker also could predict the further prognosis of breast cancer patients comparing with other already well known parameters for the prognosis of breast cancer.

**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 like disease free survival and overall survival time.

**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 not only to predict the risk using hormones in therapy but also as a prognostic biomarker in ER-positive and negative breast cancer.

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**Parallel Session: Cardiovascular disease and the aging woman**

**INV45**

**Heart disease in midlife women: True and perceived risk**

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Compared to premenopausal women, the incidence of heart disease increases significantly at midlife and beyond. Perceived risk is that heart disease is a disease of aging men; however, true risk is that each year more women face an adverse heart disease prognosis and higher mortality. This risk is not fully accounted for by age, comorbidity, coronary atherosclerotic disease, or treatment gender gaps. Women differ in presentation, diagnosis, and treatment of heart disease. Perceived risk is that heart disease symptoms include crushing chest pain, however true risk is that symptoms of heart disease in women are often more atypical, milder symptoms of angina compared to men. Further, women are also more likely to have open coronary arteries on angiography, which leads to false reassurance that they do not have heart disease. Data from the National Heart, Lung, and Blood Institute-sponsored, multi-site Women’s Ischemia Syndrome Evaluation (WISE) Study indicate that microvascular coronary dysfunction (MCD) is prevalent and a mechanistic pathway of ischemic heart disease in women. MCD is defined as persistent symptoms of angina (typical and atypical), objective evidence of ischemia by stress testing, and no obstructive CAD by angiography. This lecture will focus on true risks for heart disease in midlife women.

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**INV46**

**Vasomotor symptoms and women’s cardiovascular health**

Rebecca C. Thurston

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Vasomotor symptoms (VMS) are common menopausal symptoms, experienced by upwards of 70% of women during the menopause transition. VMS have long been understood to have important implications for quality of life during the menopause transition. However, aside from signaling a changing hormonal milieu, they have generally been conceived as having few implications for physical health. Emerging data have called that assumption into question. Research from the epidemiologic study, the Study of Women’s Health Across the Nation, indicates higher subclinical cardiovascular disease (CVD) among women with VMS compared to those without VMS, controlling for CVD risk factors
and estradiol levels. Recent findings from our laboratories using physiologic monitoring of VMS shows more frequent physiologic VMS among women with VMS associated with higher subclinical CVD in a dose-response fashion. We and others have investigated potential mechanisms that may link VMS to CVD risk (e.g., blood pressure, lipids, insulin resistance, endothelial function, inflammation, clotting, cardiac vagal control). Additional data underscore potentially important modifying roles of age of menopause stage in VMS-CVD risk associations. For example, we have found early- occurring VMS associated with higher subclinical CVD and CVD mortality across several cohorts of women. However, positive findings of CVD risk associated with VMS are not universal. For example, research from cohorts of women with exceptionally low CVD risk profiles do not find these associations. Data on links between VMS and CVD risk will be reviewed, how best to conceptualize VMS-CVD risk relations (e.g. as causal or VMS as a marker of underlying CVD risk) will be emphasized, and clinical implications of this work will be discussed. 

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Parallel Session: Women and mental health

INV47

Psychological health and disease in later life

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Starting in adolescence and persisting well through midlife, women have increased rates of mood and anxiety disorders relative to men. Reproductive transitions, such as the menopause transition, have historically been regarded as times of psychological vulnerability for women. However, whether the menopause transition is associated with increased risk for anxiety and depression has been a topic of scientific inquiry and debate. Some recent findings from large cohort studies support increased risk for mood and anxiety disorders during the menopause transition beyond aging alone. Additional data point to the importance of sleep, as sleep problems, a known risk factor for mood and anxiety problems, are frequently reported during the menopause transition. Menopausal vasomotor symptoms are also consistently linked to adverse mood and anxiety changes during the menopause. Finally, changes in social roles and major life events common during midlife also appear to importantly contribute to psychological functioning during menopause. This talk will report data investigating risk for depressed mood and anxiety over the course the menopause transition. Contributions of menopausal symptoms and life events to these mood changes will be discussed. Finally, a potential buffering role of positive psychological functioning will be noted. The talk will emphasize findings from large, prospective cohort studies that allow investigation of women's psychological health prospectively over the menopause transition.

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Parallel Session: Cardiovascular disease and the aging woman

INV48

Ovarian aging and cardiometabolic disease

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Women are born with a finite number of oocytes, which gradually decreases as they age. The size of the pool of remaining oocytes is known as ovarian reserve. The decline of ovarian reserve continues until the ovaries are ‘depleted’ at an estimated number of 1000 remaining oocytes, which heralds the onset of menopause. The median age at which this occurs is 51 years, with a normal variation between 40 and 60 years. The distribution of age at menopause is slightly skewed towards earlier ages at menopause, of which 1% are thought to occur before the age of 40, and 5% before the age of 45. The distribution of age at menopause furthermore appears to have been conserved over time and between ethnicities. Although cardiovascular disease has long been considered a disease of middle-aged males, it is the leading cause of death for women as well. Cardiovascular diseases account for 30% of deaths. Coronary heart disease (CHD) causes half of these deaths, and for 8% of the disability-adjusted life years. Morbidity and mortality graphs by sex suggest that women are relatively protected against coronary heart disease until around the age at fifty, the age at which menopause occurs.

Menopause, in particular surgical menopause, seems to be associated with an increased risk of type 2 diabetes and cardiovascular disease. The relationship between reproductive aging and cardiovascular disease has generally been ascribed to postmenopausal decreases in endogenous estrogen levels. There is also some evidence that risk factors for cardiovascular disease (e.g., smoking, high cholesterol, high blood pressure) are also risk factors for early menopause, which could imply that an earlier menopause is the consequence of vascular aging rather than the reverse. In this lecture the current evidence regarding the relationship between reproductive aging and cardiometabolic disease risk will be summarized.

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Parallel Session: Premature ovarian dysfunction

INV49

Improving fertility rate in women with premature ovarian insufficiency

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Premature ovarian insufficiency (POI) is characterized by oligo/amenorrhoea in women younger than 40 years of age, FSH >40IU/L and estradiol <50 pmol/L. In vitro fertilization failure is caused by endometrium receptivity disturbances in 2/3 of women. Factors influencing implantation rate are: hormones, growth factors, adhesion molecules, extracellular matrix, prostaglandins, lower CD8+ and higher CD4+. Glycodelin improves implantation by suppression of immune response and apoptotic and antiproliferative effects on T lymphocytes. Factors improving fertility rate in premature ovarian insufficiency are:
1. Estrogens – high FSH values are inhibited and intermittent FSH increase induces ovulation in some of 1000 remaining follicles. In a case that no dominant follicle with quality oocyte can be obtained and FSH is 10–15 IU/L (2 day of cycle) in last 6 months, oocyte donation can be advised.

2. Hyperinsulinism: decreases glycodelin, IGFBP1 and increases PAI-1. Oral contraceptives therapy during 6 months improve fertility rate.

3. Thrombophilia: Leyden V, FII, MTHFR, PAI have to be determined. Increased PAI induces miscarriages in 60%.

4. TSH has to be 1–2.5 mU/L 3 months prior to implantation.

5. Endometriosis: Disturbed expression of HOX gene decreases endometrium receptivity. Antizona pellucida antibodies are found in 40% women. Oral contraceptives therapy during 6 months improve fertility rate.

6. DHEAS increase fertilization rate by conversion to estrogens and effects on androgens.

7. Melatonin: Has a putative role by decreasing cAMP in preovulatory follicle.

**Conclusion:** Women’s body has to be completely prepared for the pregnancy before oocyte donation.

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**INV50**

**Arthritis in the perimenopause**

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The perimenopause is a common time for women to experience new or worsening musculoskeletal symptoms. Whilst not all joint pain represents arthritis and may represent arthralgia or myalgia, there is an increased incidence of both inflammatory arthritis such as rheumatoid arthritis and osteoarthritis in this population. Sudden onset estrogen deficiency associated with surgical or medical menopause has also been noted to precipitate arthralgia or arthritis. The area is reviewed, including the evidence for an association between arthritis, menopause and hormonal changes. Osteoarthritis is the commonest form of arthritis, and the association between hand osteoarthritis, female gender, and onset of menopause has long been noted. Hand symptoms may self-limit after 2–5 years, although a subgroup of patients develop more persistent symptoms and joint change causing significant pain and disability. The known effects of estrogen on joint tissues and the effects of menopausal hormonal therapy (MHT) in those with inflammatory arthritis or osteoarthritis will be discussed. Lastly, a clinical approach to the peri-menopausal patient with new onset of joint symptoms is summarised, with an overview of relevant investigations and early management.

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**INV51**

**The role of estrogen on cognitive health in post-menopausal women**

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During the last century there has been a significant increase in female life expectancy, leading to a greater number of women achieving a postmenopausal age which is generally accompanied with low estrogen levels. Although protective effects of ovarian steroids on cognitive function have been suggested, the association between endogenous estrogen levels and cognition has not been clearly demonstrated. Thus far, cross-sectional and longitudinal studies investigating whether endogenous estrogen levels are associated with cognitive function in postmenopausal women have conflicting results. These inconsistent findings might be due to differences in study populations, technical issues in measuring serum estrogen, and different test batteries used in the assessment of cognitive performance. Furthermore, findings on the effect of estrogen therapy on cognition and brain function in healthy post-menopausal women remain contradictory. Therefore, the issue of whether or not estrogen is protective against cognitive decline continues to be of pivotal importance. Studying the association of serum estrogen level with performance in different cognitive domains in larger populations of postmenopausal women may provide more robust indications of the role of estrogen in cognition. Furthermore, research on the mechanisms of estrogen and estrogen receptor signalling in neuronal tissues may help to elucidate the effects of endogenous estrogen on cognitive function.

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**INV52**

**Promoting longevity: A global approach**

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Healthy ageing is a wide notion that includes the promotion of physical and psychological health as well as a high-standard quality of life. Health has the avoidance of disease as a primary step, risk reduction being a crucial concept in that regard. This is a very motivating feature, as demonstrated for example by the interest on the impact of menopausal hormone treatment on disease risk incidence (i.e. osteoporosis). The analysis of useful tools to accomplish significant health benefit favours lifestyle and drugs among the strongest options. The progressive narrowing in the use of drugs leaves lifestyle as a decisive resource. A wealth of data supports the protective effect of physical activity on the deterioration of several body systems. There is also some evidence about its effect against different mechanisms, including inflammation, which is determining in the phenomenon of ageing. The practice of exercise has been also shown to be crucial in particular diseases, among others those of the cardiovascular area. However, the implementation...
of the regular practice of exercise at a global level has found difficulties related with adherence. There is experience derived from attempts that have tried to introduce the necessary behavioural change. Beside some psychological tools, the insertion of exercise practices within daily life and the inclusion of social engagement as a variable, are attaining some results. There is also a huge interest in the role that may be played by new ICT technologies, an alternative being promoted by European institutions.

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Parallel Session: Steroids and health in aging women

INV53

Cardiovascular risk in women with premature ovarian insufficiency compared to premenopausal women at middle age

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Aim: To compare the CVD risk profile between women previously diagnosed with premature ovarian insufficiency (POI, n = 83) and premenopausal controls (n = 266) at middle age.

Design: Cross-sectional case control study at two University Medical Centers.

Outcomes measures: Blood pressure, BMI, waist circumference, ECG, bilateral carotid intima media thickness, E2, T, androstenedione, DHEAS, SHBG, insulin, glucose, lipids, TSH, free T4, NT-proBNP, CRP, uric acid, creatinine, and homocysteine were measured. Potential associations between POI status and subclinical atherosclerosis were assessed.

Results: Women with POI (mean age 49.9 ± 4.7 yrs) exhibited an increased waist circumference (β = 5.7; 95% CI, 1.6, 9.9), CRP (β = 0.75; 95% CI, 0.43, 1.08), and free T4 levels (β = 1.5; 95% CI, 0.6, 2.4), and lower NT-proBNP (β = −0.35; 95% CI, −0.62, −0.08), E2 (β = −1.98; 95% CI, −2.48, −1.48), T (β = −0.21; 95% CI, −0.37, −0.06), and androstenedione (β = −0.54; 95% CI, −0.71, −0.38) concentrations compared to controls (mean age 50.9 ± 3.1 yrs), after adjusting for confounders. After adjustment, a trend toward increased hypertension (odds ratio = 2.1; 95% CI, 0.99; 4.56) and decreased kidney function was observed in women with POI (creatinine β = 3.5; 95% CI, −0.05, 7.1; glomerular filtration rate β = −3.5; 95% CI, −7.5, 0.46). Women with POI exhibited a lower mean carotid intima media thickness (β = −0.17; 95% CI, −0.21, −0.13) and decreased odds of plaque presence compared to controls (odds ratio = 0.08; 95% CI, 0.03, 0.26).

Conclusions: Women with POI exhibited an unfavorable cardiovascular risk profile, including higher abdominal fat, elevated chronic inflammatory factors, and a trend toward increased hypertension and impaired kidney function compared to controls. However, we observed no signs of increased subclinical atherosclerosis in women with POI. Additional studies are required to identify specific determinants of long-term CVD risk in women with POI.

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Parallel Session: Aging skin and hair

INV54

Managing hair loss in midlife women

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Hair loss is common in women, estimated prevalence of 25%. At birth, 100,000 hair follicles are present on the scalp, gradually decreasing in life, with shortening of the anagen phase and thinning of the hairs especially perimenopausal. There may be a gliding scale between physiologic aging and androgenetic alopecia. Common causes of alopecia in midlife women are alopecia androgenetica/female pattern hair loss, telogen effluvium, frontal fibrosing alopecia, central centrifugal cicatricial alopecia and adverse effects of hair styling. A correct diagnosis is important, difficult in early stages of these different, but sometimes concurrent, types of alopecia. The consultation includes an extended history on the onset and behavior of the hair loss, on patient’s general condition systemic medication and comorbidity, recent trauma or surgery, diet, signs of androgenisation, use of cosmetics/toiletries and type of hair styling. A complete inspection of the scalp including trichoscopy (dermatoscopy of the scalp), (body) hair, face and nails is necessary and sometimes a biopsy and blood tests.

Alopecia Androgenetica or Female Pattern Hair Loss: the most frequent form of alopecia in women, occurring in all ages after puberty, but present in 50% of peri-menopausal Caucasian women. The exact mechanism is still debated, the only evidence based therapy is minoxidil as a 5% foam. Widely used in women with and without androgenisation are finasteride, dutasteride, cyproteronacetate, spironolactone.

Chronic telogen effluvium: shedding > 6 months without apparent scalp thinning/alopecia. Bloodtest to exclude hypothyroidism, iron deficiency, DM. Therapy is unknown.

Frontal fibrosing alopecia, progressive cicatricial alopecia starts mostly in postmenopausal women, a symmetrical recession of the frontal and temporal hairline. Treatment is difficult.

Central centrifugal cicatricial alopecia is the most common cause of scarring alopecia in African American women. No proven therapy.

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New and herbal alternatives for hot flushes
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The abrupt decrease of ovarian estrogen production at the menopause leads to vasomotor hot flushes, which is accepted as a leading indication for MHT. Menopausal hormone therapy (MHT) with estradiol is the most effective treatment for menopausal complaints. However, many women prefer complementary or alternative remedies such as herbal preparations or nutraceuticals, which are perceived to be more natural than hormones and believed to be safer. Hop is a climbing plant of which the flower cones are an ingredient of many beers. The hop-flavonoid 8-prenylnaringenin (8-PN) is a stronger estrogen than soy isoflavones. There is some evidence that 8-PN may be efficacious against vasomotor complaints. Hops have been shown to contain one of the most potent in vitro estrogenic substance known from the plant kingdom.

Preparations of hops that contain 8PN must be considered “estrogenic”. It still is open to debate, however, whether or not they can have beneficial hormononal activity when consumed orally by humans. Whereas there are numerous animal studies and some clinical evidence that hops may contribute to the therapeutic efficacy of certain polyherbal sedative preparations, no randomized, double-blind, placebo-controlled clinical trials have been identified that would support the internal use of hops for their estrogenic properties. Considering that sleep disturbances and vasomotor complaints are frequently associated with menopause, and that hops are not only estrogenic but also used traditionally as a sedative, Hop preparations can have a rational place in menopausal medicine.

Thus, given the history of long-term and present use in humans with no significant adverse effects, an initial hypothesis is that hops are safe.

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New opportunities for ameliorating sexual disorders during premenopause and menopause
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Female sexual disorders are common during premenopause-menopause and have very complicated pathophysiological mechanisms. The diagnosis is also difficult. Most of the time, therapy which is addressed to pathophysiological mechanisms, is insufficient. A wide range of therapy has been proposed to improve the female sexual disorders.

In my topic, I try to review the role of a very special herbal medicine on sexual disorders. This is Trigonella foenum-graecum which has been widely used to treat a wide variety of disorders for years.

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Menopausal hormone therapy and breast cancer risk
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The possibility that long term Menopausal Hormone Therapy (MHT) increased the risk of breast cancer (BC) was recognised in the late 1980s. The publication of the initial results of the US WHI study in 2002 indicated that conjugated equine oestrogen (CEE) plus MPA increased the risk of BC – a later publication indicated no increase in risk associated with CEE alone. The findings from the UK Million Women Study published in 2003 indicated that all oestrogen progesterone combinations increased the risk of breast cancer within one year of exposure. The increased risk associated with oestrogen alone was only seen after more than one year. The MWS investigators calculated that HRT over a ten year period about 20,000 extra cases of breast cancer occurred in England and Wales as a result of MHT.

More than 10 years have elapsed since the publication of these alarming findings. There was an early rapid fall in the use of HRT in the UK and many other countries. The current rate of prescribing is less than a third of the level before 2001. If there is a causal association between MHT use and BC then it would be expected that the decline in its use would be associated with a decline in BC. Registration rates of BC amongst women age 50–64 years (the age group that had the highest consumption of MHT) in a number of countries (England, New Zealand, Australia, some areas in the US) show no decline.

The absence of a consistent decline in BC incidence may be due to changes in detection or changes in background incidence of the disease. If this were the case then it is remarkable that those changes were coincident with the decline in MHT use. On the other hand it is possible that the pivotal studies over estimated the risks. This explanation is the more likely.

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Non pharmacological management of fracture risk
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The compliance of bisphosphonate treatment in osteoporotic patients is very low. Netelenbos et al., 2010, demonstrated that 57% of the patients who started bisphosphonates discontinued treatment within 1 year. This was mainly due to the side effects like heartburn complaints. A further disadvantage is that bisphosphonate intake should be stopped after 5 years and the small increase of osteonecrosis of the jaw. Therefore there is an urgent need of alternative treatments. There are two bone active vitamins namely vitamin K and D. Vitamin K2 (Menaquinone-7, MK-7) has been extensively investigated by Knapen et al., 2013 and they demonstrated that 180 μg MK-7/day capsules used by healthy postmenopausal women (n = 244) during 3 years versus placebo significantly decreased the age-related decline of the bone

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Mineral density (BMD) of the lumbar spine and femoral neck. Ronn et al., 2017 performed a randomized controlled study in 148 postmenopausal women with osteopenia comparing MK-7, 375 μg daily versus placebo during 12 months. The osteocalcin level decreased in the MK-7 group however the BMD at any site did not show significant differences between both groups. Nakano et al., 2011, investigated the vitamin D and K levels in 99 female patients with a hip fracture. They concluded that patients with a femoral fracture had a severe vitamin D and K deficiency. From these data it is obvious that adequate supplementation with vitamin D and K in patients with osteopenia and osteoporosis is mandatory to prevent fractures. Adequate daily supplementation of vitamin D consists of 5000 IU and MK-7 of 200 μg. The 10 year data of the fracture and osteoporosis outpatient clinic of the Medisch Spectrum Twente Hospital Group demonstrated that only 10% of the female patients had a sufficient vitamin D serum level of >80 nmol/l. These unpublished data will be presented during the congress.

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Parallel Session: Pregnancy in women over 40

INV59

Assisted reproduction for POI patients and for (peri-)-menopausal women

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Many women with POI present with a wish to conceive. Furthermore, with postponing childbearing due to social reasons in an increasing amount of women, there is a trend towards women who are trying to conceive when they are already perimenopausal. The current presentation will address the waxing and waning of ovarian activity, and spontaneous conception rates in these women. Further focus will be placed on the exploration of the possibilities and limitations of artificial reproductive techniques in these specific groups. Finally, fertility preservation, oocyte donation and considerations regarding obstetric risks in subgroups of women with POI will be discussed.

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Parallel Session: Cross-cultural differences in the management of aging

INV60

Menopausal symptoms – Comparing East and West

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Well known are the typical “menopausal symptoms”, i.e. symptoms during the transit from pre- to peri- to early postmenopause, like vasomotor symptoms (hot flush and sweating), sleep disorders and mood changes, urogenital atrophy and dyspareunia with sexual disfunction. Very typical also are menstrual disorders, which are the basis of the definition of menopausal stages according to the “2011 Stages of Reproductive Aging Workshop (STRAW + 10) report”. By comparison of different countries or continents, resp., it should be considered that in the studies the symptoms have been assessed by different menopausal transit definitions and also by different scales, and there are also large differences dependent on study design, sampling and screening. However, there are some striking observations: Our own large recent study (n = 1225) shows that the main climacteric symptoms in Chinese women are muscle and joint pain, depression and irritability (about 60%) whereas vasomotor symptoms only in about 40% have been observed, all symptoms according Kupperman Index are higher in post-compared to perimenopause. This also is confirmed in large intercontinental reviews. An alarming increase of depression is observed also in other parts of Asia, in Eastern Europe and South Americia, e.g. also seen in the SWAN study comparing different ethnic groups within USA. Although metaanalyses and systematic reviews concluded in general no clear pattern of menopausal symptoms, in general there is an increase of all symptoms within the recent years, thus great need for treatment in every country.

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Society Symposium: European Society of Gynecology – Adrenopause, Fertilopause and Menopause: Problems and Solutions

INV61

Estradiol-based contraceptives for perimenopausal patients?

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In hormonal contraceptives primarily the progestin is the key component. Combined oral contraceptives (COC) also contain an estrogen primarily to promote cycle stability. Up to recently all COC did contain Ethinyl-Estradiol (EE). Now two E2-based COC are available, containing as progestins dienogest (DNG) or NOMAC, resp. Use of natural estradiol is expected to provide benefits compared to EE especially regarding hepatic and cardiovascular tolerability. 1.5–2 mg E2 is roughly comparable with 5–20 μg EE, depending on the target organ. Regarding the activation of coagulation factors or induction of carrier proteins such as SHBG, the hepatic activity of EE tends to be 500-fold higher compared to E2, while the proliferating effect on the endometrium or vaginal superficial cells, the osteoprotective and especially also the central effect for improving depressive mood, irritability, treating hot flushes have been proved to be higher using E2 instead of EE. These differences may have special importance for the use of COC in perimenopausal women, who have an increased risk of endometrial hyperplasia, of developing climacteric symptoms, osteoporosis and vaginal atrophy. Most important is, that risk of VTE strongly is increasing with age, and there is increasing warning to use COC containing EE in this age group. From the pharmacological point of view it already has been expected that the risk of VTE should be lower using E2-compared to EE-pills, not only because of the high hepatic affinity but also because of the frequent liver passages of EE before it is broken down to peripheral concentrations which no longer are biological active. Just now the first study in about 50,000 COC users has been published showing indeed a more than 50% lower VTE risk using the E2/DNG pill compared to COC containing EE. Although more studies are needed to prove this important difference we conclude
that E2-derived COC may be a good option for contraception in perimenopausal age.

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Society Symposium: Erasmus MC Women and cardiometabolic health: Transition through menopause

INV62

Estrogen receptor β actions in the female cardiovascular system: A systematic review of animal and human studies

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Five medical databases were searched for studies that assessed the role of ERβ in the female cardiovascular system and the influence of age and menopause on ERβ functioning. Of 9472 references, 88 studies met our inclusion criteria (71 animal model experimental studies, 15 human model experimental studies and 2 population based studies). ERβ signaling was shown to possess vasodilator and antiangiogenic properties by regulating the activity of nitric oxide, altering membrane ionic permeability in vascular smooth muscle cells, inhibiting vascular smooth muscle cell migration and proliferation and by regulating adrenergic control of the arteries. Also, a possible protective effect of ERβ signaling against left ventricular hypertrophy and ischemia/reperfusion injury via genomic and non-genomic pathways was suggested in 27 studies. Moreover, 5 studies reported that the vascular effects of ERβ may be vessel specific and may differ by age and menopause status. ERβ seems to possess multiple functions in the female cardiovascular system. Further studies are needed to evaluate whether isoform-selective ERβ-ligands might contribute to cardiovascular disease prevention.

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Parallel Session: Osteoporosis

INV63

Clinical impact of different treatments of osteoporosis

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Osteoporosis is a chronic disease which may require treatment for many years and requires not only individual management but often sequential or combination treatments. For many years, we have used antiresorptives as monotherapy, positioning each according to its mechanism of action, vertebral and non-vertebral efficacy and its side-effects. The appearance of the anabolic parathyroid hormone (PTH) agent in its two presentations (teriparatide (PTH1-34) or PTH1-84) has opened new possibilities. Thus, another approach would be to switch or even add an anabolic treatment to ongoing treatment with antiresorptives. Several anabolic and antiresorptive therapies have been combined in an attempt to reach higher bone mass and increased strength compared with monotherapy. The current possibilities are to start with antiresorptive and to keep it for a long time or to switch it to another antiresorptive or an anabolic, or even to combine them at the same time, or to begin with an anabolic and to switch it later by an antiresorptive.

When you start with an antiresorptive whether to maintain or modify the treatment depends very much on BMD. If BMD decreases after 2 years or there is a fracture and secondary causes of loss of bone mass are excluded, a more potent antiresorptive agent or sequential or combination therapy with an anabolic agent should be considered. New anabolic agents will appear and the idea of combining antiresorptives with anabolics has more and more evidence and even in specific cases begin with an anabolic agent.

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Society Symposium: British Menopause Society

INV64

Premature Ovarian Insufficiency Registry – An update (BMS symposium)

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Context: Premature ovarian insufficiency (POI) remains poorly understood and under-researched. The POI registry http://poiregistry.net has been developed using a British Research Council grant to collect national and international data in an effort to avoid fragmented research and improve our understanding of this relatively uncommon but important disease.

Objective: Retrospective and prospective registry analysis of women with POI.

Methods: Data collected on women diagnosed with POI younger than 40 years have been entered onto an online registry. The data were subsequently extracted and analysed at Imperial College London by patient ages, aetiology, ethnicity, time to diagnosis, symptom profile and bone mineral density (BMD).

Results: 45 centres have registered to enter data globally thus far. Many of the centres are in the UK but also include investigators in Australia, Brazil, Canada, Chile, China, Italy, Russia, Spain and South Africa. Retrospective (legacy) data have been entered for 484 women and prospective data for 343 women with POI thus far. Data entry includes demographics, diagnosis, presentation, management and outcomes such as bone mineral density. Collaborative work is being conducted to facilitate biobanking for genetic and biomarker analyses. A key finding from early data analysis is that delay to diagnosis results in lower bone mineral density. These and other data will be presented in detail with focus on diagnosis, presentation and management of POI.

Conclusions: The POI registry has proved successful in data collection as shown by the number of centres registered and the number of patients entered thus far. By encouraging more healthcare professionals to engage with data collection, we aim to optimize the quality and quantity of data.

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Parallel Session: Gynecological oncology

INV65

Obesity, insulin resistance and endometrial cancer risk

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Endometrial cancer (EC) is the most prevalent female genital malignancy in developed regions. It is considered a steroid hormone-dependent cancer, although its prevalence is higher during postmenopausal years (sixth and seventh decades) when ovarian function is minimal and steroid hormone levels are lower
Autosomal trisomy is the most frequent finding and is related, at least in part, to changes in the meiotic spindle that predisposes to nondisjunction. Although 9.9% of women younger than 33 years who conceive during IVF with a fresh embryo transfer have a pregnancy loss after 7 weeks of gestation with fetal heart activity observed, the rates of miscarriage progressively increase from 11.4% in the 33–34-year group to 13.7% in the 35–37-year, 19.8% in the 38–40-year, 29.9% in the 41–42-year groups, and 36.6% in women older than 42 years.

As age increases, the risks of other disorders that may adversely affect fertility, such as leiomyomas, tubal disease, and endometriosis, also increases. Women with a history of prior ovarian surgery, chemotherapy, radiation therapy, severe endometriosis, smoking, pelvic infection, or a strong family history of early menopause may be at an increased risk of decline in fertility. Given the anticipated age-related decline in fertility, the increased incidence of disorders that impair fertility, and the higher risk of pregnancy loss, women older than 35 years should receive an expedited evaluation and undergo treatment after 6 months of failed attempts to conceive or earlier, if clinically indicated. In women older than 40 years, more immediate evaluation and treatment are warranted.
anniversary of Turkish Society of Menopause and Osteoporosis in 2017, we are continuously working on new projects for the awareness of menopause among women in Turkey.

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Parallel Session: Aging skin and hair

INV69
Over-the-counter antiaging products: Science and fiction
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Both the passage of time (intrinsic ageing) and chronic exposure to environmental insults (extrinsic ageing) induce changes in skin appearance, mechanical function and architecture. In the case of intrinsic ageing these clinical signs are associated with a generalised loss of dermal extracellular matrix (ECM) components including fibrillar collagens, elastic fibres and negatively charged oligosaccharides. In contrast extrinsically aged skin is characterised by the early loss of fibrillar-microfibrils from the papillary dermis and, in more severe cases, by the accumulation of dis-organised elastotic material known as solar elastosis.

Over-the-counter (OTC) topical formulations, which often target wrinkles, are widely employed as a strategy for preventing and/or repairing aged skin. It is clear that some topical formulations can exert an effect on dermal composition, skin architecture and the prevalence of wrinkles. However due to their cosmetic nature, evidence of their efficacy and mechanism of action is, in many cases, lacking. This presentation will review commonly found OTC ingredients and the evidence for their: efficacy, potential mechanisms of action and the importance of synergistic effects between ingredients. Finally in order to characterise both the effects of ageing and the efficacy of repair strategies it is important to understand skin composition. We have recently developed a systematic literature review-based approach to defining the human skin proteome and in this talk we will conclude by discussing the application of the Manchester Skin Proteome to dermatological conditions including ageing.

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INV70
Ultraviolet exposure and skin health
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In the last decades, the term “a healthy tan” has been firmly anchored in the minds of many people (primarily among Caucasians) and the wish to tan, imparting a sense of wellbeing, is omnipresent. In addition, there is a strong enthusiasm for prolonged outdoor activities and vacations in warm and sunny areas. The increased consumption of ultraviolet radiation (280–400 nm) by a population with primarily vulnerable skin has led to rising skin cancer rates. It is therefore not surprising, that the International Agency for Research on Cancer (IARC) has classified the ultraviolet radiation as a carcinogen. At the same time, the UV-B radiation (280–315 nm) initiates the vital vitamin D synthesis in the skin (optimum: 295–303 nm). There is a well-established relationship between the vitamin D status and musculoskeletal health. Against these contrasts, current issues relating to sun exposure and sun protection are discussed:

(1) effects of solar light on normal and diseased skin,
(2) mechanism of action of sunscreens,
(3) safety of sunscreens and
(4) sun exposure and sun protection in skin aging and skin cancer.

Practical recommendations for patient education are given.

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Plenary Session: Cancer prevention

INV71
Prevention of uterine and ovarian cancer
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General population screening for uterine cancer is not cost-effective. Screening of risk groups may be relevant, but prevention is largely restricted to reduction of risk factors.

Increased estrogen levels is a major endometrial cancer risk factor in overweight women, in women suffering from polycystic ovarian syndrome and women treated with postmenopausal unopposed estrogen. Other endocrine conditions may also increase the risk and recent data suggest that the increased risk of endometrial cancer may be related to childhood obesitas. In cancer prevention in these risk-groups, oral contraceptives or progestogen treatment e.g. with an IUD should be considered if weight loss is not successful.

Risk reducing hysterectomy in combination with total colectomy may be relevant in Lynch syndrome families.

Tamoxifen treatment in breast cancer patients increases the risk of endometrial cancer. Postmenopausal bleeding in these patients should be investigated by hysteroscopy.

Although screening for ovarian cancer has been investigated using biochemical markers as well as ultrasound, none have been effective in reducing mortality.

Hereditary ovarian cancer (e.g. BRCA mutations, Lynch syndrome, Cowden’s disease and Peutz-Jegher) is responsible for about 10% of cancer cases. In high risk families early bilateral salpingo-oophorectomy should be considered, although this strategy is associated with risks related to premature menopause e.g. cardiovascular disease and osteoporosis, and not all side effects are mitigated by add back hormone replacement therapy. Recently a strategy of early salpingectomy and delayed oophorectomy has been suggested.

The incidence of ovarian cancer is also reduced by pregnancy, lactation, the oral contraceptive pill and tubal ligation. Lifestyle factors may be important and risk may be reduced by avoiding overweight in childhood as well as in the adult and avoiding long-term use of hormonal replacement therapy.

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Parallel Session: Steroids and health in aging women

INV72

Prophylactic oophorectomy and long term health risk

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Prophylactic oophorectomy significantly reduces mortality in carriers of BRCA mutations and is recommended in women with a high risk of ovarian cancer as screening so far has not been effective. Oophorectomy substantially decreases the risk of death from ovarian cancer and also reduces the risk of death from breast-cancer when performed in pre-menopausal women.

Ovarian and breast cancer is most effectively prevented by early rather than late oophorectomy, preferably as soon as childbearing is completed.

However the ovaries are not only reproductive but also endocrine organs secreting steroids before as well as after menopause having impact on other organs. Oophorectomy before menopause increases the risk of coronary heart disease and cardiovascular death as well as osteoporosis and fractures and may also be associated with an increase in the prevalence of dementia and Parkinson disease. Observational studies indicate that oophorectomy especially in premenopausal women increase all cause mortality and at no age group is associated with a lower risk of other cause-specific or all-cause mortality in women not treated with estrogen.

The optimal age for oophorectomy in high risk women is a matter of debate, since osteoporosis and cardiovascular risk increases with earlier menopause whereas ovarian and breast cancer is more effectively prevented.

Recently a two-step procedure has been suggested delaying oophorectomy while performing early bilateral salpingectomy, as the distal fimbrial end of the fallopian tubes may be primary precursor of high-grade serous carcinoma and a reduced risk of ovarian cancer has been observed in women who have had bilateral salpingectomy and/or hysterectomy. The impact on the risk of breast cancer in these women is however unknown.

Based on theoretical speculations salpingectomy may also be recommended in women with low risk of ovarian cancer at the time of hysterectomy with benign indication.

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INV73

Individualized fracture risk prediction

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Fractures are a growing problem today and an urgent public health challenge due to the increasing proportion of older people and the increasing incidence of fractures. Osteoporotic fragility fractures are common in men as well as women. More than 50% of women and more than 25% of men aged older than 50 years will sustain a fragility fracture in their remaining lifetime. Moreover, it is clear that initial fragility fractures signal much increased risk of further fractures, and several studies support the relationship between major (proximal) fragility fractures and premature mortality. Subsequent fracture risk is highest in the first years after the initial fracture. Therefore, it is important to identify patients at high risk for fractures and subsequent fractures for whom treatment would be most effective.

Numerous risk factors have been identified for predicting fracture risk, independently of each other and of bone mineral density. Based on these risk factors, fracture risk assessment tools have been developed. Some tools are individualized and some are not, some tools take into account the changes of fracture risk over time and some do not, some tools are simpler due to their limited number of risk factors and others are more complex, and some tools do take into account fall risk factors and some do not. Due to the differences between the tools, it might be better to use a tool that contains the number of falls or fractures for one patient, while for another patient it might be better to use a tool that includes more risk factors.

In conclusion, patients are at highest risk for a re-fracture in the first years after their initial fracture. This indicates the need for immediate attention to prevent subsequent fracture. Patients at high risk for an initial fracture, can also be detected by using (one of the) fracture risk assessment tools. Multiple tools are clinically relevant for case-finding and easy to use in daily practice.

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INV74

CVD risk in BRCA mutation carriers

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BRCA1/2 mutation carriers are at high risk of breast and ovarian cancer. The number of studies on non-cancer endpoints in BRCA1/2 mutation carriers is still limited. BRCA1/2 mutation carriers may be at higher cardiovascular risk due to early menopause after risk-reducing salpingo-oophorectomy (RRSO) and/or due to the potential cardiotoxic effects of breast cancer treatment (radiotherapy/chemotherapy). Moreover, BRCA genes have a role as a gatekeeper in cardiac function and structure, which may affect susceptibility to cardiac damage. In this presentation we will provide an update of cardiovascular risk among BRCA1/2 mutation carriers and share our first data on cardiovascular measures in women after preventive RRSO.

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INV75

Identification of the high risk woman for cardiovascular disease

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Sex-specific factors related to hormonal and reproductive status are known to relate to CVD risk. It is unclear yet, to which extent and within which stage(s) of life these female-specific risk factors are relevant to CVD risk estimation in women. When considering all age-groups together, reproductive and pregnancy related disorders do not seem to be relevant in 10 years risk estimation. However, when focusing on younger patients (<55 years) evidence is increasing that assessment of female-specific risk factors may indeed add to identify women at higher risk. This is especially important as young women are considered to be at low risk, until a first premature event has occurred. Reproductive and pregnancy-related
Factors may predispose to earlier signs of endothelial dysfunction, vascular inflammation and atherosclerosis. This is less relevant for the older female population, having a higher prevalence of traditional risk factors with more advanced and more easily detectable atherosclerosis. It is to be expected that a combination of genetic risk together with (several) female-specific reproductive and non-traditional risk factors related to inflammatory diseases are more predictive in identifying women at high risk for premature CVD, than one or two single factors alone. The justified weighting of these various risk variables remains to be further investigated.

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INV76

The association between AMH and cardiovascular health after menopause

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Background: Menopause is associated with an increased risk of cardiovascular disease (CVD). Recently, there have been indications that premenopausal levels of anti-Müllerian hormone (AMH) are related to CVD risk factors and occurrence. With highly sensitive AMH assays, it has become possible to detect AMH in postmenopausal women. In this study, postmenopausal AMH levels were related to CVD risk factors.

Methods: This study included postmenopausal participants from the population-based Doetinchem Cohort Study. Women were invited for visits every 5 years, with a follow-up time of 20 years. Women were divided into categories based on their AMH level (picoAMH assay): <0.002 ng/mL, 0.002–0.01 ng/mL or >0.01 ng/mL. CVD risk factors were compared between these categories for each visit using linear regression, with correction for confounders.

Results: Data were available for 1,882 women, aged between 20–80 years. The proportion of women with detectable AMH levels ranged between 19–25% per visit and the detected AMH levels ranged between 0.002–12.3 ng/mL. After adjustment for age, body mass index, hormone use and smoking, AMH levels were not associated with blood pressure or total cholesterol levels, or total number of CVD risk factors.

Conclusion: Detectable levels of AMH in postmenopausal women are not associated with differing CVD risk factors. Further research is needed to investigate the implications of detectable AMH after menopause.

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INV77

Hormones and the heart, what’s new

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Animal studies from the late Tom Clarkson and his colleagues around 18 years ago gave rise to the concept of a “window of opportunity” for HRT to prevent CHD if initiated around the time of menopause. The failure of the Women’s Health Initiative (WHI) to show overall benefit of HRT on coronary heart disease (CHD) events obscures the fact that there was benefit from estrogen alone initiated below age 60 years in postmenopausal women. This finding is in agreement with large meta-analyses of randomised clinical trials of HRT which show that there is a reduction in CHD in women initiating HRT below age 60 years or within 10 years of the onset of menopause. Further support comes from newer randomised prospective clinical trials. In the Danish Osteoporosis Prevention Study (DOPS), HRT produced a significant reduction in a composite end-point of myocardial infarction, death or heart failure compared with no treatment. The ELITE study of the effects of HRT on carotid artery intima-media thickness in healthy postmenopausal women compared initiation of HRT within 6 years of menopause onset to initiation of HRT beyond 10 years postmenopause. The early starters showed a reduction in carotid artery atheroma progression with HRT compared with placebo, whilst no difference was seen between HRT and placebo effects in the late starters. Analyses from a national registry have shown that HRT reduces CHD mortality if initiated below age 60 years, whilst stopping HRT results in a transient increase in CHD mortality. This accumulating evidence supports the use of HRT for the primary prevention of CHD in postmenopausal women.

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Society Symposium: ISGE – Sex steroids impact in breast cancer and cardiovasculcar risk

INV78

Is HRT a cardiovascular risk for older women?

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Observational studies have usually shown a benefit of HRT for both primary and secondary prevention of CHD in postmenopausal women. However, randomised clinical trials of HRT have not shown any significant benefit on CHD in older women or in those with established disease. But in women initiating HRT at a younger age and closer to the onset of menopause, more recent studies have shown a benefit on CHD events, atheroma progression, and CHD mortality. Whilst these benefits in younger women have not been shown in older women, HRT has not been shown to cause CHD harm. In the Women’s Health Initiative (WHI) combined phases (intervention and cumulative follow-up), there was no significant increase in either CHD or stroke in those women initiating estrogen-progestogen or estrogen alone HRT above age 60 years compared with placebo. This is in accordance with large meta-analyses of randomised clinical trials of HRT effects on CHD events or mortality where no significant benefit, but also no harm, is seen in women initiating HRT above age 60 years or beyond 10 years after menopause. The lack of benefit in older women may well be the result of the use of inappropriately high starting doses of HRT. Adverse cardiovascular effects of estrogen, such as coagulation activation and adverse vascular remodelling, are dose-dependent effects, and could be avoided or minimised with lower starting doses. The ELITE study showed that the benefit of HRT seen in reducing atheroma progression in women initiating HRT soon after menopause was not seen in those initiating at a later age. But whilst there may be little benefit of HRT on established atheroma, there is evidence that older and diseased arteries can still respond favourably to estrogen in terms of function. HRT use in older women may not cause cardiovascular harm providing appropriately low starting doses are used and may even provide some benefit.

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Ask the Expert: Optimizing a healthy menopause: Diet and lifestyle.
Discussion of clinical cases

ATE1

Clinical case scenarios

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Case nr 1: PBSO after age 50: necessity and safety of MHT for bothersome complaints and prevention of longterm sequelae

A 57-year-old woman ‘Mrs M’ was referred to our clinic with complaints of extreme fatigue, depressed mood, headaches, vasomotor symptoms and total loss of vitality and libido.

Three years prior she had undergone preventive bilateral salpingo-oophorectomy (PBSO) after her mother died from ovarian cancer and her aunt died from breast cancer. Both were diagnosed after age 50. Postoperative estrogen suppletion was not considered optional by her caregivers. Unprepared for the consequences of the surgery, she was unable to work and developed feelings of insufficiency and regret. She had also developed osteopenia, high cholesterol, chronic migranes and analgesic-overuse and was referred for assessment and further treatment.

Relevant findings at first assessment: G2P2; BMI 21.9 kg/m²; BP 110/70 mmHg; glucose 5.9 mmol/L, total cholesterol 6.2 mmol/L, LDL-cholesterol 4.2 mmol/L. Otherwise normal results.

Medications: triptans, antihypertensives, vitamin, Calcium and magnesium tablets.

Greene Climacteric scale score: 33; CES-D (measure for depression) score: 52; MIDAS (migraine disability) score: 67

Questions:
1. What would be optimal aftercare for Mrs M with regard to her physical, mental, psychosexual and bone health?
2. What non-hormonal options would be appropriate?
3. What kind of follow up would be advisable until what age?

Case nr 2: Coronary artery disease after laparoscopic sterilization at age 34 and subsequent untreated POI in an obese woman with unhealthy lifestyle and family history positive for acute deaths

A 59-year-old woman Mrs V was referred because of persistent vasomotor complaints ever since laparoscopic sterilization at age 34. Her periods stopped shortly afterwards and she was diagnosed with premature ovarian insufficiency (POI) when trying to conceive a pregnancy for her younger sister of 2 years who also had POI. Mrs V also complained of mood swings, constipation, uterine myomas, overactive bladder signs and vulvar lichen sclerosis. She was a vegetarian and did not exercise.

The procedure was complicated by massive bleeding in the left groin. She recovered, and almost all her unexplained symptoms disappeared. She refused to join the cardiac rehab exercise group, although she managed to reduce smoking to 5 cigarettes a day.

Clinical course: Mrs V was seen by the cardiologist and upon catheterization (percutaneous coronary intervention) 5 stents were placed and lifelong use of anticoagulants and statins was advised. The procedure was complicated by massive bleeding in the left groin. She recovered, and almost all her unexplained symptoms disappeared. She refused to join the cardiac rehab exercise group, although she managed to reduce smoking to 5 cigarettes a day.

Questions:
1. Is Mrs V a candidate for MHT for persistent vasomotor symptoms and what would be the best choice and for how long?
2. What would be the best approach to motivate her to adhere to screening and exercise programs and lose weight?

Case nr 3: Obesity and vegetarian lifestyle in a 48-years old perimenopausal woman: strategies to manage vasomotor and urogenital symptoms and prevent development of cardiovascular complications

A 48-year-old woman Mrs B was referred for irregular bleeding, and vasomotor complaints. She was overweight, had hypertension, constipation, uterine myomas, overactive bladder signs and vulvar lichen sclerosis. She was a vegetarian and did not exercise.

For treatment of lichen sclerosis and uterine myomas, removal of endometrial polyps, and insertion of a Mirena IUD, her vasomotor symptoms became more bothersome and her weight increased. She consulted the dietician and started a regimen low on carbohydrates and more wholesome on proteins and multivitamins. Upon weight loss most of her complaints were reduced and additional treatment for her vasomotor symptoms, overactive bladder or high blood pressure was no longer necessary.

Relevant findings at intake: G3P3; BMI 31.1 kg/m²; BP 140/100 mmHg
Result after 6 months: BMI 28 kg/m² and BP 140/90 mmHg

Questions:
1. Does Mrs B have cardiovascular risk factors of concern?
2. Does lichen sclerosis play a role in her cardiovascular risk profile?
3. What would be the best approach to motivate Mrs B to adhere to the diet and exercise program and prevent cardiovascular complications

Case nr 4: Undiagnosed secondary amenorrhea in a 49-years old woman with sedentary lifestyle who developed urogenital syndrome and osteopenia: how to improve QoL and urogenital and bone health

A 49-year-old nulliparous women Mrs G consulted the gynaecologist because of vasomotor symptoms, recurrent bladder infections and dyspareunia. Her periods stopped at age 43 but the menopausal and urogenital complaints started just two years ago. She was normotensive, did not exercise regularly and was recovering after 2 years treatment for ‘burn-out’. Her mother’s menopause occurred at an early age.

Relevant findings at intake: G0P0; BMI 21.6 kg/m²; BP 110/75 mmHg.

Medications: Nitrofurantoine maintenance for chronic cystitis

BMD Lumbar spine: 0.804 g/cm² with T-score −1.5 and Z-score −1.1.
BMD hip: 0.689 g/cm² with T-score −1.5 and Z-score −0.8; suggestive of WHO osteopenia.

She started transdermal Estradiol suppletion combined with oral progesterins at 3-months intervals and weekly vaginal estriol applications, also regular exercise.

Repeat BMD after 6 years showed improvement of bone density and her urogenital complaints no longer needed maintenance antibiotics.

Questions:
1. Is treatment indicated for secondary amenorrhea? What are the risks of untreated secondary amenorrhea?
2. Is local treatment of urogenital syndrome preferred over systemic hormone therapy? Can these be safely combined?
3. What would be the best approach for osteoporosis prevention in this case?

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ATE2

Clinical case scenarios

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Case 1:
52 year old woman – yearly check up – at the end of the consultation she asks whether it is normal at her age that she has no more interest in sex. … if it were not for her husband … he has started to look at pornography in the Internet.
Threat to the longstanding relationship,
How to help the woman regain some pleasure in her sexual life and help the couple to re-establish their sexuality.

Case 2:
49 year old woman, II Grav, II Para complains about “bladder problem” and some burning sensation in the urethra. Uethral swabs show chlamydia. She reports having had an extramarital affair. Her husband suffers from erectile dysfunction and they had no more intercourse for a long time.

How to manage the issue of STI and the ED of the husband.

Case 3:
68 year old patient presents after a long period of not showing up for checkups. The gynaecological exam reveals a high grade atrophy of the vaginal mucosa and some lichen at the vulva. Since many years she suffers from dyspareunia which she did hide from her husband out of fear that he may be offended.

How to help this woman to restore her sexual health

Case 4:
61 year old patient, widow, BMI 33 kg/m² presents with prolapse of the uterus. She felt ashamed and did not consult a doctor being afraid of operations. She is convinced that she has some form of cancer. Now she has a new partner and wants to have an intimate relationship with him. She is terrified by the thought that he might see her “intimate parts”.

How can we help the woman and how can we prevent the loss of sexual function and promote sexual health in middle aged women.

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ATE3

Clinical case scenarios

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Case 1 – Memory Problem
• A 50-year-old, married woman presents for her annual gynecological exam. She is generally healthy and takes no medications.
• She recently began experiencing mild hot flashes but is not bothered by them.
• Her main complaint is that she is forgetful at work and in social situations. She works in marketing and during a presentation, she could not remember the name of one of her former clients. At a work picnic, she also forgot the name of her co-worker’s husband though she did remember it later, after she returned home.
• Her mother has Alzheimer’s disease and she worries about whether she, too, might be getting dementia.
• Further discussion indicates that while she is embarrassed and worried about her memory lapses, she still is fully capable of carrying out her work-related responsibilities.
• There is no history of early onset AD in her family. Her mother was diagnosed with AD when she was 75 years old.

Case 2 – Depressive Symptoms
• Deanne is a 48-year-old woman. During her annual exam, she said her periods are not as regular as they used to be but she had not skipped any periods.
• She had a few episodes of night sweats and can get very hot and sweaty at work which she finds embarrassing.
• Her BMI is 33 and she has mild hypertension that is effectively controlled with amlodipine. Otherwise she is in good health.
• She said that she has felt sad a lot lately, has had trouble sleeping, and has withdrawn from her friends.
• These symptoms have affected her ability to maintain relationships and function at work as a corporate lawyer. She has a very demanding, high stress job and has struggled with significant feelings of worthlessness and shame due to her inability to perform as well as she always has in the past. She has missed work because she has difficulty getting out of bed after not sleeping well. She feels her reputation at work is at stake.
• Her mood worsened when she divorced a year ago.
• She reported feeling depressed for several months after the birth of her first son but she was unsure if that was due to fatigue or “true” depression.
• She said that she often wondered if her mother had depression but was not sure.
• She said she never received counseling or pharmacological treatment for these symptoms.

Case 3 – Premature Menopause
• Vienna is a 38-year-old woman with primary ovarian insufficiency. Her final menstrual period was 12 months ago. Her mother also went through menopause early.
• She has occasional mild hot flashes, but is not bothered by them.
• Her BMI is 32, but otherwise she is in good health.
• At her annual exam, she complains of memory problems and irritability.
• As a working mother of a 8-year-old, she finds that she cannot remember the names of the other parents and children in her son’s class though she has met them on multiple occasions. She can cover this up socially, but her memory is definitely not as good as it used to be. She is concerned that this change in memory might mean that she might be vulnerable to dementia, which her grandmother had before her death.
• She asks you whether this might be related to her going through menopause earlier than other women.

Case 4 – Breast Cancer and Hormone Therapy
• Jenny is a 48-year-old woman with a history of DCIS. Biopsy showed a high-grade, ER+, PR+ DCIS. She was treated with surgery, 6 weeks of radiation therapy, and tamoxifen.
• She has daily moderate to severe hot flashes. She is severely bothered by them—they disrupt her sleep, are socially embarrassing, and don’t seem to be improving.
• What guidance do you give her on treating her hot flashes?

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Clinical case scenarios

Alessandra Graziotinn

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Case 1. Clara, 52 years old, 7 years postmenopausal. She has never used menopausal hormone therapy because of fear of breast cancer. She suffers from vaginal dryness and dyspareunia. She has celiac disease and she is vegan. She does not wish to use vaginal gels or tablets, as she is not comfortable with them. Her doctor prescribed her ospemiphene. Initially she was very happy with her medication. Later, however, she began to experience leg cramps.

Case 2. Maria, 42 years old has undergone hysterectomy and bilateral oophorectomy after the diagnosis of endometrial cancer. She does not wish to receive hormone therapy because of fear of disease recurrence. Her mother has sustained a hip fracture at the age of 78 years. She is concerned about her own risk of fracture.

Case 3. Elena, 48 years old, perimenopausal. She has irregular cycles, occasionally with heavy bleeding. She has no family of breast cancer. She drinks one to two glasses of wine with her dinner every day. When she is with friends, she may have some more wine. Her mammogram reveals high density, ACR IV.

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Ask the Expert: A personalized approach to Menopausal Hormone Therapy: Discussion of clinical cases

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I – A 58-year-old postmenopausal patient (LMP was at age 52) presents with complaints of bothersome hot flashes and day time fatigue. Her last menstrual period occurred at age 52. The patient was diagnosed with type 2 diabetes mellitus at age 56 and is taking metformin. Recent HbA1c level was 6.8%. She was initiated on an angiotensin-converting enzyme inhibitor for renal protection. BP in office is 130/80 mm Hg. Patient wishes to discuss menopausal hormone therapy for management of vasomotor symptoms. This case should generate discussion on individualizing management based on patient’s risk profile.

II – A 38-year-old patient who is known BRCA1 mutation carrier (diagnosed on screening for a strong family history of breast and ovarian cancer) recently underwent a prophylactic risk reducing bilateral salpingo-oophorectomy. She is now experiencing severe vasomotor symptoms and poor sleep and these symptoms are affecting her quality of life. Her primary care provider and oncologist have strongly advised her against use of menopausal hormones. A trial of Venlafaxine has not provided much relief. This case should generate discussion on safety of menopausal hormones in BRCA mutation carriers and management options.

III – A 58-year-old otherwise healthy although overweight postmenopausal woman (BMI 29 kg/m²) presents with complaint of severe “drenching” hot flushes that have progressively worsened over the past year; she stopped menstruating at age 52 and has been using low dose transdermal estrogen (with cyclic progesterone) without much improvement in her symptoms. She is now seeking a second opinion in the hope that you will increase her dose of estrogen to help with her symptoms. This case should generate discussion on differential diagnoses of “menopause like symptoms”.

IV – 48-year-old menopausal patient is experiencing bothersome vasomotor symptoms and poor sleep. She is otherwise healthy and physically active. Past history is significant for wrist fracture at age 44 following a fall. Family history is significant for osteoporosis (maternal grandmother) and breast cancer (mother at age 58). Patient is particularly anxious regarding possibility of height loss (similar to her maternal grandmother), but is even more concerned about her risk for breast cancer given maternal history of breast cancer at age 58. How do you counsel this patient and what management options are available to address patient’s concerns and minimize future risk?

V – A 58-year-old postmenopausal woman seeking consultation for bothersome and progressive thinning of scalp hair. Menopause was at age 53. She has tried multiple hair products without any benefit, and her symptom is now affecting the quality of her life. She denies any hot flushes or night sweats, acknowledges progressive weight gain, particularly noticeable since her menses stopped. Her BMI is 32 kg/m². Examination reveals evidence of acanthosis nigricans, central obesity and evidence of moderate severity hair loss predominantly affecting the caput. This case should generate discussion on prevalence of hair loss related bother in aging women, differential diagnoses of hair loss in women and management options.

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Clinical case scenarios

Mark Brincat

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Case #1

George a 57 year old Surgeon has operated skilfully for years. He is now feeling lethargic, lacks concentration and feels that he is mentally drifting. He is not walking as briskly as he used to and feels an unnatural muscular fatigue and joint pains. He is also having problems with erectile function and has lost his early morning erections. He has lost his desire to exercise having been normally slimmer and fit. He is also developing and ever expanding waistline despite his best efforts and is for the first time in his adult life putting on weight.

He has visited numerous physicians, including cardiologists, and has been pronounced healthy for his age. His slightly raised blood pressure has been successfully controlled with a diuretic.

The only finding of note is his raised FSH in excess of 15 IU/ml and low serum testosterone at 10 μmol/l (note range 40–100 μ/l). He has therefore been referred to an endocrine clinic for advice, investigation, management and treatment.

Case #2

Gladys, a 75 year old has just sustained her second Colles fracture. She has got progressively shorter over the years and complains of persistent backache. She also complains of muscle stiffness. She had a TAH & BSO for an ovarian mass at the age of 37. She never had oestrogen replacement. For years she complained of hot flushes, vaginal dryness and discomfort but was treated topically for the latter, and told she will grow out of hot flushes. She is a slim
and tall Caucasian who retired from work as a teacher in her 60’s. She has recently been widowed and has no children.

At assessment, she was found to be osteoporotic with a vertebral and her femoral neck bone mass being below 2.5 centile of the mean.

She is otherwise fit, has no history of breast cancer, and has no significant medical problems.

What options would you consider in the management of this patient? Her primary concern is that she recovers from her fracture and improves her mobility.

**Case #3**

Corinne, 55 year old had a ductal carcinoma in situ (DCS) diagnosed at the age of 40 in her right breast and subsequently had a mastectomy and an axillary node dissection. Her axillary nodes were negative. She received radiotherapy and was on Tamoxifen for five years. Follow up at 51 revealed a small recurrence and this was once again treated surgically and with radiotherapy. This time she was put on an Aromatase Inhibitors coupled with a surgical menopause (TAH and BSO).

She has complete aversion to sex and as a result of her dyspareunia, and additionally a loss of libido. She finds it difficult to have sexual intercourse with her as yet fit husband.

She has come to you asking for relief and management of her symptoms.

**Case #4**

Phyllis is a 60 year old who had a late menopause at the age of 57 years. She subsequently had episodes of postmenopausal bleeding and hysteroscopy and D&C showed cystic hyperplasia. Phyllis has a high BMI of 38, is hypertensive and has a tendency to hyperinsulinism. She was found to be hypertensive at her pre-operative assessment and put on anti-hypertensives. It was decided to carry out a TAH and BSO. Post surgery, she complained of dry skin, itching, vulval dryness and frequency and dysuria. She also complained of hot flushes for the first time ever. She also complains of joint pains, anxiety and lack of concentration. She has no significant family history and is asking for relief of her symptoms.

**Discussion of clinical cases**

Juan Blümel

*Universidad de Chile, Medicine, Santiago, Chile*

**Background:** Vasomotor symptoms are common during menopause and perimenopause; however, in some women, it may appear at earlier ages.

**Chief complaint:** A 42-year-old woman with normal menstrual flow who has hot flushes and depressive mood.

**Questions:** Can she be a woman with climacteric symptoms or thyroid dysfunction? Can the symptoms be adverse drug effects or tumors? Are there other diagnostic options? List what you would like to know about her medical history, physical exam and laboratory and imaging diagnosis exams. What would be your treatment? What do the clinical guidelines say about the use of estrogen in women with regular menstrual periods?

**Conclusions:** Climacteric symptoms are frequent before menopause. A therapeutic test with transdermal estradiol should be attempted if symptoms impair the quality of life. Evaluate lifestyles and cardiovascular risk. We need a position statement of the scientific societies on this subject.

http://dx.doi.org/10.1016/j.maturitas.2017.03.086

**ATE7**

**Clinical case scenarios**

Mary Ann Lumsden

*University of Glasgow, Glasgow, United Kingdom*

**Case #1 Premature Ovarian Insufficiency.**

A 23 year old girl from Iran presented to the Outpatients Clinic with amenorrhoea of 10 months duration. She had a regular cycle prior to this. She complained of some hot flushings on close questioning otherwise was asymptomatic. She was engaged to be married.

On investigation her FSH was 26IU/L and LH 18IU/L. Her oestradiol was <70IU/L.

The case aims to discuss future management:

1. Repeat gonadotropin assessment
2. initial focus on fertility
3. Hormone replacement
4. Long term consequences.

Her fear was that her fiancée would leave her but he said he would support her. She rejected ovum donation and HRT was then started. She will be regularly reviewed.

**Case #2 65 year old at high risk of cardiovascular disease.**

This patient attended the clinic complaining of severe hot flushings and sweats that were intolerable. She had been on HRT until 18 months previously but had been stopped by her GP because of her age. She had hypertension and was on an anti hypertensive and a statin. She was very overweight but did not have T2DM. She was desperate to restart her HRT.

Issues for discussion.

1. Current data for women starting HRT at 65 but unknown impact of having been on it before.
2. Impact of symptoms of QoL and why so important.
3. Risk of MI, CVD episode and stroke
4. Transdermal versus oral

**Case # 3 Perimenopausal Bleeding**

A 48 year old African-American woman presents with heavy menstrual bleeding. Her periods last 7 to 10 days and are heavy for 3 with flooding and clots. She cannot leave the house. She has also had a previous myomectomy. She wishes to avoid surgery if possible. She has tried mefenamic acid and tranexamic acid without success. On examination the uterus is enlarged to 18 weeks size and ultrasound confirms the presence of at least 6 fibroids, the largest 8 cm in diameter and anteriorly. She has no menopausal symptoms as such.

Issues for discussion are the possible treatment options.

- NOT Mirena
- Uterine Artery Embolisation
- Ulipristal acetate
- MRgHIFU

Case # 4 Severe dyspareunia in a 35 year old who has breast cancer. She had a lumpectomy followed by radiotherapy 2 years previously and is currently on aromatase inhibitor. She also has severe joint pains and is feeling very low as a result.

http://dx.doi.org/10.1016/j.maturitas.2017.03.085
Issues for discussion.
Impact and importance of symptoms.
Full history.
Physiology
Possible treatment options – lubricants, moisturisers, etc
Change to tamoxifen.
Local oestrogen treatment.

http://dx.doi.org/10.1016/j.maturitas.2017.03.087

ATE8
Clinical case scenarios
Susan Davis
Monash University, Melbourne, Australia

Case #1
A 54 year old had the menopause 2 years ago and is now concerned about her flushes and her bones.
Her mother and maternal aunt were diagnosed with breast cancer in their 70s and her mother had a hip fracture at 65 and has bad kyphosis She is worried about the risk of breast cancer if she takes HRT but also about the risk of developing osteoporosis. Mammogram 2016 unremarkable
How would you advise and manage her?

Case #2
A 49 year old woman went through menopause 2 yrs ago.
Been seeing a GP who has been prescribing compounded hormone therapy.
She has a syringe containing progesterone and uses a metered dose ea day according to the "Wiley protocol" She is using a biest lozenge and another cream containing DHEA and testosterone.
She has come to see you as another GP has questioned her use of these medications and referred her to you. She is having night sweats. She hands you the results of the salivary tests she has had performed and seeks your opinion on her medication, the test results and the doses.

http://dx.doi.org/10.1016/j.maturitas.2017.03.088

Ask the Expert: How should employers treat menopausal women? Discussion of cases

ATE9
Cases scenarios
Martin Birkhäuser
Universitäts Frauenklinik, Bern, Switzerland

Case 1
Hot flushes provoked by client contact
A 52 years old female bank employee gets hot flushes as soon as a client approaches her desk. The phenomenon started 3 months ago. She panics more and more, just by thinking at her next client.

Case 2
Climacteric depression
A lawyer observes a progressive mood change in one of his assistants, a pretty married female bachelor of law, 54 years old. She looks sad, what is new for him. He fears a depression. What should/can he do?

Case 3
Pollakisuria at work
A 61 years old otherwise reliable female supermarket cashier leaves her box more and more frequently to go to the restroom, without explanation to the manager. Clients start to complain.

http://dx.doi.org/10.1016/j.maturitas.2017.03.089

ATE10
Case scenarios
Marije Geukes
Reinier de Graaf Gasthuis, Delft, The Netherlands

Poor concentration: The past few months a 52 years old female human resource manager has been struggling to keep her attention during performance interviews with employees. If she could only have a good night rest, as to regain her focus at work.

http://dx.doi.org/10.1016/j.maturitas.2017.03.090

ATE11
Case scenarios
Henk Franke
Franke Consultancy Holding BV, Enschede, The Netherlands

Case 1
A 50 year old woman works in a pastry factory. She suffers of frequent hot flushes which results in excessive sweetening. Her employer fires her because of this unhygienic situation.

Case 2
A 48 year old female teacher became indecisive and depressed lately. She also suffered of menopausal symptoms. Her general practitioner thinks she suffers of dejection and advised her to take Seroxat and report herself sick.

http://dx.doi.org/10.1016/j.maturitas.2017.03.091

ATE12
Case scenarios
Herman Depypere
Ghent University, Ghent, Belgium

Everything came at the same time for Nathalie, her long awaited appointment as head of the department and her vasomotor symptoms. How to tackle both challenges?

http://dx.doi.org/10.1016/j.maturitas.2017.03.092

Ask the Expert: Non-HRT, alternative and complementary therapies for menopause: Discussion of clinical cases

ATE13
Clinical case scenarios
Amos Pines
Tel-Aviv, Israel

Case 1
A 52-year healthy woman. Cessation of periods since one year. Suffers from 5-7 hot flushes during the day and once every night.
She says that life suddenly seems less joyful and she feels less energetic. She is working in a bank and she claims the hot flushes cause embarrassment in front of clients and colleagues. She wants to get rid of this misery. Her physician rightfully suggested to try HT. She said she heard about hormones, but is afraid of taking it because friends told her that this might be risky. She already tried some herbal products, which were not effective enough. She asked whether there are alternative medications with proven effects.

**Case 2**

A 62-year healthy woman. Cessation of periods ten years ago. Feels well, but suffers from vaginal itching, unpleasant irritation and some discharge. She has a lovely partner, but had to reduce the frequency of sex because of painful intercourse. Her physician suggested to try HRT, local or systemic. She refused because her mother and aunt had breast cancer. She tested negative for BRCA. She thought the best for her would be a non-hormonal therapy, but was not sure whether she would feel comfortable with the local administration of a cream. She returned a year later. She tried lubricants but hated the texture.

http://dx.doi.org/10.1016/j.maturitas.2017.03.093

**ATE15**

**Clinical case scenarios**

Margaret Rees

*University of Oxford, Oxford, United Kingdom*

A 45 year old woman asks advice about how her vaginal dryness can be dealt with. She has no hot flushes. What would you recommend?

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**ATE16**

**Clinical case scenarios**

Petra Stute

*Inselspital Bern, Bern, Switzerland*

1) 55-year old breast cancer survivor treated with aromatase inhibitors suffering from severe hot flushes.
2) 60-year old postmenopausal woman with severe vaginal dryness and dyspareunia but not wanting hormone therapy.
3) 50-year old perimenopausal woman presenting with depressive symptoms, hot flushes and sleep disturbances, not wanting hormone therapy.
4) 55-year old breast cancer survivor treated with aromatase inhibitors suffering from arthralgia.

http://dx.doi.org/10.1016/j.maturitas.2017.03.096

**ATE17**

**Clinical case scenarios**

Sonia Cerdas

*Clínica San Agustin, San José, Costa Rica*

**Case N 1**

- V.C. 52 years old presents with complaints of hot flushes and night sweats, 14–20/day, over the past 10 months. Her last period was one year ago.
- She reports progressive fatigue and poor sleep quality. She suspended her exercise routine and she gained seven kilograms of weight.
- Her gynecologist contraindicated the HRT use because her medical history of thrombophilia.
- She reports a history of recurrent miscarriages and at age of 35 she suffered a deep venous thrombosis with no obvious precipitating cause.
- A thrombophilia screening panel was performed documenting protein C deficiency and heterozygous mutation for factor V of Leiden and MTHFR.
- She has since been treated with folic acid and low doses of aspirin and does not want to take any other medication.

**Case N 2**

L.P. 45 years old presents with complaints of intense and frequent hot flushes and night sweats.

She reports feelings of hopelessness since her last period 2 years ago, when she started chemotherapy, followed by radiotherapy after left lumpectomy for Estrogen Receptor Positive Breast Cancer.

Medication: She is under treatment with tamoxifen.

Physical examination: excellent general health condition.

Laboratory: Normal laboratory results.

**Case N 3**

P.O. 65 years old presents with complaints of vaginal dryness and frequent urinary infections.

The symptoms have worsened during the last year. She tried using vaginal lubricants with poor results.

She was sexual active, but has progressively lost her sexual drive, with vaginal dryness and low libido.

Physical examination: severe vaginal and vulvar atrophy.

Laboratory: normal laboratory general results.

**Case N 4**

A.M. 62 years old was concerned about the diagnosis of osteopenia that was reported in a densitometry exam.
(spine 0.869 g/cm² (T-score −1.5) and, left hip 0.735 g/cm² (T-score −1.7) and neck 0.602 (T-score −2.3).

She has no personal or family history of fractures and reports asymptomatic menopause at 52 years old and she didn’t receive HRT.

She eats healthy, does not smoke, does not drink more than 3 alcoholic drinks per week and exercises regularly.

Medication: none

Physical examination: normal physical examination.

http://dx.doi.org/10.1016/j.maturitas.2017.03.097

Ask the Expert: GSM and the menopause: Counseling, drugs and lasers. Discussion of clinical cases

ATE18

Clinical case scenarios

Rosella Nappi

University of Pavia, Pavia, Italy

Julia, Breast cancer survivor, 47 yrs of age with severe dyspareunia.

Maria, 45 yrs of age, premature menopause on MHT with rUTIs.

Greta, 49 yrs of age, surgical menopause with female sexual dysfunction.

Gloria, 56 yrs of age, natural menopause with vaginal dryness.

http://dx.doi.org/10.1016/j.maturitas.2017.03.098

ATE19

Lasers in the treatment of genitourinary syndrome of menopause

Ivan Fistonič

Institute for Womens Health, Zagreb, Croatia

Genitourinary Syndrome of Menopause (GSM) stands for the variety of menopausal symptoms associated with physical changes of the vulva, vagina, and lower urinary tract, related with estrogen deficiency and process of ageing as well. GSM is chronic and is likely to worsen over time, affecting up to 50% of postmenopausal women. Local vaginal estrogen administration is the treatment of choice for vulvovaginal atrophy, although lacking long time efficacy and safety. However, many women do not accept local hormonal therapy or have absolute contraindications, such as a personal history of estrogen-dependent tumors, particularly endometrial and breast cancer.

Recently, results from studies that employ laser energy in the therapy of GSM, incontinence, vaginal distension syndrome and consequent reduced sexual performance. Micro-ablative carbon dioxide (CO₂) laser induced a significant improvement of vaginal health in postmenopausal women improving dyspareunia related to vulvovaginal atrophy and sexual global performance as well. Simultaneously, non-ablative, thermal-only SMOOTH-mode erbium YAG laser pulses are used to produce vaginal collagen hyperthermia, followed by collagen remodeling and the synthesis of new collagen fibers, resulting in improved vaginal tissue tightness and elasticity. This erbium laser technology is used for treatments of vaginal laxity, stress urinary incontinence, pelvic organ prolapse and vaginal atrophy. Several clinical studies covering all four indications were conducted with the aim to prove the efficacy and safety of this novel technology. The results have shown that SMOOTH-mode erbium laser seems to be an effective and safe method for treating vaginal laxity, stress urinary incontinence, pelvic organ prolapses and vaginal atrophy. Breast cancer survivors frequently face serious difficulties in their sexuality due to GSM. Laser thermotherapy has shown high level of effectiveness in those who were not able to use local hormonal therapy.

http://dx.doi.org/10.1016/j.maturitas.2017.03.326

EMAS Junior Mentorship Programme

Jump01

Effects of a new vaginal cream containing visnadine, prenylflavonoids and bovine colostrum on Vaginal Health Index Score and Female Sexual Function Index in post-menopausal sexually active women affected by vaginal dryness: A pilot study

Antonio Simone Lagana1,*, Francesca Basile1, Lily Stojanovska2, Vasso Apostolopoulos2, Salvatore Giovanni Vitale1, Rosario D’Anna1

1 University of Messina, Unit of Gynecology and Obstetrics, Department of Human Pathology in Adulthood and Childhood 'G. Barresi', Messina, Italy
2 Victoria University, Centre for Chronic Disease, College of Health and Biomedicine, Melbourne, Australia

Objective: To evaluate the effects of a new vaginal cream containing visnadine (0.30%), prenylflavonoids (0.10%) and bovine colostrum (1%) on Vaginal Health Index Score (VHIS) and Female Sexual Function Index (FSFI) in post-menopausal sexually active women affected by vaginal dryness.

Patients and methods: We performed a prospective pilot study, enrolling 15 post-menopausal sexually active women affected by vaginal dryness. The mean age of participants was 56.8 ± 4.6 years with parity mean 1.6 ± 1. All women gave consent and underwent VHIS evaluation and FSFI test. Following baseline evaluation, women underwent 15 days of vaginal treatment with one application per day of the new vaginal cream. Following treatment, women were evaluated again using the same methods of the pre-treatment phase.

Results: Following treatment there was significant improvement in elasticity (p = 0.03), fluid secretion type and consistency (p = 0.01), pH (p < 0.03), epithelization of vaginal mucosa (p = 0.04), moisture (p = 0.04) and total VHIS (p = 0.0001). Similarly, after the treatment there was also a significant improvement of lubrication (p = 0.01), orgasm (p = 0.01), satisfaction (p = 0.02), pain (p = 0.03) and total FSFI score (p = 0.004). No significant differences regarding desire (p = 0.57) and arousal (p = 0.61) were found. None of the women reported any local or systemic side effect during the treatment.

Conclusion: We demonstrated a significant improvement of both VHIS and FSFI score in post-menopausal sexually active women after a treatment with vaginal cream containing visnadine, prenylflavonoids and bovine colostrum. Given that our results are based on a pilot study, we postulate that the treatment with this new vaginal cream may significantly reduce vaginal dryness in post-menopausal women and improve their sexual wellbeing.

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She eats healthy, does not smoke, does not drink more than 3 alcoholic drinks per week and exercises regularly.

Medication: none

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EMAS Junior Mentorship Programme

Jump01

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Antonio Simone Lagana1*, Francesca Basile1, Lily Stojanovska2, Vasso Apostolopoulos2, Salvatore Giovanni Vitale1, Rosario D’Anna1

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Conclusion: We demonstrated a significant improvement of both VHIS and FSFI score in post-menopausal sexually active women after a treatment with vaginal cream containing visnadine, prenylflavonoids and bovine colostrum. Given that our results are based on a pilot study, we postulate that the treatment with this new vaginal cream may significantly reduce vaginal dryness in post-menopausal women and improve their sexual wellbeing.

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Evaluation of sexual function in mid-aged Ecuadorian women using the six-item Female Sexual Function Index

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2 Institute of Biomedicine, Facultad de Medicina, Universidad Católica de Santiago de Guayaquil, Guayaquil, Ecuador
3 University of Zaragoza, Faculty of Medicine, Zaragoza, Spain

Objective: To assess sexual function and related factors (including metabolic ones) in a sample of mid-aged women.

Methods: In this cross-sectional study, 202 urban-living women from Guayaquil (Ecuador), 40–69 years, were surveyed with the six-item version of the Female Sexual Function Index (FSFI-6) and a questionnaire containing personal and partner data. In addition, abdominal circumference and serum metabolic parameters were assessed.

Results: The median age of the sample was 50 years, 56.9% were postmenopausal, 5.9% used hormone therapy, 3% psychotropic drugs, 36.6% had hypertension, 4.5% hyperglycemia, 50% abdominal obesity, 17.3% had the metabolic syndrome (METS) and 67.3% had a partner (n = 136). Overall, 38.6% (78/202) of surveyed women were sexually active, presenting a median total FSFI-6 score of 19.0. Lower total FSFI-6 scores were associated to several factors such as age, educational level, menopausal status and coital frequency (bivariate analysis); while no association was found with the presence of the METS or its components. Multiple linear regression analysis found that higher total FSFI-6 scores, indicating better sexual function, of androgen supplementation (per os, transvaginal testosterone; dehydroepiandrosterone sulfate (DHEA-S); tibolone] on HSDD in postmenopausal women and to meta-analyse data from randomized controlled trials asking this specific research question.

Methods: PubMed, EMBASE and Cochrane electronic databases were comprehensively searched from conception until December 2016. Six RCTs fulfilled the inclusion criteria and were included in the meta-analysis. Data extraction and risk of bias assessment was performed in duplicate for each study. Three scales of Female Sexual Function Index (FSFI) [FSFI-(D)esire, FSFI-(A)rousal, FSFI-(T)otal] were used to quantify HSDD. The random effect model was applied. Meta-analysis was conducted by R Studio for Mac (version 1.0.44).

Results: Androgen supplementation resulted in increase in FSFI-D [mean difference (MD) 1.01, 95% confidence interval (CI) 0.42–1.60, p < 0.001, heterogeneity (I²) 90.5%], FSFI-A (MD 1.00, 95% CI 0.74–1.26, p < 0.001, I² 0%) and FSFI-T (MD 3.45, 95% CI −1.73 to 8.63, p > 0.05, I² 94.5%). Publication bias, sensitivity analysis, subgroup analysis (according to type of menopause and type of androgen) and meta-regression (moderators: age, years since menopause, body mass index, dosage of androgen) techniques were used to explain heterogeneity among studies.

Conclusions: Androgen supplementation results in improved HSDD parameters. Therefore, it should be considered in the treatment of postmenopausal women with HSDD.

This study has been conducted in the frame of EMAS mentoring program (JuMP).

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Androgen supplementation for hypoactive sexual desire disorder in postmenopausal women: A systematic review and meta-analysis

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2 Aristotle University of Thessaloniki, Unit of Reproductive Endocrinology, First Department of Obstetrics and Gynecology, Thessaloniki, Greece
3 Poznan University of Medical Sciences, Department of Gynecological Endocrinology, Poznan, Poland

Context: Postmenopausal period has been associated with increased prevalence of Hypoactive Sexual Desire Disorder (HSDD). Although androgen supplementation, on top of estrogen replacement therapy (ERT), has been proposed as possible treatment for HSDD, data are conflicting.

Objective: To evaluate the best available evidence concerning the effect of androgen supplementation (per os, transvaginal testosterone; dehydroepiandrosterone sulfate (DHEA-S); tibolone] on HSDD in postmenopausal women and to meta-analyse data from randomized controlled trials asking this specific research question.

Methods: PubMed, EMBASE and Cochrane electronic databases were comprehensively searched from conception until December 2016. Six RCTs fulfilled the inclusion criteria and were included in the meta-analysis. Data extraction and risk of bias assessment was performed in duplicate for each study. Three scales of Female Sexual Function Index (FSFI) [FSFI-(D)esire, FSFI-(A)rousal, FSFI-(T)otal] were used to quantify HSDD. The random effect model was applied. Meta-analysis was conducted by R Studio for Mac (version 1.0.44).

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Parathyroid hormone levels in menopause: Associations with demographic characteristics, calcium supplementation and sex hormone profile

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Aim: The aim of the study was to investigate possible determinants of circulating parathyroid hormone (PTH) in a sample of peri- and postmenopausal women.

Methods: This is a retrospective analysis of 538 charts of peri- and post-menopausal women from a Menopause Clinic. Charts of women known to have premature ovarian failure, gynecological malignancy, clinically overt or treated CVD, VTE, familial hypercholesterolemia, inflammatory disease, diabetes or hyperparathyroidism were excluded from the study. A complete medical history was obtained, including anthropometric measurements. Laboratory measurements included PTH, Testosterone, E2, FSH, LH, SHBG, as well as 25(OH)-vitamin D and Calcium levels.

Results: 117 women were using Calcium and Vit.D supplementation, while 421 patients served as controls. No significant differences were noted in PTH levels, as well as in the hormonal profile between the two groups. Vitamin D was more elevated in the
supplementation group (22.9 ± 9.1 vs 19.5 ± 11.0, p = 0.029). Calcium levels did not differ between the two groups. In the total sample PTH levels correlated significantly with Vit D, TSH, FSH and levels (r = −0.188/p = 0.003, r = 0.135/p = 0.043, r = −0.182/p = 0.024 and r = −0.142/p = 0.053, respectively), as well as with patient age, years since menopause, and BMI (r = 0.259, p < 0.001, r = 0.297, p < 0.001, r = 0.209, p = 0.001, respectively). The demonstrated significant correlations, though, indicate a moderate effect on PTH levels needing careful interpretation, as r values remain relatively low.

Conclusions: Our results confirm that PTH levels rise in the years following menopause with advancing age of women. A higher BMI is also associated with increased PTH levels, while Calcium and Vit D supplementation were not associated with elevated PTH levels. Compliance to treatment was not accounted for and may explain the lack of association between PTH and calcium/Vitamin D supplementation.

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Jump05

Impact of risk reducing salpingo-oophorectomy on quality of life in BRCA mutation carriers. A study protocol

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Introduction: BRCA 1 and 2 are two tumour suppressor genes and certain mutations of these genes can turn into an increasing risk of developing breast and ovarian cancer.

In order to prevent these neoplasms, certain strategies have been investigated. Thus clinical and radiological regular tests can help us to diagnose early stage breast cancers. Tamoxifen has demonstrated the reduction on contralateral breast cancer as and adjuvant treatment for breast cancer. Talking about surgical strategies, bilateral prophylactic mastectomy is the best option to reduce the incidence of breast cancer with reductions up to 90% but no clear benefit on overall survival. On the other hand, risk reducing salpingo-oophorectomy (RRSO) has demonstrated a 50% reduction on breast cancer incidence, a 90% reduction on ovarian cancer reduction and an increase on overall survival of these patients.

Nevertheleass, RRSO can induce the appearance of certain symptoms (e.g: hot flushes, genitourinary syndrome of the menopause, sexual dysfunctions) that could negatively impact on these patients’ quality of life (QoL).

Objective: To check if RRSO worsens quality of life in BRCA mutation carriers.

As secondary objectives we will explore which are the most annoying symptoms on these patients and analyse the evolution of the QoL on these patients.

Methods: The present study protocol has been submitted to the Ethics Committee at our hospital planning to star recruitment on March 1st 2017.

BRCA mutations carriers on which a RRSO is going to be performed will be invited to participate in this study.

Patients will be asked to fulfil the Menopause Rating Scale, the Cervantes Scale short form and the Female Sexual Function Index preoperatively, 1 and 6 months after surgery.

Type of BRCA mutation, age, presurgical menopausal status and personal history of breast cancer will be recorded for each patient.

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Jump06

Evolving endocrine and metabolic milieu of PCOS with aging

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Introduction: While clinical presentation, endocrine and metabolic profiles are well characterized in populations diagnosed with PCOS, the available data are overwhelmingly accrued in young women, with limited information available on the natural history of the disorder. We herein attempt to determine if features of PCOS vary across a defined spectrum of chronological aging.

Methods: In a cross-sectional population of 2595 pre-menopausal PCOS women, subjects were categorized into 3 groups by age: young (Y – 18–30 years, n = 2116), middle (M – 31–37 years, n = 386) and late reproductive age (L – 38–50 years, n = 93).

The following parameters were available: age, body mass index (BMI), blood pressure (BP), menstrual history, hirsutism severity, hormonal data (FSH, LH, FSH:LH, estradiol (E2), testosterone (T), cortisol, DHEAS and metabolic data (fasting glucose and insulin, glycaemic response during 75 g OGTT, total cholesterol (TCh), lipoproteins (LDL, HDL), triglycerides (TG)).

Results: In women with PCOS, hormonal and metabolic profile varied across the different age groups. Comparison of Y vs. M groups showed higher LH, DHEAS and lower estradiol concentrations in Y group. Y group presented better metabolic profile. When comparing M vs L groups we found higher DHEAS levels in M group and lower BMI, OGTT glucose concentrations. We also found significant differences between Y and L groups: higher LH, T, DHEAS, cortisol; lower E2, BP, fasting and OGTT glucose, TCh, LDL. Incidence of hypertension was highest in M group, whereas impaired glucose tolerance or diabetes was highest in L group.

Conclusions: While endocrine aberrations are more apparent in the young, metabolic deterioration dominates the profile of older women with PCOS. Our findings underscore the importance of ongoing surveillance of women with PCOS beyond the reproductive years and considerations for preventative interventions to minimize lifetime risk of cardiovascular morbidity that this population is deemed at risk for.

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Jump07

**Calcium metabolism in relation to subclinical arterial stiffness in asymptomatic, non-diabetic postmenopausal women**

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**Background:** Disorders in mineral metabolism have been related to cardiovascular events in patients with impaired renal function as well as in the general population. This study aimed to evaluate the association between indices of calcium metabolism that are frequently affected in menopausal women by the accelerated osteoclastic bone resorption due to estrogen deficiency and pulse wave velocity (PWV)-a commonly used marker of arterial stiffness and predictor of CVD mortality.

**Methods:** The study population consisted of 433 healthy post-menopausal women with no documented cardiovascular disease or diabetes. We evaluated the association between serum calcium (Ca), phosphorus (P), magnesium (Mg), parathormone (PTH) and 25-hydroxyvitamin D levels, calcium-phosphorus (Ca-P) product and carotid-femoral pulse wave velocity (PWV).

**Results:** The mean age of the participants was 56.7 years. We observed that phosphorus (3.53 ± 0.49 mg/dl, r-coefficient = −0.122, p-value = 0.023) and the Ca-P product (33.7 ± 4.9, r-coefficient = −0.126, p-value = 0.021) correlated negatively with PWV while PTH (40.9 ± 14.9 pg/ml, r-coefficient = 0.153, p-value = 0.022) was the only index with a positive association with PWV. In addition, the phosphorus levels and the Ca-P product in the group of women with PWV > 8.5m/s were significantly lower than in the group of women with PWV < 8.5m/s [(3.45 ± 0.46) mg/dl vs. (3.58 ± 0.50) mg/dl, p-value = 0.013 and (32.9 ± 4.7) vs. (34.2 ± 5.1), p-value = 0.031 respectively]. The inverse association between the Ca-P product and PWV remained significant after adjustment for age, years since menopause, systolic blood pressure, diastolic blood pressure, smoking and PTH.

**Conclusion:** Among ambulatory postmenopausal women, lower serum phosphorus levels and lower Ca-P product, even within the normal range, are associated with elevated PWV. The effects of calcium metabolism on PWV still remain controversial and further studies are necessary in order to clarify these associations.

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Jump08

**Maternal obesity – A negative long-term prognostic factor for the offspring**

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**Objective:** To examine whether metabolic imprinting in utero by maternal obesity affects health in offspring and subsequent generations.

**Methods:** An animal model using pregnant female Wistar rats weighing between 200 and 250 g was used to analyze the influence of gestational obesity on lipid peroxidation levels and placental histopathology. Obesity was induced with high-fat, high-calorie food intake for all rats; half of them received normal diet during pregnancy as controls. Lipid peroxidation and antioxidant levels (malondialdehyde, thiols from maternal serum and placental homogenates) and placental histopathology were assessed in 15 obese rats and 15 controls. After planned breeding, rats were closely monitored for suggestive signs of pregnancy: cessation of estrus cycle, copulatory plug after mating, hair loss around nipples, nest building, enlarged lower abdomen. After birth the female offspring from both groups (25, respectively 27) were given the same normal diet for the rest of their lives.

**Results:** Malondialdehyde levels were significantly higher and glutathione levels lower in the high-fat group compared to the normal diet one. Placental histopathology showed dysplastic epithelial and mesoderm cells in the yolk sac, a higher density of inflammatory cells and heavily congested blood vessels, some showing thrombotic areas and glycogen trophoblast deposits in the high fat group. The offspring of rats with receiving the obesogenic diet weighed significantly more at birth and 72% became obese in adulthood compared to 41% in the control group. We repeated the experiment for the female pups exposed to high fat diet in utero and found that their offspring showed the same metabolic alteration.

**Conclusions:** Metabolic imprinting affects subsequent generations. Our study suggests that early life exposure to maternal obesity is a mediator for programming insulin resistance in the fetus with metabolic phenotypic manifestations in adult life.

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Physicians’ attitude to sexual problems in menopausal women. The 5th minute study

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Objectives: To evaluate the hypothesis that sexual problems in the menopause in Spain may be underdiagnosed, due to the physician’s attitude who do not ask about sex.

Methods: For this observational study, we first sent a survey via e-mail to the members of the Spanish menopause association (AEEM). In this survey it was asked if they routinely addressed sexuality with their patients.

Secondly, a multi-center cross sectional study was performed in 10 different Spanish hospitals. Menopausal patients were attended in medical consultations and no questions about sexual issues were performed. After 5 min time it was asked to all patients who had not referred any sexual problem in the first 5 min about sexual issues. The prevalence of sexual problems diagnosed in the first 5 min and the prevalence after asking about sexual problems were registered.

Results: Only 53.3% of the AEEM members who answered the survey did routinely, ask about sexual problems during medical consultation.

Preliminary results show a difference in cumulative incidence of more than 15% after asking about sexual problems in the 5th minute.

Conclusions: Sexuality is a key aspect of women’s health. It is known that the prevalence of sexual dysfunctions increases after menopause. Gynecologists, because of specialization in the female genital tract and reproductive health, have the possibility of talking openly about sexuality with patients. If we do not ask openly about sex, sexual problems may remain underdiagnosed and undertreated.

Jump10

Determinants of circulating PTH and effect on BMD in menopause

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Introduction: Parathyroid hormone (PTH) determines calcium homeostasis and may contribute to the development of postmenopausal osteoporosis as serum PTH levels and bone mineral density (BMD) seem to be inversely correlated. However, the role of PTH in the modulation and support of bone mass has not been thoroughly defined. This review focuses on PTH determinants and its effect on BMD.

Methods: A literature review was performed using the Medline database (keywords: PTH; postmenopausal osteoporosis; calcium; 25(OH) vitamin D; TSH; LH; FSH; SHBG; testosterone; estradiol; BMI; age; BMD). Based on title and abstract; 152 studies were extracted out of 4,830 citations screened. Only articles published in English between 2005 and 2016 were considered.

Results: The studies included (n = 26) found a positive correlation between serum PTH and a number of biochemical and demographic factors such as serum calcium, 25(OH) vitamin D, TSH, BMI, and age, respectively. An inverse correlation between PTH and 25(OH) vitamin D has been demonstrated, whereas a positive association of BMI with PTH values was found. In contrast, the impact of estradiol, LH, FSH, testosterone and SHBG remains controversial. Importantly, the extend of postmenopausal bone loss may be determined by circulating PTH. Adequate calcium intake and adjusted levels of 25(OH) vitamin D seem to be necessary for maintenance of bone mass within satisfactorily levels and may restrict the risk of osteoporotic fractures.

Conclusion: The role of PTH determinants in the development of postmenopausal osteoporosis warrants further investigations.

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Jump11

The role of polymorphism – 634 G/C (rs2010963) of VEGF – A gene in the development of hypertension and obesity in perimenopausal women

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In recent years much attention of researchers focused on genetic dependencies of cardiovascular disease factors and endothelial dysfunction.

Purpose: To determine the effect of genetic polymorphism – 634G/C (rs2010963) of the VEGF-A gene and formation of AH combined with obesity in perimenopausal women.

Materials and methods: 115 women with stage II of AH, grade 1–2 and obesity I–II gr., aged 45–53 years in perimenopause. All patients were divided into groups according to menopausal status: 45 women without premenopausal and 50 menopausal women. The control group was consisted of 20 healthy menopausal women matched by age. The VEGF concentration was determined by ELISA. The study of the allelic polymorphism –634 G/C (rs2010963) VEGF-A gene was performed by polymerase chain reaction.

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Results: The VEGF level was significantly higher in women with the GG genotype (436.4 [315.2; 772.8]) comparing with the genotype CG (314.6 [222.9; 449.4]) \((p = 0.040)\) and the genotype CC (261.8 [127.5; 268.8]) \((p = 0.005)\). There were any significant differences among women with the CG and CC genotypes \((p = 0.156)\) in the premenopausal group. The VEGF level was significantly higher in the menopause group with the GG genotype (535.2 [290.5; 726.8]) comparing with the genotype CC (252.4 [177.0; 363.8]) \((p = 0.003)\) and the genotype CC (226.9 [197.9; 252.8]) \((p = 0.001)\). There were any significant differences of the VEGF level among women with the genotype CC and CC \((p = 0.148)\). The VEGF level was significantly higher among women with the genotype GG comparing to the CC \((p = 0.010)\).

Conclusion: It was found that the level of VEGF was significantly higher among perimenopausal women with the GG genotype polymorphism -634 G/C (rs 2010963) of the VEGF-A gene compared with genotypes CC and CG patients \((p < 0.05)\). The relationship between the level of VEGF and the carriage of GG genotype polymorphism -634G/C (rs 2010963) VEGF-A, that can be regarded as predictor of AH in premenopausal women with obesity.

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Jump12

Effect of aromatase inhibitors on serum calprotectin levels in an animal experimental model

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Introduction: There is evidence that aromatase inhibitors can influence liver architecture by inflammation processes. Aim was to investigate if Anastrozole (ATZ) and Letrozole (LTZ) in rats can influence serum Calprotectin, a marker for hepatic inflammation.

Methods: 55 female Wistar rats (4-week-old) were maintained in weather controlled chambers \((20 ± 1 \text{ C}, \text{ humidity 55 ± 5\%})\) under lightning \((12 \text{ h light/day})\) for 30 days to adapt to their new environment. After ovariectomy the animals were randomized in three groups. The first group did not receive any drug regimen (control group). The second group received ATZ, the third group LTZ. Blood samples were collected using capillary tubes from the medial retro-oval venous plexus under light ether anesthesia at the beginning \((T1)\), at 2 months \((T2)\) and at the end of the study \((4 \text{ months} – T3)\).

Results: At T1, Calprotectin levels significantly differed among control group (OVA) and ATZ (OVA-A, \(p < 0.01)\) and LTZ group (OVA-L, \(p < 0.05)\). At T2, Calprotectin levels significantly differed between OVA and OVA-A \((p < 0.01)\) and OVA-L group \((p < 0.001)\). At T3, the lowest levels of Calprotectin were observed in OVA group. Specifically, we observed significantly lower rates of Calprotectin in OVA group compared to OVA-A \((p < 0.001)\) and OVA-L group \((p < 0.001)\). OVA-L group presented significantly higher rates of Calprotectin \((p < 0.001)\) compared to OVA-A.

Conclusion: LTZ and ATZ administered to ovariectomized rats are associated with significantly higher levels of Calprotectin. To our knowledge this is the first study suggesting possible effects of ATZ and LTZ on hepatic inflammation via effects on Calprotectin. In our study significantly higher levels of Calprotectin seem to occur with the use of aromatase inhibitors compared to a control group, and these alterations should be considered in future clinical studies.

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Jump13

Sexual function, dysfunction and effect of aging in women with PCOS

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Introduction: Based on recognized endocrine, metabolic and psychological associations that been linked with female sexual dysfunction (FSD), women with PCOS may be deemed susceptible to FSD. The aim of this prospective cross-sectional study is to assess female sexual function and the prevalence of FSD in women with PCOS, and to determine if this differs by age.

Materials: Sexual function was assessed in 102 premenopausal women diagnosed with PCOS. Participants were categorized into 3 groups based on age: \((Y = 18–30 \text{ years}, n = 56); \) middle age \((M = 31–37 \text{ years}, n = 35)\) and late reproductive age group \((L = 38–50 \text{ years}, n = 11)\). Institutional approval was obtained and participants provided informed consent.

Methods: Sexual function was assessed by completion of female sexual function index (FSFI) questionnaire that assesses sexual function across 6 domains: desire, arousal, lubrication, orgasm, satisfaction and pain. Prevalence of FSD (score \(≤ 26.55)\) and its relationships with clinical (body mass index (BMI), hirsutism, endocrine (FSH, LH, estradiol, testosterone, DHEAS) and metabolic (fasting glucose, insulin) parameters was assessed across the three age categories.

Results: The overall prevalence of FSD in the studied population \((\text{age } 28 ± 7)\) was 43%. There was no observed relationship between FSD with hormonal or metabolic indices of PCOS. Older age was associated with FSD with the prevalence being highest \((55\%)\) in L group in comparison to Y and M groups \((44\%\) and \(40\%, \) respectively, \(p = 0.04)\). The sexual function domains that were most affected by aging were of arousal, lubrication, orgasm and satisfaction. There was a negative correlation between BMI and general FSFI score \((r = -0.64, p = 0.04)\). We failed to show any correlation with hirsutism score in this population.

Conclusions: Prevalence of FSD is high among patients diagnosed with and is higher in late-reproductive age women in comparison to younger groups. High BMI negatively affects sexual functioning of PCOS women.

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O01

Associations of steroid sex hormones and sex hormone-binding globulin with N-terminal pro-brain natriuretic peptide in postmenopausal women: The Rotterdam Study

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Background: Amino-terminal pro-B-type natriuretic peptide (NT-proBNP) has a well-documented prognostic value for cardiovascular disease and sex-hormones are suggested to modulate NT-proBNP levels. However, little data are available on the association of sex-hormones with NT-proBNP in postmenopausal women.

Objectives: To examine whether endogenous sex-hormones are associated with NT-proBNP levels in postmenopausal women free of cardiovascular disease (CVD).

Methods: Total estradiol (TE2), total testosterone (TT), androstenedione (AD), dehydroepiandrosterone sulfate (DHEAS), dehydroepiandrosterone (DHEA), sex hormone-binding globulin (SHBG) and NT-proBNP were assessed in 4527 postmenopausal women free of CVD from the prospective population-based Rotterdam Study. Free androgen index (FAI) was calculated as ratio of TT to SHBG concentration. Regression coefficients and 95% Confidence Intervals (CI) were calculated using multivariable linear regression models adjusting for confounders.

Results: In models adjusted for multiple confounders (age, reproductive, life style and cardiovascular risk factors) higher TE2 levels (per 1 standard deviation (SD) increase, β = 0.02, 95% CI = 0.003, 0.05) and lower levels of TT (per 1 SD increase, β = −0.03, 95% CI = −0.05, −0.01), FAI (per 1 SD increase, β = −0.11, 95% CI = −0.14, −0.09), DHEAS (per 1 SD increase, β = −0.07, 95% CI = −0.10, −0.05), DHEA (per 1 SD increase, β = −0.07, 95% CI = −0.09, −0.04) and SHBG (per 1 SD increase, β = 0.14, 95% CI = 0.11, 0.16) were associated higher levels of NT-proBNP. Further adjustment for upstream hormones attenuated the association between TE2 and NT-proBNP but did not materially affect the associations of other sex hormones or SHBG with NT-proBNP. No association was found between androstenedione and NT-proBNP.

Conclusions: Our findings support the hypothesis that higher androgens might be associated with lower natriuretic peptide levels in postmenopausal women.

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O02

Association between blood markers of malnutrition with functional status and mortality in elderly patients with high comorbidity

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Objectives: The states of malnutrition can have negative repercussions on functional status and can increase hospitalization.

The purpose of the study is to assess how nutritional analytical parameters can alter both the functional dependence of the patient, impact on hospital admissions as well as mortality.

Methods: Observational study of patients included in Multimorbidity Chronic Unit of Navarra. We analyzed the serum levels of total proteins, albumin, ferritin and transferrin and calcidiol and how these factors could influence the Barthel index, the number of hospital admissions as well as mortality.

For the data analysis, \( \chi^2 \) was used to compare categorical variables, and univariate linear and logistic regression.

Results: We included 282 patients 83 ± 1.5 years (W/M 139/143). Mean total protein levels were 6.6 g/dl, albumin 3.7 mg/dl, ferritin 210 µg/l and transferrin 231.4 mg/dl and calcidiol 20.4 mg/dl.

We found that patients with normal levels of protein, ferritin and transferrin had significantly lower hospital admissions (beta coefficients – 0.39, 95% CI 0.57–0.21, \( p < 0.001 \); beta coefficients 0.0009, IC95% 0.0003–0.001, \( p = 0.003 \); beta coefficients –0.003, 95% CI –0.006 to 0.0004, \( p = 0.262 \), respectively).

The mean of Barthel index was 75 points. Patients with a Barthel greater than 60 points had albumin levels higher than 3.5 g/dl (OR 2.45, 95% CI 1.16–5.19, \( p = 0.019 \)).

The overall mortality of the study was 23%. Albumin levels higher than 3.5 g/dl are associated with significantly lower mortality (OR 0.14, 95% CI 0.06–0.38, \( p < 0.001 \)).

Conclusions: Depending on our results, there is a clear relationship between malnutrition’s markers, as measured by analytical parameters, with functional impairment, risk of hospital admissions and mortality.

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O03

Metabolic endotoxaemia as a cause of obesity related androgen deficiency

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Obesity is associated with a chronic state of low grade inflammation and impaired testosterone production. Recently we suggested that inflammation triggered by the passage of intestinal bacteria into the circulation may be an underlying cause of androgen deficiency in obese men (GELDING theory [1]). The intestine contains trillions of bacteria bearing the potent immune stimulant endotoxin (Lipopolysaccharide, LPS). The consumption of fatty food and obesity is associated with a breakdown in intestinal mucosal
integrity that then allows passage of bacterial endotoxin into the systemic circulation – so called “metabolic endotoxaemia”. Since administration of endotoxin to animals is known to impair testicular function, we hypothesized that a similar process may occur in men.

An initial observational study observed that adiposity (% body fat) was positively associated with both metabolic endotoxaemia (LBPol, $r = 0.366$, $p = 0.009$) and inflammation (CRP, $r = 0.531$, $p < 0.001$; IL-6 $r = 0.463$, $p = 0.001$), while also being negatively correlated with serum testosterone ($r = -0.403$, $p = 0.004$). Furthermore, serum testosterone levels were negatively correlated with inflammation ($CRP = -0.471$, $p = 0.001$; IL-6 $r = -0.516$, $p < 0.001$) and metabolic endotoxaemia status (LBPol) after adjusting for serum LH levels ($p = -0.317$, $p = 0.03$). A later interventional study where low dose LPS (0.8 ng/kg body weight) was administration to healthy volunteers produced an inflammatory response and a corresponding fall in serum testosterone, thereby confirming endotoxin’s ability to impair testosterone production.

These studies are the first to link metabolic endotoxaemia with androgen deficiency in men. The potential implications of these findings in the management of androgen deficiency, infertility and cardiovascular disease will be discussed.

**Reference**


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**Oral Communications 2**

**004 Self-compassion and climacteric symptoms in postmenopausal BRCA1/2 mutation carriers**

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**Objective:** To reduce ovarian cancer risk, BRCA1/2 mutation carriers are advised to undergo risk-reducing salpingo-oophorectomy (RRSO) around the age of 40, which may induce severe climacteric symptoms. Dealing with these symptoms may be difficult and success is related to several coping strategies. Successful coping depends in part on self-compassion. This describes a positive and caring way of relating toward the self when facing difficult experiences: it is a skill that can be taught. The aim of this study was to explore the association between climacteric symptoms and self-compassion in late postmenopausal BRCA1/2 mutation carriers.

**Methods:** This cross-sectional study using questionnaire data examined climacteric symptoms, self-compassion, physical fitness in 165 BRCA1/2 mutation carriers who underwent an RRSO ≤ 45 years, at least 5 years ago.

**Results:** Late postmenopausal BRCA1/2 mutation carriers reported low levels of climacteric symptoms and being highly self-compassionate. Higher self-compassion was associated with less climacteric symptoms. Furthermore, anti-depressant use was associated with more climacteric symptoms, whereas physical fitness with less symptoms.

**Conclusions:** Being self-compassionate and physically fit, and not using anti-depressants was associated with less climacteric symptoms in oophorectomized BRCA1/2 mutation carriers. Future research is needed to investigate the effect of self-compassion training on climacteric symptoms after RRSO in BRCA1/2 mutation carriers.

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**005 REPLENISH trial: Endometrial protection with a 17β-estradiol and progesterone combination (TX-001HR) in postmenopausal women with vasomotor symptoms**

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**Introduction:** TX-001HR (TherapeuticsMD, Inc., Boca Raton, FL) is an investigational hormone therapy (HT) of combined naturally occurring 17β-estradiol and progesterone (which some call bio-identical) in a single, oral softgel capsule developed to treat menopause-related vasomotor symptoms (VMS). More than 3M women are estimated to use unapproved compounded bi-identical HT (BHT) in the US, and it is also used outside of the US. Compounded BHT may be associated with endometrial cancer.

**Objective:** To determine the endometrial safety of four doses of TX-001HR vs placebo in women seeking relief for VMS.

**Methods:** REPLENISH (NCT01942668) was a phase 3, randomized, double-blind, placebo-controlled, multicenter trial that evaluated TX-001HR in postmenopausal women (n = 1835; 40–65 years) with an intact uterus and vasomotor symptoms. Women received daily TX-001HR estradiol/progesterone: 1.0 mg/100 mg (n = 415), 0.5 mg/100 mg (n = 424), 0.25 mg/50 mg (n = 421), 0.25 mg/50 mg (n = 424) or placebo (n = 151). The primary safety endpoint was the 12-month incidence of endometrial hyperplasia based on a consensus read of 2 out of 3 pathologists. Adverse events (AEs) were also monitored.

**Results:** The incidence of endometrial hyperplasia or malignancy was 0% (by consensus read) with all four TX-001HR doses and placebo after 12 months of therapy. A high incidence of amenorrhea was achieved with all TX-001HR doses.

**Conclusions:** TX-001HR had a safe endometrial profile in postmenopausal women seeking relief for VMS. No endometrial hyperplasia or malignancy, or unexpected safety issues were observed, which is in contrast to what has been reported with compounded BHT. If approved, TX-001HR may be an alternative option of naturally occurring estradiol and progesterone that can be used to treat hot flushes for the estimated millions of postmenopausal women currently using unregulated, unapproved, compounded BHT, whose efficacy and safety have not been studied in rigorous clinical trials.

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REPLENISH trial: TX-001HR (17β-estradiol and progesterone combination) significantly improved moderate to severe hot flushes in postmenopausal women

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Introduction: TX-001HR (TherapeuticsMD, Inc., Boca Raton, FL) is an investigational hormone therapy (HT) of naturally occurring 17β-estradiol combined with progesterone (which some call bio-identical) in a single, oral softgel capsule developed to treat menopausal vasomotor symptoms (VMS). No similar combination HT product has been approved yet in the US or Europe.

Objective: To determine efficacy of four TX-001HR doses vs placebo in women with moderate-to-severe hot flushes.

Methods: REPLENISH (NCT01942668) was a phase 3, randomized, double-blind, placebo-controlled, multicenter trial evaluating TX-001HR in postmenopausal women (n = 1835; 40–65 years) with an intact uterus. The VMS substudy included women with moderate to severe hot flushes (>7 hot flushes/day or ≥50/week) were randomized to daily TX-001HR estradiol/progesterone 1.0 mg/100 mg (n = 141), 0.5 mg/100 mg (n = 149), 0.5 mg/50 mg (n = 147), 0.25 mg/50 mg (n = 154) or placebo (n = 135). Four co-primary endpoints were change from baseline in frequency and severity of hot flushes at weeks 4 and 12 vs placebo.

Results: TX-001HR 1.0 mg/100 mg or 0.5 mg/100 mg met all 4 co-primary endpoints, with significant improvements from baseline in frequency and severity of moderate to severe hot flushes at weeks 4 (all, P < 0.05) and 12 (all, P < 0.001) compared with placebo. Women treated with TX-001HR 0.5 mg/50 mg had significant improvements in hot flush frequency and severity at week 12 (both, P < 0.05) vs placebo, while those taking 0.25 mg/50 mg had significant improvements in frequency, but not in severity, at weeks 4 and 12 (both, P < 0.001).

Conclusions: TX-001HR 1.0 mg/100 mg or 0.5 mg/100 mg effectively treated menopause-related moderate to severe hot flushes. If approved, TX-001HR—the first combination HT product containing naturally occurring 17β-estradiol and progesterone—may provide an alternative option for the estimated millions of women currently using unregulated, unapproved, compounded bio-identical HT.

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Preliminary Brazilian analysis of the Portuguese language 6-item Female Sexual Function Index (FSFI-6)

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Aim: To present preliminary analysis of the Brazilian Portuguese version of 6-item Female Sexual Function Index (FSFI-6).

Methods: A cross-sectional study from Brazilian southern cities included 420 mid-aged women (40–61 years), which completed the 6-item Female Sexual Function Index (FSFI-6), the Menopause Rating Scale (MRS) and a socio-demographic questionnaire. A confirmatory factor analysis (CFA) was conducted. Chi-square of degrees of freedom (χ²/df), the comparative fit index (CFI), the Tucker–Lewis index (TLI) and root mean square error of approximation (RMSEA) were used as indices for goodness of fit. Cronbach’s alpha coefficient (α) and correlations were carried out for FSFI-6 and MRS question related to female sexual problems to assess criterion reliability and validity. All analysis were performed using SPSS and AMOS version 21.0.

Results: In total, 200 women of the sample presented low sexual function (FSFI-6 total scores ≤19). The CFA showed an acceptable fit (χ²/df = 4.921; CFI = 0.974; TLI = 0.959; RMSEA = 0.097 CI 95%: 0.074–0.121 [p = 0.001]). A good reliability was established for FSFI-6 and MRS question (α = 0.79). Although moderately correlated, both FSFI-6 and MRS question related to female sexual problems presented, as expected, a negative and significant association (r = −0.403; p ≤ 0.0001).

Conclusions: The Brazilian Portuguese version of the FSFI-6 presented good psychometric properties. However, further analyses are required (e.g. taking into account health and menopause-related variables; invariance analysis).

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O09

Hormone replacement therapy (HRT) is effective in relieving oestrogen deficiency symptoms (ODS) and improves quality of life in breast cancer patients: The UK randomised HRT trial experience

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Introduction: The UK trial of HRT in early breast cancer (EBC) patients with ODS randomised women to HRT or information about non-hormonal, prescription and complementary alternatives for 2 years. After the HABITS trial reported an apparent increased recurrence risk with HRT the UK trial closed prematurely in July 2004 with 197 women recruited. Results on ODS relief, quality of life and cancer outcomes are presented.

Methods: Co-primary endpoints of disease-free (DFS) and overall survival (OS) were analysed on an intention-to-treat (ITT) basis using Kaplan–Meier estimates, log-rank tests and Cox proportional hazards regression. Secondary endpoints of ODS relief and quality of life were measured using self-completed questionnaires (i.e. oestrogen-deficiency symptom checklist, FACT-B, FACT-ES), analysed by ITT and censoring patients at treatment cessation comparing incidence of symptoms (chi-squared or Fisher’s exact test), impact of symptoms and quality of life (Wilcoxon signed rank pairs test) between groups.

Results: Median follow-up at time of data snapshot was 11.9 years (IQR 11.0–12.4). At baseline, 69% (67/97) of women allocated HRT and 65% (65/100) allocated to no HRT were taking tamoxifen. The median duration of HRT use was 23.7 months (range 0 to 128.4). There was no evidence of a difference in OS (HR for HRT 0.81, 95% CI 0.37–1.79) or DFS between randomised groups (HR for HRT 1.02, 95% CI 0.56–1.84); small numbers limited further sub-group analysis. HRT reduced the proportion of hot flushes (P < 0.001) their impact on daily life (P < 0.001) and explained quality of life improvement with HRT+ concurrent tamoxifen. Minimal impact on vaginal dryness was likely due to topical oestrogen use in both groups.

Conclusion: The UK trial confirms HRT’s effectiveness in relieving ODS in EBC patients. Research to identify symptomatic patients who could benefit without increased recurrence risk is needed and been recommended by the 2015 UK NICE menopause guidance.

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O11

What are workplaces and key stakeholders being advised to do about menopause at work? A review of guidance in the UK

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With an aging workforce, governments and policy makers are increasingly recognising that more women will be working through their menopause than ever before. For some women this is not a problem; around 53% of women find managing work difficult in relation to their menopause. To help workplaces, various guidance materials have been produced from relevant professional bodies. However, what is being suggested, are guidance consistent, and how much of this guidance is based on empirical evidence? The present paper explores guidance materials produced by key professional bodies and trade unions in the UK. These guidance materials are designed to help employers, trade union/health and safety representatives, as well as menopausal working women address the issue of menopause at work. 130 UK trade union websites, Google, and a large UK trade union library were searched for relevant documentation. 25 documents were found, which were, on average, 8 pages in length. 15 trade unions had produced materials representing around 9% of UK trade unions. An inductive thematic

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Tibolone and risk of ovarian and endometrial cancer
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Background: Use of unopposed estrogen therapy or combined estrogen/progestin therapy increase ovarian cancer risk. For endometrial cancer addition of continuous progestin decrease the estrogen induced increased risk. Less in known about the influence of tibolone a synthetic steroid with estrogenic, progestagenic, and androgenic properties.

Objective: To assess the influence of use of tibolone on the risk of endometrial and ovarian cancer.

Design: In a prospective cohort study, all Danish women 50–79 years of age without previous cancer was followed 1995–2009. The National Prescription Register provided individually updated exposure information and The Danish Cancer Registry provided data on cancer including histology. Confounding factors were obtained from other national registers. Poisson regression analyses with 5 years age bands included hormone exposures as time-dependent covariates.

Results: More than 900,000 women were followed. During an average of 9.8 years, 4513 were diagnosed with ovarian cancer and 6202 with endometrial cancer; of which 2221 were serous ovarian tumours and 4972 Type I endometrial tumours. Compared to women never on postmenopausal hormone therapy, women on tibolone had an increased incidence rate ratio (RR) for ovarian cancer of 1.42 (95% confidence interval [CI], 1.01–2.00) and of 2.21 (1.48–3.32) for serous ovarian tumours. The risk increased with duration of use; most explicit for serous ovarian tumours: Long-term use (+10 years) showed a RR of 3.15 (1.40–7.03). The risk of endometrial cancer was 3.56 (95%CI 2.94–4.32) among current users of tibolone and 3.80 (3.08–4.69) of Type 1 endometrial tumours. The steepest risk increase with duration of use was for Type 1 tumours. The RR with long-term use was 4.70 (3.13–7.04).

Conclusion: Tibolone increases the risk for ovarian and endometrial cancer overall; and particular the risk of serous ovarian tumours and Type 1 endometrial tumours. The risk increases with increasing durations of use.

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O13

Menopause Rating Scale (MRS) and the 10-item Cervantes Scale (CS-10): Comparisons in a sample of Brazilian women
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Aim: To compare both Brazilian scales: Menopause Rating Scale (MRS) and the 10-item Cervantes Scale (CS-10).

Methods: A cross-sectional study from Brazilian southern cities included 420 mid-aged women (40–61 years), which completed the 10-item Cervantes Scale (CS-10), the MRS and a socio-demographic questionnaire. Both scales were divided into symptoms domains addressed by their questions (e.g. hot flashes, palpitations, sleep difficulties, joint stiffness, aches and pains, tiredness, depression, anxiety and mood changes, urinary incontinence, and vaginal dryness or sexual discomfort). Each domain was analysed individually by Cronbach’s alpha coefficient (α), Receiving Operating Characteristic (ROC) curve and Correlations to assess criterion reliability and validity. All analysis was performed using SPSS, version 21.0.

Results: Except for tiredness (α = 0.69), all other domains presented a good reliability between MRS and CS-10 (α ≥ 0.73). Besides tiredness (α = 0.69), all other domains presented a satisfactory performance when considering area under a smoothed ROC curve (≥ 0.75). CS-10 presents a specific domain about changes in skin texture or tone, not contemplated by the MRS. Although from moderated to highly correlated, both MRS and CS-10 domains related to menopausal symptoms presented, as expected, a positive (r ≥ 0.596) and significant association (p ≤ 0.0001). Comparisons between the sums of both scales also revealed a great reliability (α = 0.92), and a positive and significant association (r = 0.851, p ≤ 0.0001).

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Conclusion: The Brazilian Portuguese version of the CS-10 presented good psychometric properties in assessing menopause symptoms.

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014

Cigarette smoking and the risk for premature and early natural menopause: Results from pooled analysis of data from 51 450 women

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Introduction: Premature menopause and early menopause are known risk factors for adverse health outcomes in later life. While cigarette smoking is an established risk factor for earlier age at menopause, the overall size and strength of its relationship with premature or early menopause is yet to be fully elucidated.

Objectives: To quantify the magnitude of the relationship between cigarette smoking status with the age at final menstrual period (FMP).

Methods: The International collaboration for a Life course Approach to reproductive health and Chronic disease Events (InterLACE) enables the use of pooled data on 51 450 women from nine longitudinal observational studies in the UK, Scandinavia, Australia and Japan. Age at FMP was confirmed by at least 12 months of cessation of menses and categorised as: premature menopause (FMP before age 40), early menopause (FMP 40–44 years), 45–49 years, 50–51 years, 52–53 years, or 54 or more years. Cigarette smoking was categorised as current smoker, past smoker, or never smoker. Multinomial logistic regression was used to identify associations with age categories for FMP, after adjusting for birth year, age at menarche, education level, marital status, parity, and body mass index during midlife.

Findings: Overall 18% of the women were smokers, with a mean age at FMP of 48.9 years (SD 4.2). The mean (SD) for never or past smokers was 50.1 (4.2) years. Current smokers were at a higher risk of having premature menopause (RRR 1.48, 95% CI 1.17 to 1.88), early menopause (RRR 1.70, 1.43 to 2.03), FMP at 45–49 years (1.43, 1.31 to 1.56) compared with never smokers. Past smokers had similar risks as never smokers.

Conclusions: This study identified robust evidence for the effect of cigarette smoking on the timing of menopause before the age of 50, with the effect being highest for early menopause. Findings underscore support for smoking prevention and quitting programmes for women of reproductive age.

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015

Latent class analysis of patterns of well-being after hysterectomy in the United States

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Objective: To evaluate patterns of well-being 3 months after hysterectomy using latent class growth analyses.

Methods: This prospective cohort study identified women undergoing hysterectomy for benign indications. Patterns of well-being were examined over time, using latent class growth analyses. Demographic and clinical characteristics of each class were also analyzed.

Results: A total of 245 women were included in the study. Three patterns of well-being were identified.

Class 1 (16 patients [6.5%]) showed a well-being trajectory that started lower than the other 2 classes and had little improvement postoperatively.

Class 2 (87 patients [35.5%]) and Class 3 (147 patients [60.0%]) were similar in trajectory, except that class 2 began at a lower well-being score and had a slight deceleration in its early trajectory.

Length of stay and body mass index showed statistically significant differences among the 3 classes (p ≤ 0.005). Readmission rate, uterine weight, and baseline pain (dichotomized as yes/no) all differed as well (p < 0.05) with each class.

Those in class 1 tended to be the most likely to have reported pain during the baseline interview, the smallest average uterine size, length of stay > 1 day, and a readmission.

Those in class 2 were the least likely to have a length of stay > 1 day and had the largest average body mass index.

Those in class 3 were the least likely to have a readmission or report pain at baseline and had the largest average uterine weights. Classes did not differ in their racial compositions, ages, indications for hysterectomy, surgical approaches or procedure duration, or in their rates of transfusions, complications, cervix removal, or oophorectomy.

Conclusion: This work may offer guidance around shared decision making, when planning hysterectomy. In our study, patients with low uterine weight, non-fibroid uterus, and higher baseline pain were less likely gain as much improvement as the other groups postoperatively.

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016

Misoprostol for cervical priming prior to hysteroscopy in postmenopausal and premenopausal nulliparous women: A multicentre randomised placebo controlled trial

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Objective: To evaluate the reduction of pain by Misoprostol compared to placebo prior to hysteroscopy in postmenopausal and premenopausal nulliparous women.

Design: Randomised multicentre double-blind placebo controlled trial.

Setting: Two Dutch teaching hospitals and one Dutch university medical centre.

Methods: Patients were randomised to receive either 400 mcg Misoprostol or placebo 12 and 24 h before hysteroscopy. Pain was quantified by the use of real time pain measurement by the Continuous Pain Score Meter (CPSM) and by VAS scores.

Main outcome measures: Primary outcome was pain measured by the CPSM during passage of the hysteroscope through the cervical canal, quantified by the Area Under the Curve (AUC). Secondary outcomes included VAS scores, other CPSM parameters, failures and side effects.

Results: 149 patients were randomly assigned to either Misoprostol (n = 74) or placebo (n = 75). The AUC during introduction did not significantly differ between the intervention and the placebo group.

The VAS score during introduction however, demonstrated a significant difference in premenopausal nulliparous women favouring Misoprostol: 2.9 (95%CI: 1.3–4.4) versus placebo 5.5 (95%CI: 3.9–7.1), p = 0.02, as well as the AUC during the entire procedure: 618 (95%CI: 410–827) vs 1126 (95%CI: 671–1580), p = 0.04.

Failures were equally distributed between the Misoprostol (16%) and placebo group (13%). Intestinal side effects occurred significantly more frequent in the Misoprostol group (67%) compared to the placebo group (32%) (OR 4.2 [95%CI 2.1–8.3], p < 0.01).

Conclusion: Misoprostol prior to hysteroscopy reduces pain in premenopausal nulliparous women, but not in postmenopausal women. It does cause side effects.

Keywords: Hysteroscopy, pain, Misoprostol

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O18

Effect of androgen supplementation on activity-rest patterns in old males

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Like elderly men, old male rhesus monkeys show attenuated circulating levels of testosterone and dehydroepiandrosterone sulfate (DHEAS), and many of them also show reduced levels of daytime activity. It is unclear, however, if this age-associated behavior is causally related to the underlying decrease in circulating androgen levels. To test this possibility, old male rhesus monkeys were given daily supplements of testosterone and DHEA for 6 months, designed to mimic the 24-h circulating hormone patterns of young adults. Compared to the young adults, the old controls showed attenuated daytime activity levels. However, there was no difference between the androgen-supplemented old animals and the aged-matched controls, even after 6 months of treatment. The data suggest that age-associated decreases in circulating androgen levels might not be a primary reason for altered activity-rest patterns in elderly men, and that physiological androgen supplementation paradigms offer no obvious therapeutic benefit.

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O36

Reduced breast cancer incidence in women treated with subcutaneous testosterone, or testosterone with anastrozole: 9-year interim analysis

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Objective: To determine the long-term effect of testosterone therapy on the occurrence of breast cancer.

Methods: A 10-year prospective study (approved March 2008) was designed to follow pre and postmenopausal women treated with subcutaneous testosterone (T) or testosterone combined with anastrozole (T+A) for symptoms of hormone deficiency for the occurrence of breast cancer. 1387 patients were accrued through 2013: 119 control patients and 1268 treated patients (>2 pellet insertions). An interim analysis was performed February 2017 to determine the incidence of breast cancer per person-years (p-y) of therapy. P-Y of therapy was calculated using first pellet insert until 240 days following last insert”.

Results: Between March 2008 and January 2017 a total of 12 invasive breast cancers (2-2010, 2-2011, 2-2012, 2-2013, 2-2014, 2-2015, 0-2016) have been diagnosed in treated/active patients on T therapy in 6319 p-y of T therapy. This translates to an incidence of 190/100,000 p-y, which compares favorably to never users from the Million Women Study (325/100,000), our control group (390/100,000) and SEER age specific incidence rates for ages 60-64 (347/100,000). Ten tumors were ER-positive and two were ER-negative, consistent with an expected ratio of 80% for ER-positive tumors.

As of January 2016, 527 (of 1268) patients had received implants within the previous 240 days (active). Mean age at time of analysis (January 2017) in this group was 60.1 ± 8.6 y and mean length of therapy was 8.1 ± 1.8 y. No invasive breast cancers were diagnosed in these 527 patients through January 2017 (year 2016). One patient was diagnosed with low-grade ductal carcinoma in situ, had surgical treatment, and continued testosterone therapy

Conclusion: Subcutaneous testosterone therapy reduced the occurrence of ER-positive and ER-negative invasive breast cancers.

*Duration of action of subcutaneous implant therapy

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O20

Muscle and joint pains in middle-aged women are associated with insomnia and low grip strength

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Objectives: Muscle and joint pains are among the most common symptoms in menopausal transition, whereas the precise underlying mechanism is not known. This study aims to investigate the factors associated with the symptom in middle-aged women.

Study design: Cross-sectional.

Main outcome measures: The first-visit 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 the institutional review board. The prevalence of muscle and joint pains was estimated based on women’s responses to the Menopausal Health-Related Quality of Life Questionnaire. Effects of background characteristics, including age, menopausal status, body composition, cardiovascular parameters, physical fitness, and other menopausal symptoms of vasomotor, depression, anxiety, and insomnia were assessed using multivariate logistic regression analysis.

Results: Daily bother by muscle and joint pains were reported by 56.1% of women. Factors associated with the symptom were: low stature; high body fat percentage; low grip strength; high vasomotor/depression/anxiety/insomnia symptom scores. Multiple logistic regression analysis revealed independent associations between daily bother by muscle/joint pains and low grip strength (adjusted odds ratio with 95% confidence interval, 0.92 [0.87–0.97]), and high insomnia symptom score (1.20 [1.07–1.34]).

Conclusions: Muscle and joint pains are highly prevalent in middle-aged women, and are associated with insomnia and low grip strength.

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O21

Quantifying the mediating effect of body mass index on the association between hysterectomy status and incident diabetes in a mid-aged cohort of Australian women

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Introduction: Hysterectomy is a common gynaecological procedure that has been linked with metabolic syndrome and markers of pre-diabetes and diabetes. Mechanisms underlying these associations may be related to changes in hormone levels that occur post-surgery; however other explanatory factors may also be at work. Women with a hysterectomy tend to be more obese and obesity is one of the strongest risk factors for diabetes. It is therefore plausible that the associations between hysterectomy and diabetes may be mediated through high body mass index (BMI).

Objectives: To formally quantify the mediating effect of BMI on the association between hysterectomy and the incidence of
diabetes. Women who had a hysterectomy before age 50 years were compared with women who did not have a hysterectomy.

**Methods:** Data from the mid-aged cohort of the Australian Longitudinal Study on Women’s Health were used in this analysis (N=6829). Women with existing diabetes at baseline were excluded from the analysis. A causal inference framework for mediation analysis was used to estimate the total, natural direct, and natural indirect effects of hysterectomy status on incident diabetes over an 8-year period, and to estimate the proportion mediated through BMI, after adjusting for age, level of physical activity, age at menarche, highest education level, and gestational diabetes.

**Results:** Preliminary results suggest that the total effect of having a hysterectomy before the age of 50 increases the odds of diabetes in later life (adjusted odds ratio 1.92 [95% CI: 1.39, 2.64] compared with women without hysterectomy), using BMI as a mediator. Approximately 23% of the relationship between hysterectomy status at baseline and incident diabetes was mediated through BMI.

**Conclusion:** Findings highlight that health professionals should encourage women with a hysterectomy, who have high BMI, to lose weight to reduce their risk of developing diabetes in midlife.

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**O22 Factors associated with climacteric symptoms in a sample of Brazilian women**

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**Aim:** To verify factors associated with climacteric symptoms in a sample of Brazilian women.

**Methods:** A cross-sectional study from Brazilian southern cities included 420 mid-aged women (40–61 years), which completed the Menopause Rating Scale (MRS) and a socio-demographic questionnaire. Questions about lifestyle and habits were analysed using SPSS, version 21.0, considering menopausal status. Comparisons between status, by Kruskal-Wallis test, and correlations among all variables were carried out. Categorical variables were expressed as relative frequencies (n%) and continuous variables as median [25–75 percentiles].

**Results:** Most women were married (70%), multiparous (64%), employed (67%), non-smokers (68%), had a sexual partner (88%), had similar educational level (11.76[11.41–12.47]), and family income (in minimum wages, 3.20[2.13–6.40]). They moderately to never consume hot beverages (60%) or alcohol (68%), but frequently drink coffee (82%) and exercise (52%). They were categorized in pre (n = 154), peri (n = 53) or postmenopausal (n = 213) women, and the median age of menopause was 48.00[46.16–47.41] years. Pre-menopause women displayed lower hot flashes (compared to post and peri groups, p < 0.0001), heart palpitations (compared to perimenopause group, p = 0.013) and vaginal dryness complaints (compared to postmenopause group, p < 0.0001). Hot flashes were positively related to age, smoking, alcohol, and menopause status, but they showed a negative relation to the age of menopause. Heart palpitations positively correlated to menopausal status and psychologic disorders. Additionally, vaginal dryness complaints were positive related to menopause status, and showed a negative relation to being married or having a sexual partner.

**Conclusion:** Considered together, age, menopausal status, alcohol intake, smoking, psychological disorders, and marital status were presented as risk profiles to symptoms related to menopause.

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**O23 Immigrant women’s experiences and perceptions of the menopausal transition and post-menopausal life: A systematic review**

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Immigration affects all aspects of women’s health and well-being. We conducted a systematic review to evaluate the available evidence relating to immigrant women’s experiences of menopause; strategies to manage menopausal symptoms; and perceptions of menopause-related health care.

The search yielded 728 papers of which 24 reporting on 20 separate studies met inclusion criteria. Five studies were conducted in two countries simultaneously (Germany/Turkey, Germany/China, Tunisia/France, US/South Korea and United Kingdom/India), six in Australia, five in the USA, two in Israel, and one each in Spain and Sweden.

**Experience of menopause:** Overall, immigrant women attributed joint and muscle pains and reduced physical strength and stamina more frequently than vasomotor symptoms to menopause. Poorer mental health was linked to lower socioeconomic status, employment status and less social support.

**Strategies to manage menopausal symptoms:** Most women viewed menopause as a natural event. Tolerating and accepting menopausal symptoms, using traditional medical therapies known in their country of origin and life style changes were the most commonly used ways of managing menopausal symptoms. Lack of knowledge and inability to access reliable information were perceived as barriers for postmenopausal health.

**Perceptions of menopause related health care:** Common complaints about health care providers were that they did not provide adequate information and direction about how to manage menopausal symptoms. Studies reported that women received medical treatments which they regretted having undergone or with which they silently disagreed and either never commenced or ceased taking after a short time.

**Conclusion:** Culturally competent menopause-related clinical care should include comprehensive information about symptom
management and mechanisms to ensure that consent to treatment is informed.

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O24

Age at period cessation and verbal memory across adult life: Findings from the MRC National Survey of Health and Development

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Whether earlier menopause is associated with earlier or faster cognitive decline and risk of dementia has long been of interest. We used data from the British 1946 birth cohort to investigate whether verbal memory assessed between 43 and 69 years was associated with timing of natural or surgical menopause; and whether associations were explained by hormone therapy (HT), childhood cognition and sociobehavioural covariates. Verbal memory (word learning) was assessed at 43, 53, 60–64 and 69 years. Age at period cessation was derived from 11 questionnaires between 43 and 64 years. We fitted multi-level models based on 3631 observations on 1153 women with linear and quadratic age terms, stratified by natural or surgical menopause, and adjusting for: HT use, body mass index, and smoking at each cognitive assessment; and adult occupational class, educational qualifications, and childhood cognition. Later age at natural menopause was consistently associated with higher verbal memory from 43 to 60–69 years (0.18 words per year, 95% CI 0.08, 0.27, p-value < .001). An association remained after adjustment for covariates (0.10 words per year, 95% CI 0.03, 0.18, p-value = .007); HT use was not associated with verbal memory. Verbal memory increased with later age at surgical menopause (0.16, 95% CI 0.08, 0.27, p value < .001) but no association remained after adjustment. Lifelong oestrogen exposure rather than short-term menopausal fluctuations may be the underlying mechanism.

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O25

Age at natural menopause and life expectancy with and without type 2 diabetes

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Background: Early onset of menopause is associated with increased risk of type 2 diabetes (T2D) and all-cause mortality. However, little is known about the effects of early age at natural menopause (ANM) on years lived with and without T2D.

Objective: We aimed to examine the association of ANM with the number of years lived with and without T2D.

Methods: We included 3.623 postmenopausal women aged 45+ years from the Rotterdam Study, a prospective population-based cohort study. Multistate life tables were built to calculate total life expectancy (LE) and LE with and without T2D among women who experienced early (<44 years), normal (45 to 55 years), and late menopause (>55 years, reference). For life table calculations, we used prevalence, incidence rates and hazard ratios (HR) for 3 transitions (free of T2D to T2D, free of T2D to death and T2D to death) stratifying by ANM and adjusting for confounders.

Results: We identified 306 incident cases of T2D. Early (HR 1.8, 95% CI 1.17; 2.76), but not normal ANM (HR 1.1, 95% CI 0.77; 1.64), was associated with increased risk of T2D. Also, early ANM was associated with mortality in women without T2D (HR 1.4, 95% CI 1.02; 1.96), but not in women with T2D (HR 1.5, 95% CI 0.83; 2.54), whereas no association was found between normal ANM and mortality in either groups. Compared with those who experienced late menopause, women who experienced early and normal onset of menopause lived 3.2 (95% CI: −5.8; −1.0) and 0.9 (95% CI −2.6; 0.8) years fewer overall of which 5.0 (95% CI −9.5; −1.2) and 1.4 (95% CI −4.1; 0.9) years fewer without T2D, respectively. In addition, although not significant, women who experienced early menopause lived 1.8 (95% CI −1.4; 5.8) years longer with T2D than women who experienced late menopause.

Conclusions: The increase in the risk of T2D and mortality from early onset of menopause represents an important decrease in total LE and LE free of T2D.

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Stakeholder perceptions of what makes a care home homely

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Background: This doctoral study explored the concept of homeliness as perceived by residents, relatives and staff of Scottish care homes for older people. Following ethical approval from the West of Scotland Research Ethics Committee seven relatives, five residents and four staff participated in the study.

Aims: To explore the concept of creating a home like environment and whether a ‘homely’ care home is a priority in the expressed needs and wishes of residents, staff and the relatives who visit care homes.

Methods: A mixed methodology design was selected using both an observational environmental assessment tool and Q methodology. The literature review concluded that homeliness was a complex concept, which was highly individual, and this information used to inform the first interviews with the participants. These interviews were then thematically analysed and mapped against the literature. Statements representing each theme were developed and 30 formed the Q-set. A pilot study concluded that the concourse was adequately represented by these 30 statements.

Findings: Three factors were extracted from analysis of the completed Q-sorts. Relatives and staff loaded on Factor 1 (Standards Driven) while Factors 2 (Making the Most of It) and 3 (A Sense of Belonging) were representative of residents, staff and relatives. By mapping these factors onto Maslow’s Hierarchy of Need it could be seen that these Factors could be related to the journey that individuals make when moving from home to the care home.

Conclusion: The results suggested that meeting the standards of care required by the inspection bodies was of importance, but not enough to engender a feeling of homeliness.

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Skeletal muscle and vitamin D level in women of various ages

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Introduction: In recent years there has been a number of studies examining the correlation between vitamin D status and skeletal muscles. However, there are many different approaches to the role of vitamin D metabolism and function of skeletal muscles.

The aim of the research conducted at the SI dF. Chebotarev Institute of Gerontology NAMS of Ukraine was to study the correlation between skeletal muscles and vitamin D level in women of different ages.

Materials and methods: The study involved 122 healthy women aged 20 to 83 years. According to the gerontological classification, the examined women were divided into groups: younger – up to 44 years (n=35), middle – 45–59 years old (n=26), older – 60–74 years (n=44), senile age – 75–89 years (n=17). Lean mass of the total body, upper and lower extremities was evaluated using Dual X-ray absorptiometry (Prodigy, GEHC Lunar, Madison, WI, USA). Strength of skeletal muscle was evaluated using springy carpal dynamometer. To determine the functional capacity of skeletal muscle we used a «four-meter» test. To determine the level of 25(OH)D electrochemicalinescent method was used with Elesys 2010 analyzer (Roche Diagnostics, Germany).

Results: We determined a significant correlation between parameters of lean mass (r = 0.45; t = 2.08; p = 0.05) and the level of vitamin D in women of middle (45–59 years) age: skeletal muscle functionality (r = −0.51; t = −2.29; p = 0.04) and the level of vitamin D in women of older (60–74 years) age. We did not find the significant correlation between parameters of muscle strength and level of vitamin D.

Conclusion: Significant correlation between parameters of lean mass, skeletal muscle functionality and the level of vitamin D was determined in women of middle and older age.

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Oral Communications 5

Metabolic effects of the Cimicifuga racemosa extract Ze 450 in vitro and in ob/ob mice

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Metabolic changes have been often described in perimenopausal women. Therefore, the present experiments evaluated the potential antidiabetic effects of the Cimicifuga racemosa extract Ze 450. Ze 450 and some of its components (23-epi-26-deoxyactein, protopine and cimiracemoside C) were investigated in vitro for their effects on AMP-activated protein kinase (AMPK) compared to metformin in HepaRG cells. Ze 450 (given orally (PO) and intraperitoneally (IP)), metformin (PO) and controls were given over 7 days to 68 male ob/ob mice. Glucose and insulin concentrations were measured at baseline and during an oral glucose tolerance test (OGTT). Ze 450 and its components activated AMPK to the same extent as metformin. In mice, Ze 450 (PO/IP) decreased significantly average daily and cumulative weight gain, and daily food and water intake, while metformin had no effect. In contrast to metformin, PO Ze 450 virtually did not change maximum glucose levels during OGTT, but, prolonged elimination. Ze 450 administered PO and IP decreased significantly glucose-stimulated insulin, whereas metformin did not. HOMA-IR index of insulin resistance improved significantly after IP and PO Ze 450 but only slightly after metformin. In summary, the results demonstrate that Ze 450 reduced significantly body weight, plasma glucose, improved glucose metabolism and insulin sensitivity in diabetic ob/ob mice. In vitro experiments suggest that part of the effects may be related to AMPK activation. Therefore, Ze 450 may have utility in the treatment of type 2 diabetes. Thus, Ze 450 given for the treatment of menopausal symptoms in perimenopausal women may give an additional benefit. However, longer term studies in additional animal models or patients with disturbed glucose tolerance or type II diabetes may be of use to further investigate this hypothesis.

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O29

Study of the effects of Tribulus terrestris on sexuality in post-menopausal women by inventory of sexual satisfaction – Female version (GRISS)

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**Objective:** To study the effects of Tribulus terrestris on sexuality in post-menopausal women.

**Method:** A prospective, randomized, placebo-controlled, double-blind trial involving 60 post-menopausal women with sexual dysfunction was carried out. Study participants were split into two groups: Group I (control) n = 30, and Group II (Tribulus) n = 30. Both groups were assessed for three months based on two questionnaires: the Inventory of Sexual Satisfaction - Female Version (GRISS).

**Results:** The GRISS questionnaire showed a significant improvement in global scores in Group II compared to Group I (P < 0.001). A significant improvement on the GRISS domains of Infrequency, Non-communication, Female sexual avoidance, Female non-sensuality, Vaginismus and Anorgasmia, was seen in Group II compared to Group I (P < 0.05). No significant improvement in the Female dissatisfaction domain (P = 0.845) was found. In terms of collateral effects, no significant difference was detected between the two Groups. No improvement was seen in the Female sexual dissatisfaction domain on the GRISS assessment.

**Conclusions:** A ninety-day treatment using Tribulus terrestris in post-menopausal women with sexual dysfunction led to improvements in several aspects of sexuality according to scores on the GRISS questionnaires, applied before and after the treatment. No improvement was seen in the Female sexual dissatisfaction domain on the GRISS assessment.

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O30

Bisphosphonate and denosumab “holiday” in postmenopausal osteoporosis: A systematic review of randomized-controlled trials

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**Introduction:** Long-term bisphosphonate and denosumab use is associated with osteonecrosis of the jaw (ONJ) and atypical femoral fractures (AFF), raising the issue of discontinuation (“drug holiday”). The present systematic review presents data on the effect of “drug holidays” on fracture risk, bone mineral density (BMD) and ONJ/AFF risk.

**Methods:** MEDLINE, Scopus, EMBASE and Cochrane databases were searched (up to January 2017) for randomized controlled trials (RCTs).

**Results:** Fracture risk. Extending alendronate treatment to 10 years reduced clinical vertebral fracture risk by 55%, without benefit on morphometric vertebral or non-vertebral fractures (one study, 5-year “holiday”). Extending zoledronic acid treatment to 6 years reduced the risk of new morphometric vertebral fractures by 49%, without benefit on clinical vertebral or other fractures (one study, 3-year “holiday”). Treatment extension was beneficial for patients at high risk (occurrence of new fractures or femur neck T-score < -2.5). No anti-fracture benefit exists for 9 years of continuous zoledronic acid use (one study). Risedronate discontinuation for 1 year did not increase fracture risk (one study). No RCT was found for ibandronate and denosumab. Denosumab discontinuation may be associated with rebound fractures. BMD, in all studies, lumbar BMD was sustained above pre-treatment values during “drug holiday”, although femur neck BMD was reduced. Adverse events. No increased risk of ONJ or AFF was shown in any study. Alendronate discontinuation reduced AFF risk (one study).

**Conclusions:** Bisphosphonate discontinuation may be considered after 5 years of treatment with alendronate and 3 years with zoledronic acid and risedronate, for up to 5, 3 and 1 year, respectively, since the fracture risk is low. Regular reassessment and re-initiation of anti-osteoporotic treatment, in case fracture risk remains high, is suggested. No safe recommendations can be made for ibandronate or denosumab.

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O31

Low BMD is a red flag for sarcopenia in climacteric women as shown in a data preliminary analysis

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**Background:** During climacteric a significant loss of bone and muscle mass is seen. A low muscular mass (sarcopenia) could be a more sensible predictor than osteoporosis for bone fracture; therefore a prompt diagnosis should be warranted.

**Objective:** Could BMD be considered as a predictive marker of a poor muscle mass existence?

**Material and method:** 493 BMD exams of women 30 to 80 years old taken during a voluntary gynecological checkup were analyzed. BMD taken with a Lunar Dpx densitometer were evaluated at both femoral necks and the appendicular muscle mass (four extremities). Muscle mass index, a sarcopenia marker,
was computed dividing the muscular mass by the height (square meters). The Baumgartner (<5.45 kg/m²) cutting point was used.  
**Results:** Largest BMD (0.975 g/cm²) in 40–49 age group, smallest (0.821 g/cm²) in the older group (>69 years), statistically significant difference (p<0.0001) between groups. Highest muscular mass index, 5.995 kg/m², in 40–49 years old group falling to 5.826 in group over 69 (p < 0.05). In the highest BMD (first quartile group) a 14.4% of low muscular mass index (sarcopenia) groups with poorest BMD had a 39.9% (OR: 3.04; 95% CI: 1.56–6.0).

**Conclusions:** It is shown in this sample that the lower femoral neck BMD value is associated with a highest presence of sarcopenia. Therefore, we propose that when detecting a low bone mineral density in a routine examination an immediate evaluation of muscle mass index and muscle function should be performed, in order to install the adequate measures to diminish a following sarcopenia risk, one of the leading causes of fracture and of postmenopausal low quality of life.

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**O32**

**Health promoting effect of synbiotic yogurt containing pomegranate polyphenols: Scientific evidence**

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**Objective:** To evaluate the effects of a synbiotic yogurt, a novel product on lipid profile and blood pressure (BP) in mildly to moderately hypercholesterolemic and hypertensive subjects.  

**Methods:** Synbiotic yogurt contained probiotic cultures, L. rhamnusis and L. acidophilus, 2% prebiotic fructooligosaccharide, inulin and 20% pomegranate juice concentrate (PJC) was used as dietary supplement. This product had 90% probiotics survivability, 72% total phenolic compounds and 68% antioxidant activity over a 4-week period of refrigerated storage. To assess its health benefits, an 8-weeks parallel, double-blinded, randomised trial was conducted with 48 male and female volunteers, aged 30–65 years, consuming a daily serve of 200 g yogurt. Subjects were assigned to 3 groups:

- a control;  
- group 2 consumed the synbiotic yogurt without PJC; and  
- group 3 consumed the same synbiotic yogurt containing 20% PJC.

Fasting blood samples, 3d dietary records, anthropometric measurements and BP were collected at baseline, end of 4 and 8 weeks.  

**Results:** Lipid profile parameters showed that consumption of the synbiotic yogurt containing PJC resulted in 6% decrease in total cholesterol and 8.3% decrease in low-density lipoprotein cholesterol (LDL-C) levels compared with the controls. Systolic blood pressure was reduced by 3.70 mmHg and diastolic blood pressure by 2.33 mm Hg. No significant changes from the baseline were observed in triglycerides and HDL-C levels. Total cholesterol: HDL-C ratio and LDL-C: HDL-C ratio as atherogenic indices significantly decreased in group 3 that consumed synbiotic yogurt containing PJC compared with the control group.

**Conclusion:** This study indicates the combined effectiveness of probiotics, prebiotics and polyphenols in the synbiotic yogurt in modulating total cholesterol and LDL-C levels in mildly to moderately hypercholesterolemic population and its effectiveness in ameliorating cardiovascular disease risk factors in both women and men.

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**O33**

**Prescribing for the oldest old**

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**Background:** The oldest old (usually classed as 85+) are the fastest growing cohort in the ageing population. While there is a growing body of literature on treating the oldest old, much of this work is confined to specialist geriatric literature.  

A major issue in prescribing for people over the age of 85 is that guidelines for diseases are based on single disease management and take no account of the interaction of drugs used in managing several diseases. Therefore all professionals who prescribe need practical help in prescribing for the oldest old.  

**Aim:** To explore the positive and negative influences on prescribing practices for the oldest old.  

**Method:** A narrative literature review was carried out from January 2010 to January 2016. The keywords used were frail elderly, iatrogenic disease, GP assessment, primary care.  

**Results:** The search strategy sourced 94 records. Following screening, 49 articles were reviewed.  

The papers showed four distinct themes concerning positive and negative influences on prescribing practices: These were

- Potentially Inappropriate Medications (12 papers),  
- Geriatric Assessment (9 papers),  
- Clinical Decision Making (13 papers),  
- General Practitioner Training (15 papers).

However, what became apparent was the lack of uniform definitions for co morbidity and polypharmacy in the articles reviewed. Most tellingly, we found no consensus on the definition of the ‘oldest old’.  

**Discussion:** General practitioners are time limited and need practice related information and the opportunity to exchange knowledge with colleagues in order to prevent professional isolation.  

**Recommendations:** It is clear that single disease standards of treatment are not useful when managing frail older people with multiple pathologies and reduced functional reserve. Grouping conditions means that multiple methods of treatment can be planned.

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**O34**

**Bone mineral density and trabecular bone score in Ukrainian men with obesity**

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The aim of this study is to determine the connection between the bone mineral density (BMD) and trabecular bone score (TBS) parameters in Ukrainian men suffering from obesity.
**Materials and methods:** We examined 396 men aged 40–89 years, depending on the body mass index (BMI) all the subjects were divided into 2 groups:

Group A – 129 men with obesity whose BMI was ≥30 kg/m² (mean age – 59.9 ± 10.4 years; height – 174.4 ± 6.8 cm; weight – 100.0 ± 9.8 kg, BMI – 32.9 ± 2.6 kg/m²) and

Group B – 267 men without obesity and BMI of <30 kg/m² (mean age – 60.9 ± 12.5 years; height – 174.3 ± 6.7 cm; weight – 77.1 ± 9.8 kg, BMI – 25.3 ± 2.6 kg/m²). The BMD of total body, lumbar spine at the site L1–L4, femoral neck and ultra-distal forearm were measured by DXA (Prodigy, GEHC Lunar, Madison, WI, USA). The TBS of L1–L4 was assessed by means of TBS iNsight software installed on our DXA machine (product of Med-Imaps, Pessac, France).

**Results:** In total group we found that obese men have significantly higher BMD in comparison with men without obesity of lumbar spine (A – 1.289 ± 0.212 g/cm², B – 1.172 ± 0.237 g/cm²; \( F = 22.59, p < 0.001 \)), femoral neck (A – 0.964 ± 0.148 g/cm², B – 0.914 ± 0.150 g/cm²; \( F = 25.18, p < 0.001 \)), total body (A – 1.277 ± 0.098 g/cm², B – 1.185 ± 0.118 g/cm²; \( F = 57.38, p < 0.001 \)) and ultra-distal forearm (A – 0.555 ± 0.086 g/cm², B – 0.494 ± 0.095 g/cm²; \( F = 37.57, p < 0.001 \)). TBS (L1–L4) was significantly lower in obese men compared to non-obese men (A – 1.053 ± 0.161, B – 1.197 ± 0.167; \( F = 66.48, p < 0.001 \)). Fat mass and BMD status showed a significant positive correlation at various sites. The correlation between the fat mass and TBS of L1–L4 was also significant, although negative.

**Conclusion:** In Ukrainian men obesity negatively affected on TBS L1–L4, despite significantly higher BMD at all measured sites compared with men without obesity. The study results reveal a significant positive correlation between fat mass and BMD. Correlation between fat mass and TBS L1–L4 was significant and negative.

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**O35**

**Neurokinin 3 receptor antagonism as a novel treatment for menopausal hot flushes: A phase 2, randomised, double-blind, placebo controlled trial**

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**Background:** Hot flushes affect 70% of menopausal women, can be long-lasting, and often severely impact on physical, psychosocial, sexual, and overall wellbeing. Hormone replacement therapy is effective but not without risk. Neurokinin B signalling is increased in menopausal women, and has been implicated as an important mediator of hot flushes.

**Methods:** This phase 2, randomised, double-blind, placebo-controlled, crossover trial assessed the effectiveness of an oral neurokinin 3 receptor antagonist (MLE4901) on menopausal hot flushes in an ambulatory setting (Clinicaltrials.gov NCT02668185). Sixty-eight women were screened between February and October 2016 in a single-centre, of which 37 were randomised and included in an ITT analysis. Twenty-eight participants (aged 49–62 yrs, experiencing > 7 hot flushes/24 h some of which were reported as bothersome or severe), completed the trial, and were included in a Per-Protocol analysis. They received 4 weeks of MLE4901 and placebo in random order separated by a washout period. Randomisation was completed by a central computer, and participants were allocated to treatment number in numerical order. Primary outcome was total number of hot flushes during the final week of both treatment periods. Funding was obtained from the Medical Research Council (UK) ((MR/M024954/1)).

**Findings:** MLE4901 significantly reduced the total weekly number of hot flushes by 45% compared to placebo (adjusted means: placebo 49.01 (CI: 40.81–58.56), MLE4901 19.35 (CI: 15.99–23.42), \( p < 0.0001 \) (ITT)). MLE4901 also significantly reduced weekly hot flush severity, bother, and interference compared to placebo by 41% (\( p < 0.0001 \)), 45% (\( p < 0.0001 \)), and 58% (\( p < 0.0001 \)) respectively. Treatment was well tolerated.

**Interpretation:** Treatment with a neurokinin 3 receptor antagonist (MLE4901) could be practice changing as it safely and effectively relieves hot flush symptoms without the need for...
oestrogen exposure. Larger scale studies of longer duration are now indicated.

http://dx.doi.org/10.1016/j.maturitas.2017.03.319

Poster Session
P001

Serotonin receptor targeting activities for Cimicifuga racemosa dry extract (BNO 1055) as active component of Klimadynon®

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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-HT1A and 5-HT-7 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-HT1A, 5-HT2A and 5-HT7 in vitro using radioligand binding assays and second messenger (cAMP) activation assays.

The BNO 1055 dry extract demonstrated binding to serotonin receptors 5-HT1A (IC50: 2 µg/ml) and 5-HT7 (IC50: 7 µg/ml) rather than 5-HT2A. Binding was biologically functional as revealed by second messenger assays (EC50: 5 µg/ml for each, 5-HT1A and 5-HT7). N-methylserotonin, an ingredient of the CR extract, has been tested positive in terms of 5-HT1A and 5-HT7 activation (EC50: 11 ng/ml and 0.12 ng/ml). Additionally, serotonin receptor activation of BNO 1055 and Klimadynon® was analyzed in comparison to four other best-selling CR-containing products in Germany. Binding of BNO 1055 and Klimadynon® was considerably more efficacious than most of the competitors’ products as reflected by EC50 values of 5 µg/ml (5-HT1A) and 1-3 µg/ml (5-HT7) for BNO 1055 and Klimadynon® as compared to EC50 values ranging from 10 to 98 µg/ml (5-HT1A) and from 2-26 µg/ml (5-HT7) for the competitors.

In summary we showed that Klimadynon® contains herbal substances with selective agonistic serotonin receptor activity. Furthermore, Klimadynon® is one of the most effective of all tested CR dry extract-containing phytotherapeutics regarding serotonin receptor 5-HT1A and 5-HT7 activation. Thus, we hypothesize that the well-documented therapeutic effect of Klimadynon® is due, at least in part, to substances such as N-methylserotonin that activate serotonin receptors.

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P002

Menopause Symptoms Severity Inventory (MSSI) revised: Preliminary study for the adaptation with a Portuguese sample

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Introduction: A previous instrument (Menopausal Symptoms Severity Inventory), which assesses both intensity and frequency of symptoms, is being revised in an ongoing Portuguese study (EVISA).

Hence, the aim of this study is to present the preliminary analysis done with the MSSI revised version.

Methods: A total of 229 peri- and post-menopausal Portuguese women (aged 40–86 years old; M = 50.78; SD = 8.02) filled in all instruments, including the MSSI revised version, a socio-demographic and menopausal-related questionnaire. The MSSI revised version includes several new items and other improved items (e.g., wording, scale of measurement).

Results: The exploratory factor analysis entailing 43 items/symptoms, assessed both in terms of frequency and intensity, yielded a 6-factor structure (composed of 26 symptoms):

1) Pain/Tiredness;
2) Vasomotor;
3) Appearance;
4) Psychological;
5) Urovaginal; and
6) Sexual.

The confirmatory factor analysis showed an acceptable fit (χ²/df = 2.259; CFI = .846; TLI = .836; RMSEA = .074, C.I. 90% .071 – .078; p < .001). All factorial weights are above .48, except for items 19 (λfreq = .28; λint = .38) and 29 (λfreq = .26; λint = .27), both from Urovaginal subscale. The convergent validity was explored through the average variance extracted (.29 ≥ AVE ≤ .66). An excellent reliability was established (.81 ≥ Cronbach’s α ≤ .96) and the sensitivity was adequate (|ku| < 7 and |sk| < 3).

Conclusion: These preliminary analyses show promising psychometric characteristics of the MSSI revised version, in a Portuguese sample. Nonetheless, it should be noticed that further studies are required (specifically, a separate analysis considering menopausal statuses, since it is expected that the measurement models show some disparities among women in pre-menopause and counterparts in peri-/post-menopause). Despite this, the current study presents a valid instrument, which is useful, both in normative and clinical settings of research and intervention.

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Studies suggested an agonistic effect of CR towards serotonin receptors 5-HT1A and 5-HT7 resulting in modulation of vasomotor activity as potential mechanism of action against hot flushes. Earlier studies suggested an agonistic effect of CR towards serotonin receptors 5-HT1A and 5-HT7 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-HT1A, 5-HT2A and 5-HT7

in vitro using radioligand binding assays and second messenger (cAMP) activation assays.

The BNO 1055 dry extract demonstrated binding to serotonin receptors 5-HT1A (IC50: 2 µg/ml) and 5-HT7 (IC50: 7 µg/ml) rather than 5-HT2A. Binding was biologically functional as revealed by second messenger assays (EC50: 5 µg/ml for each, 5-HT1A and 5-HT7). N-Methylserotonin, an ingredient of the CR extract, has been tested positive in terms of 5-HT1A and 5-HT7 activation (EC50: 11 ng/ml and 0.12 ng/ml). Additionally, serotonin receptor activation of BNO 1055 and Klimadynon® was analyzed in comparison to four other best-selling CR-containing products in Germany.

Binding of BNO 1055 and Klimadynon® was considerably more efficacious than most of the competitors’ products as reflected by EC50 values of 5 µg/ml (5-HT1A) and 1-3 µg/ml (5-HT7) for BNO 1055 and Klimadynon® as compared to EC50 values ranging from 10 to 98 µg/ml (5-HT1A) and from 2-26 µg/ml (5-HT7) for the competitors.

In summary, we showed that Klimadynon® contains herbal substances with selective agonistic serotonin receptor activity. Furthermore, Klimadynon® is one of the most effective of all tested CR dry extract-containing phytotherapeutics regarding serotonin receptor 5-HT1A and 5-HT7 activation. Thus, we hypothesize that the well-documented therapeutic effect of Klimadynon® is due, at least in part, to substances such as N-methylserotonin that activate serotonin receptors.

The confirmatory factor analysis showed an acceptable fit (χ²/df = 2.259; CFI = .846; TLI = .836; RMSEA = .074, C.I. 90% .071 – 078; p < .001). All factorial weights are above .48, except for items 19 (λfreq = .28; λint = .38) and 29 (λfreq = .26; λint = .27), both from Urovaginal subscale. The convergent validity was explored through the average variance extracted (.29 ≥ AVE ≤ .66). An excellent reliability was established (.81 > Cronbach’s α ≤ .96) and the sensitivity was adequate ([k]u < 7 and [sk] < 3).

Conclusion: These preliminary analyses show promising psychometric characteristics of the MSSI revised version, in a Portuguese sample. Nonetheless, it should be noticed that further studies are required (specifically, a separate analysis considering menopausal statuses, since it is expected that the measurement models show some disparities among women in pre-menopause and counterparts in peri-/post-menopause). Despite this, the current study presents a valid instrument, which is useful, both in normative and clinical settings of research and intervention.

Methods: A total of 229 peri- and post-menopausal Portuguese women (aged 40–86 years old; M = 50.78; SD = 8.02) filled in all instruments, including the MSSI revised version, a sociodemographic and menopausal-related questionnaire. The MSSI revised version includes several new items and other improved items (e.g., wording, scale of measurement).

Results: The exploratory factor analysis entailing 43 items/symptoms, assessed both in terms of frequency and intensity, yielded a 6-factor structure (composed of 26 symptoms):

1) Pain/Tiredness;
2) Vasomotor;
3) Appearance;
4) Psychological;
5) Urovaginal; and
6) Sexual.

Preliminary validating analysis of the Portuguese language 6-item Female Sexual Function Index (FSFI-6)

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Aim: To present preliminary analysis of the validation of the Portuguese Language 6-item Female Sexual Function Index (FSFI-6).

Methods: A total of 252 mid-aged Portuguese women (45-65 years; mean: 52.2 ± 4.6 years) completed the FSFI-6 and a sociodemographic questionnaire. A confirmatory factor analysis (CFA) was conducted. Chi-square of degrees of freedom (χ²/df), the comparative fit index (CFI), the Tucker–Lewis index (TLI) and root mean square error of approximation (RMSEA) were used as indices for goodness of fit. Convergent validity was evaluated by average variance extracted (AVE) and reliability using Cronbach’s alpha.
Results: In total, 50% of the sample presented lower sexual function (FSFI-6 total scores ≤19). The CFA showed an acceptable fit ($\chi^2/df = 2.161$; $CFI = 0.992$; $TLI = 0.982$; $RMSEA = 0.068$, CI 90% 0.017–0.115; $p = 0.226$). Good values were evidenced both in terms of factorial weights ($\lambda_{it1} = 0.53$; $\lambda_{it2} = 0.86$; $\lambda_{it3} = 0.93$; $\lambda_{it4} = 0.79$; $\lambda_{it5} = 0.68$; $\lambda_{it6} = 0.79$), as well as regarding the multiple squared correlations ($r^2 > 0.28$). The convergent validity also presented a good result (AVE = 0.60). An excellent reliability was established ($\alpha = 0.89$), and the FSFI-6 items' sensitivity was adequate ($|ku| < 7$; $|sk| < 3$). Although weakly correlated, both FSFI-6 and Sexual QoL subscale presented, as expected, a negative and significant association ($r = -0.29$; $p = 0.001$).

Conclusion: The Portuguese language version of the FSFI-6 presented good psychometric properties. However, further analyses are required (e.g. taking into account health, menopause-related variables and invariance analysis).

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P004

The 10-item Cervantes Scale (CS-10): Preliminary analysis of its validation in a sample of mid-aged Portuguese women

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Aim: To present preliminary analysis of the validation of the 10 item Cervantes Scale (CS-10) in a Portuguese sample of mid-aged women.

Methods: A total of 292 Portuguese women, aged 45–65 years (mean: 52.6 ± 4.8 years) completed the CS-10 and a socio-demographic questionnaire. A confirmatory factor analysis (CFA) was conducted. Chi-square of degrees of freedom ($\chi^2/df$), the comparative fit index (CFI), the Tucker–Lewis index (TLI) and root mean square error of approximation (RMSEA) were used as indices for goodness of fit. Convergent validity was evaluated by average variance extracted (AVE) and reliability by Cronbach’s alpha coefficient ($\alpha$). Correlation between the CS-10 and the Utian Quality of Life Scale (UQoLS) was calculated to assess criterion validity.

Results: The CFA showed an acceptable fit ($\chi^2/df = 1.997$; $CFI = 0.975$; $TLI = 0.963$; $RMSEA = 0.059$, CI 90% 0.037–0.080; $p = 0.237$). All factorial weights were above 0.51, except for item 8 ($\lambda = 0.47$). Likewise, all multiple squared correlations were above 0.26, with the exception of item 8 ($r^2 = 0.22$). The convergent validity was below the expected value (AVE = 0.42); however, an excellent reliability was established ($\alpha = 0.88$). Moreover, the CS-10 items’ sensitivity was adequate ($|ku| < 7$; $|sk| < 3$). Although weakly correlated, both CS-10 and UQoLS presented, as expected, a negative and significant association ($r = -0.34$, $p < 0.001$).

Conclusion: These preliminary analyses show promising psychometric validation characteristics of the CS-10 Portuguese language version, useful for both clinical and research settings. Nonetheless, it should be noticed that further analysis is required, namely, a multi-group comparison taking into account menopausal status since it is expected that premenopausal women differ from their peri/postmenopausal counterparts.

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P005

Factors associated to impairment quality of life in Afro-Colombian climacterics. Assessment with Cervantes scale

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Objective: Assess factors associated to impairment quality of life in Afro-Colombian climacterics women with use Cervantes Scale (CS).

Methods: CAVIMEC (Calidad de Vida en la Menopausia y Etnias Colombianas) is a cross-sectional study, accredited by the ethics committee of the Universidad de Cartagena, Colombia. Study without risks. Participated women that will recognize self be Afro-Colombian, black skin and daughters of black mother and father, living in Caribbean and Pacific Coast. Participation anonymous, voluntarily, with informed consent, were asked to fill sociodemographic questionnaire and CS, that measures health conditions with 31 questions, setting 0–155 point, to higher score, worse evaluation. It was considered impairment quality of life to scores above average of the CS. Statistical analysis done using EPI-INFO-7. It was performed logistic regression to associated factors risks. $P < 0.05$ was considered statistically significant.

Results: A total of 646 women were studied, mean age of the whole sample was 48.7 ± 5.7 years, 41.9% premenopausal, 17.4% perimenopausal and 40.5% postmenopausal. Cronbach’s alpha 0.719. Global score 39.2 ± 22.6. Were scored above average 257 (39.7%). The 76.4% felt hot flashes suddenly, 73.1% hot flushes, 71.3% aching in muscles and/or joints, 61.8% cannot get sufficient sleep, 50.4% skin dryness. Risk factors were: age group 55–59 years OR: 4.1 [2.5–6.8], 50–54 years OR: 3.6 [2.1–5.9], overweight OR: 0.9 [0.6–1.4], obesity OR: 1.7 [0.9–3.5], more than twelve years of study OR: 0.3 [0.2–0.4], primary education OR: 4.1 [2.4–6.9], smoking previously OR: 3.6 [2.1–6.2], Smoke now OR: 6.4 [3.4–11.8], absence of hormonal therapy OR: 1.4 [0.7–2.9], postmenopause OR: 2.6 [1.9–3.7], postmenopause over 11 years OR: 2.0 [0.9–4.5].

Conclusions: We identified modifiable and non-modifiable considerations that behave as risk factors for deterioration of quality of life.

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P006

The importance and the content of a comprehensive model of care for menopausal patients?

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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.

**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.

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**P007**

Case report of use of Black Cohosh for carbamazepine induced hot flushes in a post menopausal woman

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We report on a 66 year old female, 15 years post menopause, with a background of trigeminal neuralgia on carbamazepine 400 mg daily referred to the menopause clinic for hot flushes. The onset of the flushing was 3 months after starting the carbamazepine at the age of 64. She had not had any flushing previously. The flushing was affecting her sleep and function. She was otherwise well with no fever, skin or mucosal involvement. Vital signs were normal. Her full blood counts, thyroid and liver function and ESR were normal. There with no evidence of drug induced hypersensitivity. The hot flushes were attributed to carbamazepine. The carbamazepine was changed to pregabalin. The flushing stopped, but facial pain was uncontrolled. Decision was made to restart carbamazepine. The flushing recurred after 2 months of restarting carbamazepine. We gave the patient Remifemin (Black Cohosh) for treatment of her flushing. Patient has been free of facial pain as well as flushing for the last 6 months.

**Discussion:** Carbamazepine being a CYP 1A2 and 3A4 inducer induces the metabolism of conjugated estrogen and estradiol. This could be a possible explanation for this effect. The Search of medical literature did not reveal any cases of carbamazepine induced hot flushes. However, ehealthMe website mentions hot flushes in 17 out of 21,399 reported carbamazepine related adverse events.

To the best of our knowledge this is the first report of successful treatment of carbamazepine induced flushing with Black Cohosh [1–3].

**Reference**


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**P008**

Effect of Foeniculum vulgare (fennel) vaginal cream on vaginal atrophy in postmenopausal women: A double-blind randomized placebo-controlled trial

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**Objective:** Vaginal atrophy is one of the main concerns of postmenopausal women. The aim of the present study was to investigate the effect of fennel vaginal cream on vaginal atrophy in postmenopausal women in Ahvaz, Iran.

**Materials and methods:** This double-blind randomized controlled trial was conducted on 60 postmenopausal women (45–65 years of age) in Ahvaz, Iran. The study participants were randomly divided into one of two groups, receiving either a placebo (n = 30) or fennel 5% vaginal cream (n = 30) administered as one application per day (5 g/day) for 8 weeks.

**Main outcome:** The vaginal pH and maturation vaginal index (MVI) were measured at baseline and 8 weeks after the intervention, while the vaginal atrophy symptoms was measured at baseline and at 2, 4, and 8 weeks after the intervention. The data were analyzed using the independent t-test, chi-square test, paired sample t-test, and the generalized estimating equation.

**Results:** The number of superficial cells increased significantly in the fennel group after 8 weeks compared to the control group (76.1 ± 15.3 vs. 11.8 ± 8.8, p < 0.001). The number of intermediate and parabasal cells decreased significantly in the fennel group compared to the control group (p < 0.001). The vaginal pH decreased significantly at the 8-week follow-up in the fennel group compared to the control group (100% vs. 7.4%, p < 0.001). All women in the fennel group had an MVI of 65–100 at the 8-week follow-up, whereas almost half (40.7%) of the women in the control group had an MVI of 50–64 (p < 0.001).

**Conclusion:** According to results of this study, fennel is an effective means to manage the symptoms of vaginal atrophy in postmenopausal women and is devoid of side effects. Larger studies are necessary to confirm the positive impact of fennel for vaginal conditions occurring among postmenopausal women.

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Palmitoleic acid (C16:1 n-7) or Omega-7 (O-7) is a monounsaturated fatty acid. It is biosynthesized from palmitic acid by the action of the delta-9 desaturase. It can also be obtained from sea buckthorn (Hippophae rhamnoides), macadamia nuts (Macadamia integrifolia) and marine sources (anchovies). The nutritional and biological functions of palmitoleic acid are complex and scientific understanding of the biological significance on human health is limited.

Palmitoleate may increase cell membrane fluidity, attenuate insulin resistance, and reduce inflammation associated with diabetes and heart disease.

**Results:** Multiple studies have demonstrated the health benefits of palmitoleic acid over the last decade. They have shown beneficial effects on regeneration of skin and mucous membranes, and improving immune functions, reducing oxidation and strengthening cardiovascular health.

- B. Yang & E. Erkola demonstrated beneficial effects of O-7 from SBA 24® on the overall condition of the mucous membranes of patients of Sjögren’s syndrome.
- In 2014, P. Larmo & B. Yang, showed O-7 beneficial effects, on vaginal health, indicating it is as a potential alternative for mucosal integrity for those women not able to use estrogen treatment for vaginal atrophy.

These results have provided enough data to justify further research on a higher purity palmitoleic acid extract (Provalin®) void of the high levels of palmitic acid (saturated fat) naturally found in H. rhamnoides. Sea buckthorn and macadamia oils typically contain around 9–40% palmitic acid, the negative effects of which can negate the benefits of the O-7.

**Conclusion:** Purified palmitoleic acid (Provalin®) has shown a potent anti-inflammatory and lipid-modulating effect compared with placebo in a double-blinded, placebo controlled trial.

Further studies with promising results are being published using Provalin® in dry eye, prevention of metabolic syndrome, including cardiovascular disease and insulin resistance.

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In the third session, the above exercises together with warming-up exercises were done in a park by a trainer and cooperation of the participants and the way of cooling down was instructed. The correct way of walking and respiration were educated in the fourth session. Finally, the DVD consisting of exercises at home were given to the participants. Finally, data were analyzed by SPSS (20) and repeated measure ANOVA. A two-tailed p value, lower than 0.05, was considered to be statistically significant.

Result: The mean age of women was 54.12 ± 11.25 years. The mean of exercise was increased in case group after intervention (p < 0.001). The paired t-test showed the means of menopausal symptoms like physical, mental, anxiety and depression were decreased significantly in postmenopausal women after intervention in case group but there was significant. But, changes in the control group were not significant.

Conclusion: The exercise program (aerobic exercises and walking) can decrease menopausal symptoms in postmenopausal women.

Keywords: Exercise, Menopause symptoms, Postmenopausal women, Walking

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P012

Systematic review and meta-analysis on the effect of exercise on insulin resistance in postmenopausal women: A study from the Health Outcomes and Systematic Analyses (HOUSSAY) group

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Background: Insulin resistance is common among aging women. However, the extent of this problem is not clear and there are controversial results regarding the effect of exercise on insulin resistance-related outcomes (IRRO) after menopause.

Methods: We performed a systematic review and meta-analysis of randomized controlled trials (RCTs) assessing the effect of programmed exercise vs non-exercise control for at least 12 weeks on IRRO in postmenopausal women. Searches were conducted in 5 databases for studies evaluating insulin resistance markers (insulin, C-peptide, homeostatic model assessment-insulin resistance [HOMA-IR], insulin growth factor [IGF-1] and IGF-binding proteins). Interventions were classified as “mid-term exercise intervention” (MTEI, 3–4 month duration) and a “long-term exercise intervention” (LTEI, 6–12 month duration). A random effects model was used for meta-analysis, and the effects were expressed as mean differences (MD).

Results: We selected 7 RCTs (n = 508); there were 4 RCTs evaluating MTEI, and 4 RCTs evaluating LTEI. In 3 studies, MTEI significantly lowered fasting insulin levels (MD = −6.50 pmol/L, 95% CI −11.19 to −1.82; p = 0.006) and HOMA-IR values (MD = −0.18, 95% CI −0.34 to −0.03; p = 0.02) when compared to controls. LTEI had no significant effect on fasting insulin levels (p = 0.19) or HOMA-IR values (p = 0.68) in 4 and 3 studies, respectively. Heterogeneity of effects among studies was moderate to low.

Conclusion: Implementation of a mid-term exercise intervention for 3–4 months was associated with a significant decrease in insulin resistance markers in postmenopausal women. However, the positive effect did not last when exercise programs were long-term.

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P013

The effect of intervention on physical activity among menopausal women based on Transtheoretical Model

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Introduction: This study aimed at investigating the effect of intervention on physical activity among menopausal women based on Transtheoretical Model.

Methods: This quasi-experimental study was done on 142 menopausal women were randomly assigned to the case and control group. SEQ, processes of change, decisional balance and self-efficacy questionnaire and IPAQ were used for data gathering in pre-intervention, 3 and 6 months after intervention intervention based on Transtheoretical Model (TTM) was performed in the case group for participants in pre-Contemplation, Contemplation, preparation and action by using processes of change. Finally, data were analyzed by SPSS (20) and repeated measure ANOVA, independent t-test was used. A two-tailed p value, lower than 0.05, was considered to be statistically significant.

Results: The mean of physical activity in case group was 225.98 ± 270.55 METS. Three months after the intervention, the mean of physical activity has increased and 6 months after the intervention was 863.44 ± 809.43 METS. Repeated measure ANOVA showed no statistically significant difference in control group in times (p < 0.001). The ANOVA test showed the means of processes of change, self-efficacy, pros, and cons were significant in the case group. But, the mean of pros and cons was not significant in the control group. The mean of BMI was decreased in intervention group from before intervention 28.75–27.96 after intervention (p < 0.001). But changes in the control group were not significant.

Conclusions: The interventional program based on TTM can improve physical activity among menopausal women.

Keywords: Physical activity, Educational program, Menopausal women, Body mass index

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P014

Prevalence of sexual dysfunction the Brazilian postmenopausal women attended at Santa Casa of São Paulo

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Introduction: The sexual health process involves overall well-being, quality of life, stable identity, normal function and satisfying
sexual relationship. A range of instruments are available for assessing Female Sexual Dysfunction (FSD) including the Sexual Quotient-female version (SQF) questionnaire (Abdo, 2006).

**Objective:** To assess the prevalence of sexual dysfunction in menopausal women.

**Casuistic and methods:** A total of 520 women aged between 40 and 70 years were assessed by applying the SQF questionnaire, containing ten objective questions, at the Menopausal Phytotherapy Outpatient clinic, between April 2009 and March 2016.

**Results:** Among participants, mean age was 53.6 ± 6.1 years, and 70.6% reported lack of desire, 15.9% that foreplay failed to stimulate continuation of intercourse, 46.3% inability to relax the vagina to allow penis penetration, 32.4% inability to achieve orgasm, and 34.8% complained of lack of lubrication. Regarding level of satisfaction with intercourse, 46.2% reported no desire to have sex again on other days. With regards to dyspareunia, 12.6% consistently felt pain during intercourse.

**Conclusion:** The Sexual Quotient-Female version (SQF) is a brief, easy-to-apply questionnaire useful for screening FSD. The high prevalence of sexually-related complaints in women aged older than 40 years might be explained by the transition phase, marked by numerous physiological, hormonal and emotional changes. These findings are similar to data reported in the International literature.

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**P015**

**The impact of chronic vulvar dystrophy on sexual function at menopause**

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Chronic vulvar dystrophy is defined as growth of abnormal skin on the vulva, having two types according to the thickness of the skin – thin as lichen sclerosus, or thick like squamous hyperplasia. Lichen sclerosus appears as white, shiny patches of parchment-like tegument on the labia affecting mainly menopausal women. Symptoms are variable, from no obvious manifestations to intense itching and increasing vulvar pain. The affected skin area can easily bleed sometimes just by touch, often making sexual intercourse impossible. With squamous hyperplasia the vulvar skin becomes thick with white elevations, causing intense itching. Treatment includes topical corticosteroid and testosterone application, retinoids to reduce the connective tissue destruction and in advanced cases surgery. We examined a number of 25 menopausal patients, aged between 48 and 64 diagnosed with vulvar dystrophy in the interval 2014–2016. A percentage of 92% experienced difficulties in engaging sexual intercourse due to local pain, itching, dryness sensation, bleeding or labial fusion. From these, a number of 14 patients (56%) declared that vulvar symptoms determined them to cease any sexual activity because of intense complaints (40%) or physical impossibility caused by labial fusion (16%). All patients declared that the vulvar dystrophy had a negative impact on their sexual function and couple activity, affecting their quality of life between 7 and 10 on a visual analog scale. Topical corticosteroid and testosterone application was useful in most cases, relieving the symptoms after 3 months in 72% of the cases, while in the rest of the cases where the disease caused scarring or fusion of the labia surgical treatment was necessary. In conclusion, based on our study group we can affirm that chronic vulvar dystrophy can be a debilitating disease, affecting greatly menopausal women’s quality of sexual life with long-term psychological implications.

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**P016**

**Sexual medicine in older couples**

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Studies show that older men and women consider sexuality an important part of their couple relationship and at the same time they report a high frequency of sexual problems. To respond to these needs we have tried to answer the following questions:

a) What are the special conditions and challenges of sexual healthcare for older couples
b) Which are the specific diagnostic and therapeutic requirements when treating older couples with sexual problems.

d) Which are the specific diagnostic and therapeutic requirements when treating older couples with sexual problems.

**Methods:** Review of the literature, case presentations.

**Results:**

The challenges are:

- Communication: Emotional barriers (shame, feelings of guilt, insecurity).
- Chronic multimorbidity and pharmacological treatments having an impact on sexual health in both individuals.
- Chronic, long-lasting relationship dysfunction with unresolved conflicts and communication deficits.

The specific elements of the therapeutic approach in older couples are:

- Active Listening and accepting thus providing emotional relief,
- Information, Education and Counselling; Dispelling and Correcting myths,
- Help couples to understand the medical and psychological factors contributing to their problems,
- Help couples to define their treatment objectives differentiating between acceptance, rehabilitation, restitution,
- Focus on resources (salutogenic approach),
- Develop a treatment plan selecting an individualized combination of medical and psychotherapeutic interventions.

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**P017**

**Sexual function in menopausal patients with gynecological cancer**

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**Objective:** Assessment of female sexual function in patients undergoing to treatment gynecological cancer who request care in
the sexual health unit after receiving treatment for gynecological cancer.

**Method:** The Female Sexual Function Index (FSFI) was used in 55 gynecological oncological patients who demanded to be attended by a sexologist at the sexual health unit of the Reina Sofia University Hospital. During the first consultation, a structured interview and a psychometric test were performed for the evaluation of desire, arousal, lubrication, orgasm, satisfaction and pain during sexual in these patients.

**Results:** We studied a total of 55 women with natural or induced menopause induced by oncological treatment, aged between 36 and 71 years.

No significant differences were found between groups of patients with different types of gynecological cancer. Low scores were evident in most of the items, in all the analyzed areas.

**Conclusions:** The scores obtained in the Female Sexual Function Index (FSFI) in the patients who demanded attention in the Sexual Health consultation indicate the need to establish easy access routes for the sexual care and counseling of these patients in the oncological units.

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**P018**

**The association between sexual dysfunction and metabolic syndrome among Turkish postmenopausal women**

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**Aim:** The aim is to determine the association between sexual dysfunction and metabolic syndrome among Turkish postmenopausal women.

**Material and methods:** 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 in this prospective survey. Sexual function was assessed using the Female Sexual Function Index (FSFI). A FSFI total score of less than 26.5 was suggestive of sexual dysfunction. Metabolic Syndrome (MS) was assessed by the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria.

**Results:** Sexual dysfunction prevalence among postmenopausal women was 64.6% in relation to 42.1% in premenopausal women (p = 0.001). MS prevalence was 13.5% among premenopausal and 15.5% among postmenopausal women (p = 0.57). The total FSFI score and each score in desire, arousal, lubrication, orgasm, satisfaction, dyspareunia domains of FSFI did not differ between pre- and post-menopausal women, regarding the MS status. In the premenopausal group 45.7% of women without MS and 37% of women with MS had lower sexual dysfunction (p = 0.40); whereas, in the postmenopausal group 62.2% of women without MS and 77.4% of women with MS had lower sexual function (p = 0.22).

**Conclusion:** In our study population, the rate of sexual dysfunction increased in postmenopausal women in contrast to that in premenopausal women. The MS status did not make a difference in terms of sexual dysfunction either in pre- or post-menopausal women. 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.

**Keywords:** Menopause, Sexual dysfunction, Metabolic syndrome, FSFI, MS

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**P019**

**Vaginal lubrication in oncological gynecological patients**

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**Objectives:** To know the level of vaginal lubrication in a group of 55 women undergoing gynecological cancer who come to the sexual health unit of Reina Sofia University Hospital, Córdoba, Spain.

**Methods:** We performed a descriptive analysis of the factors that influence the sexual response of patients with gynecological oncological processes who attend the HURS sexual health consultation. For this we have used the Sexual Female Function Index (FSFI) and a structured interview.

**Results:** A total of 55 women aged between 36 and 71 years were studied. In our study, we obtained a high percentage of patients with changes in their vaginal lubrication pattern. The rated items: frequency of lubrication, difficulty in lubrication, maintenance of lubrication until the end of the relationship and difficulty in maintaining it.

**Conclusions:** The majority of women with gynecological oncological processes attending the sexual health clinic present alterations in their pattern of vaginal lubrication. This consultation shows the need to intervene to improve the health of these women and their quality of life.

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**P020**

**Negligible to very low systemic absorption of estradiol with TX-004HR for the treatment of symptomatic vulvar and vaginal atrophy (VVA): Clinical phase 1 and 3 trials**

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**Introduction:** Many women with VVA symptoms are untreated, in part due to concerns about perceived risks with estrogen exposure. TX-004HR (TherapeuticsMD, Inc., Boca Raton, FL) is an investigational, applicator-free, muco-adhesive, low-dose, vaginal softgel capsule containing solubilized estradiol (E2), shown to treat dyspareunia and vaginal dryness.
Objective: To present pharmacokinetic (PK) data from TX-004HR studies demonstrating negligible to very low systemic E2 absorption with significant improvements in VVA.

Design: REJOICE was a randomized, double-blind, placebo-controlled, phase 3 trial of TX-004HR 4 μg, 10 μg, and 25 μg in postmenopausal women with moderate-to-severe dyspareunia that included a PK substudy (N = 72). Treatments were self-administered daily for 2 weeks then twice/week for 10 weeks. Two single-dose, 2-way crossover, relative bioavailability phase 1 trials compared the PK of TX-004HR with FDA/EMA-approved vaginal E2 tablets (10 or 25 μg). Estradiol PK parameters are reported here.

Results: No differences in systemic E2 levels for 4 and 10 μg TX-004HR vs placebo were found at day 14 for AUC and Cmax. E2 AUC and Cmax with 25 μg TX-004HR were higher than placebo (P < 0.05), but Cavg (<9.1 pg/mL) remained within the normal postmenopausal range. E2 levels at day 84 were similar to placebo. The phase 1 studies (n = 36 for each) of TX-004HR 10 or 25 μg resulted in significantly lower E2 absorption than an approved E2 tablet at identical doses (P < 0.05), with 25 μg TX-004HR demonstrating AUC < 1/3 that of the approved tablet (P < 0.0001).

Conclusion: Systemic mean E2 absorption was similar to placebo for TX-004HR 4 and 10 μg, while 25 μg demonstrated negligible to very low systemic absorption within postmenopausal levels. TX-004HR 10 and 25 μg also had lower systemic E2 exposure vs identical doses of an approved E2 tablet. All three TX-004HR doses significantly improved dyspareunia and vaginal dryness with minimal systemic exposure, demonstrating a local estrogenic effect.

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P021

Hormone replacement therapy has a beneficial effect on hypertensive postmenopausal women: Results from the KNHANES 2010-2012

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Objectives: Hypertension is the most important risk factor of cerebrovascular diseases in Korea. The relative risk of cardiovascular diseases after menopause is greater than premenopausal period. The relationship between hypertension and hormone replacement therapy (HRT) has not been clearly determined. Therefore, we examined the effects of HRT on hypertension in Korean postmenopausal women.

Materials and methods: The data were acquired from the Fifth Korean National Health and Nutritional Examination Survey conducted from 2010 to 2012. Questionnaires were used to collect a medical history about women’s health and cardiovascular diseases. Each woman also had her blood pressure (BP) taken and provided a blood sample for risk factor assessment.

Results: This study involved 2,260 postmenopausal women. The participants in stage 4 hypertension showed lower proportion of HRT than other groups (P for trend = 0.027). After adjustment of several lifestyle factors and cardiovascular risk factors, the HRT group showed lower systolic blood pressure (SBP) and diastolic blood pressure (DBP). Hormone replacement therapy was independently related to the control rate of hypertension. Longer duration of HRT led to lower BP and better control rate of hypertension. The proportion of participants with stage 4 blood pressure decreased from 4.3% in the non-HRT group to 0.4% in the long HRT group.

Conclusion: The hormone therapy group showed lower BP, and presented greater hypertensive control rate. Longer duration of hormone therapy led to lower BP and higher hypertensive control rate. These data suggest that HRT in hypertensive postmenopausal women may be helpful for controlling BP.

Keywords: Hormone replacement therapy, Estrogen, Progestin, Hypertension, Blood pressure, Menopause

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P022

Effects of apolipoprotein E genotype on lipid profile and changes in lipid profile during hormone therapy in postmenopausal Korean women

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Objective: Apolipoprotein E (apoE) e4 allele is associated with a higher risk of coronary heart disease. This study was conducted to evaluate the effects of apoE genotype on serum lipid profile [total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C)] and changes in lipid profile with hormone therapy (HT) in postmenopausal Korean women.

Methods: This retrospective cohort study included 272 healthy postmenopausal women who did not have any cardiovascular risk factor and received oral HT for six months. Women were divided into two groups according to the presence of the apoE e4 allele: e4 carriers (n = 49) and non-carriers (n = 223). Serum lipid profile was measured at baseline and after 3 and 6 months of HT. Baseline levels and changes with HT were compared by the presence of e4 allele.

Results: No significant difference was found in baseline clinical characteristics between the two groups except parity. After adjusting for age, body mass index, parity and history of menopause (age and type of menopause and years since menopause), baseline level of TG was significantly higher and that of HDL-C was significantly lower in e4 carriers than those in e4 non-carriers. In addition, TC and LDL-C were higher in surgically menopausal women with e4 allele. Although TG and LDL-C were decreased and HDL-C was increased with HT, changing pattern of lipid profile was not different according to the presence of e4 allele.

Conclusion: Presence of apoE e4 allele might be associated with the higher TG and lower HDL-C in postmenopausal Korean women. However, changes in lipid profile with HT did not differ by apoE genotype.

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P023

A survey of hormone therapy compliance in Korea

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Objective: To verify compliance with hormone therapy (HT) in a population of female gynecology outpatients in Korea.

Material and methods: During 2010, a total of 1970 female patients were seen in the gynecologic outpatient clinic of our university hospital, and participated in the survey. The questionnaire comprised basic characteristics and 14 items. Patients less than 50 years old (G1), 50–59 years (G2), and 60 years or older (G3) were classified with respect to knowledge of HT (Q1), intention to take HT (Q2) and anxiety regarding HT (Q3). According to HT, we divided groups into never users (NT), current users (UT) and past users (PT).

Results: The mean age was 57.6 ± 9.92 years and 1572 patients (79.8%) were postmenopausal; they had stopped menstruation for a mean of 6.95 ± 6.26 years. The mean BMI was 22.52 ± 2.86 kg/m². Of the population, 864 women had taken HT and 1106 had not. Among the 1572 postmenopausal women, 708 were NTs (45.04%), 754 were UTs (47.96%), and 110 were PTs (7%). Women with considerable knowledge of HT and intention to take HT had decreased anxiety regarding HT. Knowledge of the degree of use of the hormone and HT showed a positive correlation (r = 0.518, p < 0.001). The intention to take HT increased as knowledge of HT increased (0.54). In contrast, the intention to take HT decreased as anxiety regarding HT increased (0.05).

Conclusions: HT is the most effective treatment for symptoms of menopause, but the thought of effectiveness of HT was unclear for Korean women. It is important to educate women regarding HT and change social attitudes. Postmenopausal women receiving HT had greater knowledge of HT than the untreated group. Current users had higher intention to take HT than never users. As menopausal women 50–59 years of age were aware of the side effects of HT, they tended to stop the treatment. HT and education of patients regarding hormone therapy is thus important in Korea.

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P024

The effects of five-year hormone therapy, alendronate, tibolone, and raloxifene on bone mineral density in postmenopausal women (second study)

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Objectives: To evaluate the effects of ten-year hormone therapy, tibolone, alendronate and raloxifene on bone mineral density (BMD) in postmenopausal women.

Methods: We studied 348 postmenopausal women who had visited the menopausal clinic of Dongguk university hospital between January 2001 and December 2010. These patients were divided into estrogen therapy (ET) (n = 51), estrogen-progesterone therapy (EPT) (n = 84), tibolone (n = 70), alendronate (n = 82) and raloxifene (n = 61) groups. The mean patients age, height, weight and body mass index were 55.28 ± 3.34 (range of 45–67) years, 157 ± 5 cm, 60.12 ± 7.22 kg and 24.18 ± 6.37, respectively. We evaluated BMD by measuring lumbar spines (L1–4) and femoral neck at baseline, 1, 2, 3, 4 and 5 years after treatment.

Results: The BMD of the femoral neck increased significantly in the alendronate group by 6.6, 7.4, 7.9, 8.3 and 8.5% at 1, 2, 3, 4, and 5 years after treatment initiation, respectively. It increased in the EPT group by 3.4 and 2.5% at 1 and 2 years after, respectively. It increased in the tibolone group by 2.2 and 2.7% at 1 and 2 years after, respectively. It increased by 2.1% in the raloxifene group at 2 years after.

The BMD of the lumbar spine increased significantly in the alendronate group by 3.4, 5.7, 5.3, 5.3 and 4.7% at 1, 2, 3, 4, and 5 years after treatment initiation, respectively. It increased by 1.2% in the EPT group at 1 year after. It increased by 1.4% in the raloxifene group at 1 year after.

Conclusion: Thus, these findings suggest that alendronate is most effective in improving the BMD levels. In postmenopausal women, any treatment with hormone therapy, alendronate, tibolone or raloxifene increases bone mineral density in the femoral neck and lumbar spines.

Keywords: Bone mineral density, Hormone therapy, Alendronate, Tibolone, Raloxifene

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P025

Hormonal therapy over 60 years old: A possibility?

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Introduction: Hormone therapy (HT) is recommended at the lowest effective dose ≤59 years old, due to breast cancer, cardiovascular (CV) or thromboembolic (TE) risks. Maintenance of therapy, when necessary, is possible in patients with a valid risk-benefit. The lowest estrogen dose, 17B Estradiol, transdermal administration and (when necessary) progestagen derived from natural progesterone (PDNP) should be used, given the benefits in CV sistem and breast tissue.

Objectives: To characterize symptoms in ≥60 years old, HT use and their evaluation at 5 years.

Material and methods: A retrospective study with ≥60 years followed in 2010 was conducted. There were analyzed through the clinical files: symptomatology, HT use ≥60 and unfavorable events at 5 years of follow-up.

Results: Of the 151 ≥60 years old which had already used HT, 70% maintained symptoms. Of these, an expectant attitude was attempted in 72% and a progressive dose decrease in 28%, with an HT maintenance need in 76% and 72%, respectively. Overall, HT was maintained in 73% of symptomatic women: 41% with mild and 59% with moderate to severe symptoms, with an average treatment duration of 43 months. Isolated estrogens were used in 17% and combined TH in 83% of patients. In 82%, low or ultra low dose was used, 18% transdermal administration, 99% 17B Estradiol and 22% PDNP. In 8 cases Tibolone was used, all with resolution of symptomatology. In 3 cases, soy isoflavones were used, with no
Hormone replacement therapy and the impact of “gap time” in cardiovascular versus breast cancer risk

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The gold standard for menopause symptoms, hormone replacement therapy (HRT) should be individualized for each patient, corresponding to her need, expectations, history and benefits should always out weigh the risks.

Following WHI (Women Health Initiative) results, studies have tried to explain the heart paradox, as well as estrogen effects related to age or the moment of treatment initiation. ELITE (Early versus Late Interven tional Trial with Estradiol) concludes that estrogen has a favorable effect on atherosclerosis and cardiovascular events when administrated in early menopause comparing to its neutral or even adverse effect in older women, when started later than 10 years after the menopausal onset. Knowing that estrogen has thickening effects on the blood, the therapy should be initiated before the development of advanced atherosclerotic plaques, because, when administrated later, together with the increase in the production of clothing factors, it makes the blood more likely to clot.

Regarding breast cancer (BC), the time hypothesis is also supported by various studies. Starting therapy later than 5 years after the onset of menopause is associated with a significant reduction of BC risk, because the estrogen deprivation associated to menopause determines a sensitization of breast cancer cells to the proapoptotic effects of estrogen, whereas immediately initiation has no advantageous effects. Furthermore, hormone receptors-positive breast cancers in postmenopausal women respond to treatment with high dose estrogen therapy, while similar tumors in premenopausal women do not. This paradoxical response to addition or deprivation of estrogen can explain both decrease in BC after initiation of HRT and the decrease following cessation of treatment.

Unfortunately, “gap time” cannot optimize both benefits and risks for cardiovascular diseases and breast cancer.

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P027

Cimicifuga racemosa for treatment of vasomotor symptoms: Mode of action

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Worldwide, 50–85% of women experience disabling symptoms during menopausal transition; these significantly affect their well-being and quality of life. Cimicifuga racemosa (CR) has shown its efficacy against Vasomotor Symptoms (VMS). The pathophysiology of VMS is still unclear; the mode of action is still being debated. The role of circulating levels of estrogen in triggering VMS has been critically discussed. The most probable site of thermoregulatory dysfunction appears to be the hypothalamic thermoregulatory center. Estrogen fluctuations affect several neurotransmitter systems and cause imbalances in the serotonin- and noradrenaline-levels in the hypothalamic thermoregulatory center, which have been shown to result in VMS.

The aim of this pharmacological overview is to discuss the relevant pharmacological properties of CR, which may contribute to the mechanism of action for the relief of VMS. Literature (e.g. MEDLINE, EMBASE, BIOSIS) was collected till 2016 and analyzed for CR extracts and its constituents interacting with brain receptors or modulating brain metabolism and activity.

The current data suggest that alleviation of VMS by CR is not caused by estrogen-agonistic effects. Several publications verified that CR contains substances that bind to serotonin, dopamine, GABA and µ-opioid brain receptors leading to receptor-mediated functional activity. CR modulates the ratio of cerebral monoamines and metabolites as well as brain activity (EEG). Moreover, CR and its constituents exert anti-inflammatory, antioxidant and radical scavenger activities. These counteract inflammatory processes and oxidative stress caused by estrogen fluctuations whereby neurons recover their sensitivity to temperature changes.

We hypothesize that CR restores imbalanced thermoregulation and mitigates VMS occurrence by a multifaceted mechanism. This includes direct action on serotonin, dopamine and µ-opioid receptors and anti-inflammatory, antioxidant and radical scavenger effects.

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P028

Use of vaginal CO₂ laser for the treatment of genitourinary syndrome of menopause.

Experience at the Hospital General de Cataluña – Quiroalsal group

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GUSM affects more than half of all menopausal women. Moisturizers and lubricants along with local estrogen therapy are the treatments of choice for these patients. However, not all patients feel comfortable with this type of treatment and others cannot use estrogens because they have a contraindication (i.e.: an active cancer).

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The vaginal laser treatment offers an alternative for these women suffering from GUSM but cannot or do not want to use estrogens.

We have reviewed 10 cases of women with GUSM criteria from the Hospital General de Cataluña’s Menopause Unit that were treated with two separated sessions of CO2 laser for 4 weeks. In all cases they were confirmed postmenopausal women. The average age is 57 years old.

The most common symptoms reported by the patients were dyspareunia, vaginal dryness, 3 out of 10 had mild urinary incontinence and in 2 cases urinary urgency.

To evaluate the response to treatment, we used two tests: the ICQ-IU-5F to assess urinary function and the questionnaire on female sexual function (FSFI), as well as the clinical assessment and subjective symptoms relieve assessment.

Patients are evaluated both before and after each session and once again 6 months later. The results show clinical and numerically improvement in all cases without being statistically significant. No negative effects were detected nor reported in any case. Additionally in all cases there was a symptomatic improvement.

The results are positive and show a clear improvement tendency but the sample is small so this may cause lack of statistical significance in the results obtained. However, the results show improvement so the vaginal CO2 laser represents an effective treatment alternative for those women who suffer from the effects of GUSM and are not candidates for classic treatments with local lubricants, moisturizers or estrogens.

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P029
Effects of combination therapy of alendronate and hormonal therapy on bone mineral density in postmenopausal Korean women: A multicenter, randomized controlled clinical trial
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Objective: This study was performed to investigate the effects of combination treatment with alendronate (ALEN) and hormone therapy (HT) on bone mineral density (BMD) in postmenopausal Korean women.

Methods: This multicenter, randomized, controlled clinical trial enrolled 344 postmenopausal women with low BMD. The women received HT (0.625 mg/day of conjugated equine estrogen and 2.5 mg/day of medroxyprogesterone acetate) alone or in combination with ALEN (10 mg/day) for 1 year. Changes in BMD and biochemical markers of bone turnover were evaluated.

Results: Data from 203 women (HT alone, 99; combination treatment, 104) who completed this study were analyzed. BMD at the lumbar spine and total hip increased significantly in both treatment groups after 1 year. There were no significant differences between HT alone versus the combination of ALEN and HT in mean BMD increase at the lumbar spine (6.9% vs. 7.9%) and total hip (3.7% vs. 3.8%). Combined therapy suppressed serum osteocalcin and urinary deoxypyridinoline to a greater extent than HT alone.

Conclusions: Compared to HT alone, combination treatment with ALEN and HT for 1 year did not offer a benefit in BMD in postmenopausal Korean women with low BMD.

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P030
Body mass index and 25-hydroxyvitamin D levels for obesity in healthy postmenopausal women
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Purpose: Obesity is associated with alterations in vitamin D (VtD) system. We evaluated the correlation between vitamin D level and BMI, as the standard for obesity in menopausal women.

Materials and methods: To study the relationship between VtD levels and obesity, we recruited 310 healthy menopausal women between January 2005 and March 2016 and analyzed the correlation between BMI and serum 25-hydroxyvitamin D (25-OH-VtD) level. We also analyzed the relationship between serum VtD level and bone health status such as bone mineral density measured by DXA, bone turnover marker, and PTH.

Results: With a standard for VtD deficiency at 30 ng/ml, 98.9% patients showed a VtD deficiency, while 87.8% patients showed a vitamin D deficiency with a 20-ng/ml standard. VtD levels had no significant correlation with age, height, weight, BMI, or bone turnover markers. Parathyroid hormone (PTH) level and serum 25-OH-VtD level showed a negative correlation. VtD level showed negative correlation with BMI, but statistically not significant.

Conclusion: In this study, most of menopausal women (more than 87.8%) had a VtD deficiency, and VtD level showed negative correlation with BMI, but was not statistically significant.

Keywords: 25-hydroxyvitamin D, Body mass index, Postmenopausal women

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P031
Intervertebral disc height in premenopausal women treated and untreated postmenopausal women and postmenopausal women with osteoporotic vertebral fractures
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The objective of this study is to assess Intervertebral Disc Height in premenopausal women, hormone treated and untreated postmenopausal and postmenopausal women with radiographically confirmed vertebral fractures.

Methods: One thousand and eight women were collected randomly from a large database of a bone density unit. These were randomly recruited from the DEXA directory.
Results: 1080 women were divided in five groups according to the menopausal/menstrual status. One hundred and twenty-nine (129) menopausal women were on HRT, 258 women were untreated menopausal women, 208 menopausal women were on bisphosphonates, 235 women were on calcium supplements, 70 women were premenopausal and 38 women had confirmed vertebral fractures. Age and weight differences were noted across groups and statistical.

The vertebral fracture group was noted to have the lowest disc height (1.38 ± 0.3 cm) of the 3 discs D1−D3. The D1−D3 disc height in the HRT and premenopausal groups were similar (1.92 ± 0.35 cm) and (1.92 ± 0.3 cm) respectively. The disc heights in the other three groups (calcium 1.49 ± 0.48, untreated menopausal group 1.49 ± 0.48 cm, Bisphosphonates 1.41 ± 0.47 cm) were significantly lower than the oestrogen replete groups but were significantly higher than the osteoporotic vertebral fracture groups (p < 0.001).

Conclusion: Postmenopausal women with vertebral fractures have significantly low disc heights. The disc heights are significantly lower than HRT treated and premenopausal women. The disc heights of the calcium and bisphosphonate groups were also significantly lower than the HRT treated and premenopausal women. These results suggest that the discoid shape and viscoelastic properties of the intervertebral discs may be relevant to the genesis of osteoporotic vertebral fractures and nonhormonally treated menopausal women also have significantly low disc heights.

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P032

Effect of isolated vitamin D supplementation on the bone turnover markers in postmenopausal women: Randomized, double-blind, placebo controlled trial

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Objective: To evaluate the effect of supplementation of vitamin D (VD) alone on the bone turnover markers in postmenopausal women.

Methods: In this double-blind, placebo-controlled trial, 160 women were randomized in VD group, vitamin D3 supplementation 1000 IU/day/orally (n = 80) or placebo group (n = 80). Women with amenorrhea ≥12 months, age 50–65 years, with normal bone mineral density (BMD) were included. The intervention time was 10 months. Serum levels of total calcium, parathormone (PTH), alkaline phosphatase (AP) and calciuria in 24 h-urine were determined. The s-CTX (serum C-terminal telopeptide of type I collagen) as a marker of bone resorption and P1NP (procollagen type I amino-terminal fragments) of bone formation were measured by immunoassay (Kit Elecsys, Roche®). The plasma concentrations of 25-hydroxyvitamin-D [25(OH)D] were measured by HPLC/high-performance liquid chromatography. Statistical analysis was by intention-to-treat (ITT), using ANOVA, Student’s t-test, Tukey test and Gamma distribution.

Results: After 10 months, there was increase in the 25(OH)D concentrations from 15.0 ± 7.5 ng/ml to 27.5 ± 10.4 ng/ml (+45.4%) in VD group, and decrease from 16.9 ± 6.7 ng/ml to 13.8 ± 6.0 ng/ml (−18.5%) in placebo group (p < 0.001). In VD group, there was significant decreased (−21.3%) in PTH values (p < 0.001). No significant differences were observed in the other laboratory parameters (total calcium, AP and calciuria) in both groups (p > .05). In comparison of bone turnover markers, there was significant reduction in s-CTX values (−24.2%, p < .0001) and P1NP (−13.4%, p = .003) in VD group. In the placebo group was not observed significant variations on bone turnover markers. For the participants who completed the study, adherence was 92% for the study intervention (VD or placebo group).

Conclusion: In postmenopausal women with VD deficiency, the isolated supplementation of 1000IU of vitamin D3 for 10 months may be associated with a reduction in the bone turnover markers.

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P033

Relation between DXA and osteoporotic fractures in postmenopausal women

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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. Observational transversal multicentric study recruiting 228 patients in fourteen Spanish hospital between November 2015 and May 2016.

Postmenopausal women visiting a gynecologist’s office and signing the informed consent were included. Exclusion criteria included women with regular menses, patients receiving oncological treatment, patients with a severe medical or psychiatric condition, women unable to understand the questionnaires and women not signing the informed consent.

The median age of the patients was 58 years (47–66). The median of bone mineral density, 49.7% (np = 89) had osteopenia and 28.5% (np = 43) had osteoporosis.

Results: The median age of the patients was 58 years (47–66) 179 of them having dual X-ray absorptiometry performed. According to DXA values, 21.8% (np = 39) of the patients had normal bone mineral density, 49.7% (np = 89) had osteopenia and 28.5% (np = 43) had osteoporosis.

Overall, at least one osteoporotic fracture was diagnosed in 28.1% of the patients (np = 64).
Osteoporotic fractures prevalence in postmenopausal women

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Objective: To study the prevalence of osteoporotic fractures in postmenopausal women and the relation between those fractures and known risk factors for osteoporosis.

Methods: Observational transversal multicentric study recruiting 228 patients in fourteen Spanish hospital between November 2015 and May 2016.

Postmenopausal women visiting a gynecologist’s office and signing the informed consent were included. Exclusion criteria included women with regular menses, patients receiving oncological treatment, patients with a severe medical or psychiatric condition, women unable to understand the questionnaires and women not signing the informed consent.

All the patients had a lateral lumbo-sacral spine X-ray and their results were evaluated according to Genant scale. Data were collected in a Microsoft Access Database and analyzed using IBM SPSS Statistics 20.0 software for MAC.

Results: The median age of the patients was 58 years (45–66). Regarding clinical risk factors for osteoporosis fractures, 2.2% of the patients had a BMI < 19, 0.4% had an excessive alcohol consumption, 0.9% had long-term immobilization, 9.6% had hypocalcemia, 17.1% were smokers, 3.1% were on glucocorticoid therapy and 21.9% had a family history of hip fracture.

At least one osteoporotic fracture was diagnosed in 28.1% of the patients (n = 64). 62.5% of these fractures (n = 40) were diagnosed during the present study 97.8% of them being vertebral fractures and the remaining 2.2% being Colles fractures.

A family history of hip fracture was the only independent statistically significant risk factor for osteoporotic fracture (HR 3.409; 95% CI 1.7–7.0; p = 0.001).

Osteoporotic fracture prevalence was 13.3% in women <50 years, 25% in women between 50 and 59 years and 35.2% in women >60 years these differences not being statistically significant.

Conclusion: Up to 62.5% of osteoporotic fractures could remain unnoticed in women visiting a gynecologist and 98% of them could be diagnosed with a lumbar spine X-ray.

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P035

Combination therapy with raloxifene and alendronate for treatment of osteoporosis in elderly women

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This 3-year prospective randomized study was carried out to determine whether raloxifene and the alendronate in combination are efficacious and safe.

Patients and methods: Sixty-two postmenopausal women (mean age 68.9 ± 0.5 years) attending gynecologic osteoporosis clinics with established osteoporosis were randomly allocated into one of four treatment groups and monitored for 3 years. All patients enrolled in this study including the control group (n = 14) received 1.0 g elemental calcium and 400 units vitamin D per day. The raloxifene group (n = 16) received raloxifene 60mg/Evista® per day; the alendronate group (n = 17) received low dose alendronate 5 mg (Maxarvil®) per day; and the combined therapy group (n = 15) received both raloxifene 60 mg and alendronate 5 mg. BMD was measured in the lumbar spine and the hip before treatment and at 1, 2 and 3 years after treatment.

Results: In patients who received the combined therapy, BMD increased in the lumbar spine by 9.8% (P < 0.001) and in the hip by 6.2% (P < 0.001) at 3 years. For patients treated with alendronate, these increases were 7.1% (P < 0.001) and 2.1% (P < 0.05), and with raloxifene, the increases were 5.6% (P < 0.001) and 2.8% (P < 0.01) in the vertebrae and femora, respectively. The group treated with calcium and vitamin D lost 2.1% (P < 0.05) and 2.7% (P < 0.01) of BMD in the vertebrae and femora, respectively, after 3 years. Patients who received combined therapy had significantly higher BMD in both the vertebrae and in the femora (P < 0.05) in comparison with patients who were treated with raloxifene or alendronate alone after 3 years.

Conclusion: This 3-year randomized study showed an additive effect of alendronate and raloxifene on hip and spine BMD in elderly postmenopausal women with established osteoporosis.

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**SP036**

Comparative effects of denosumab or bisphosphonate treatment on bone mineral density and calcium metabolism in postmenopausal women

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**Aim:** The aim of this retrospective follow-up study was to investigate the effect of denosumab compared with that of bisphosphonates on bone density and indices of bone metabolism in postmenopausal women.

**Methods:** One-hundred-thirteen postmenopausal osteoporotic women aged 53–66 years were recruited for this study. The treatment lasted at least 12 months and all the patients were treated either with denosumab or with a bisphosphonate. Bone densitometry and laboratory tests were performed before and 12 months after the initiation of treatment.

**Results:** Femoral neck BMD increased significantly in both groups (denosumab 0.69 ± 0.07 to 0.75 ± 0.09, p = 0.0001, bisphosphonates 0.69 ± 0.06 to 0.71 ± 0.07, p = 0.001). Denosumab treatment resulted in significant increases in lumbar spine BMD (0.83 ± 0.14 to 0.89 ± 0.14, p = 0.0001) while bisphosphonate treatment resulted in marginally significantly increases in lumbar spine BMD (0.84 ± 0.10 to 0.87 ± 0.11, p = 0.09). Treatment with denosumab but not with bisphosphonates was associated with a significant increase in serum parathyroid hormone (44.87 ± 17.54 to 53.27 ± 15.77, p = 0.04), an effect that occurred independently of vitamin D levels before the initiation of treatment. No changes in serum calcium, phosphate or 25OHD were observed in either of the two treatment groups. Similarly, BMD change from baseline at month 12 was significantly higher with denosumab compared to bisphosphonates at femoral neck (denosumab 8.7% ± 8.5, bisphosphonates 3.8% ± 7.3, p = 0.004). The same was apparent for lumbar spine BMD, the difference, however, did not reach statistical significance (denosumab 9.03% ± 11.3, bisphosphonates 4.5% ± 11.6, p = 0.154).

**Conclusion:** In this sample of postmenopausal women both treatments increased BMD, however, 12 months of treatment with denosumab resulted in higher increase in femoral neck BMD compared to 12 months of treatment with bisphosphonates.

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**PO37**

Bone mineral density and trabecular bone score in Ukrainian postmenopausal women with metabolic syndrome

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**Aim:** The aim of our study was to estimate the bone mineral density (BMD) and trabecular bone score (TBS) in Ukrainian postmenopausal women with metabolic syndrome (MS).

**Methods:** The study involved 1013 50–79 yrs old women in postmenopausal period (mean age – 64.44 ± 8.11 yrs; mean duration of menopause – 14.51 ± 8.21 yrs). Patients were compared into two groups:

- **A** – included 691 women without obesity (BMI ≤ 29.9 kg/m²),
- **B** – contained 322 female with MS (IDF, 2005).

Additionally groups were divided on subgroups according to age of patients (50–59 yrs; 60–69 yrs; 70–79 yrs). The BMD of lumbar spine (L1–L4) was measured by the DXA method (Prodigy, 2005). The quality of bone tissue (TBS L1–L4) was assessed by the TBS iNsight® software package installed on DXA machine (Med-Imaps, Pessac, France).

**Results:** We estimated that women without obesity in total group have significantly lower BMD of lumbar spine (A – 0.950 ± 0.178 g/cm², B – 1.113 ± 0.199 g/cm²; p < 0.001) compared to patients with MS. Analyze of BMD depending on age showed the same results (50–59 yrs – 1.009 ± 0.169 vs 1.139 ± 0.200 g/cm² (p < 0.001), 60–69 yrs – 0.932 ± 0.180 vs 1.089 ± 0.201 g/cm² (p < 0.001), 70–79 yrs – 0.912 ± 0.169 vs 1.117 ± 0.195 g/cm² (p < 0.001)). In total group of women we found that TBS L1–L4 was significantly higher in non-obese patients in compare to another ones (A – 1.195 ± 0.146, B – 1.153 ± 0.175 g/cm²; p < 0.001), especially, due to 50–59 yrs old group (A – 1.263 ± 0.125; B – 1.193 ± 0.172, p < 0.001). There was no significant difference of this index between A and B group women in other age groups. It was found significant positive correlation between BMI and BMD of lumbar spine in all groups and subgroups of patients (p < 0.05). Correlation between BMI and TBS L1–L4 was significantly negative in total group of women (p < 0.05).

**Conclusion:** Ukrainian postmenopausal women with MS have significantly better BMD indexes of lumbar spine, but quality of bone tissue is significantly worse in compare to females without obesity.

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P038

Bone mineral density and quality, body composition of women in postmenopausal period

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The aim of the study was to examine the bone mineral density and quality, body composition of women depending on the duration of the postmenopausal period (PP); correlation of total fat mass (TFM) with bone mineral density (BMD) and trabecular bone score (TBS).

Materials and methods: 179 women (mean age – 58.5 ± 0.4 yrs; duration of the PP – 11.6 ± 0.6 yrs) were examined. The examined were divided into the following groups: A – women in the premenopausal period (n = 18); B – women in PP with a duration of less than 5 yrs (n = 32); C – women in PP with a duration of 5–9 yrs (n = 39); D – women in PP with a duration of 10–14 yrs (n = 56); E – women in PP with a duration of 15–20 yrs (n = 34).

BMD of lumbar spine, femur and body composition (total fat and lean (TLM) masses) were measured by DXA method (Prodigy, GEHC Lunar, Madison, WI, USA) and TBS (L1-L4) were assessed by TBS Insight software package installed on our DXA machine (Med-Imaps, Pessac, France).

Results: BMD at the femoral neck was likely decreasing with age (p < 0.001). The changes in TFM (p = 0.01) and TLM (p = 0.05) in patients with various postmenopausal durations were improbable. Relationship among TBS, BMD and TFM of women in premenopausal period (A-group) was found unjustified (p = 0.2 and p = 0.2 respectively). In B-group this relationship was equally improbable (p = 0.9 and p = 0.5 respectively). In C-group regression relationship between the bone indicators and TFM was insignificant (p = 0.4). With increasing TFM, BMD at the spine (p = 0.008) and femoral neck (p = 0.000004) was significantly increasing. In D-group similar results were observed. The regression relationship between TBS and TFM was improbable (p = 0.3), and with the growth of TFM accompanied the increase of BMD at the spine (p = 0.000004) and femoral neck (p = 0.0001).

Conclusion: BMD and TBS probably deteriorate with advancing of PP. TFM and TLM ratio is not likely to change with age. In middle and late PP, the BMD of spine and femoral neck increases along with TFM.

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P039

The effect of parity and lactation on postmenopausal osteoporosis in the Korean National Health and Nutrition Examination Survey (KNHANES)

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Introduction: Maternal skeletal loss during pregnancy is minimal despite the fetal demand for calcium. However, in case of some pregnancies with risk factors, the maternal skeleton undergoes more progressive bone loss due to excessive bone resorption. Loss of trabecular mineral content resulted by lactation is expected to be subsequently restored, but only a few studies in Korea have investigated the effects of pregnancy and lactation on postmenopausal osteoporosis.

Materials and methods: The initial study included a total of 2360 menopausal women who had undergone the bone mineral density (BMD) screening between 2010 and 2011, through the 5th Korean National Health and Nutrition Examination Survey (KNHANES). Of the 2360, excluded were women with thyroid disease, under medication for osteoporosis, unconfirmed age at menarche or menopause, and unconfirmed duration of lactation, leaving a total of 522 menopausal women for subject for analysis.

Results: The 522 menopausal women were classified into three groups based on the duration of their lactation as <25 months (group 1), 25–60 months (group 2), >60 months (group 3). In the adjusted model, osteoporosis was significantly less prevalent in group 2 (p = 0.008) and group 3 (p = 0.007) than group 1, indicating that the risk for osteoporosis significantly decreased with increased duration of lactation. No significant difference was found in femur neck BMD among the three groups. However, for lumbar spine, it was revealed that the risk for osteoporosis was significantly decreased with increased duration of lactation.

Conclusion: According to this study, parity or reproductive life span did not affect the development of osteoporosis in Korean menopausal women, and it was found that the risk of osteoporosis for lumbar spine decreases with increased duration of lactation. The protective effect of lactation on the postmenopausal BMD of lumbar spine in the study could be a good reference to encourage breastfeeding.

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P040

Osteoporotic risk in patients with gynaecologic cancer

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Objective: Patients with cervical cancer have lower bone mass than women without cancer, whereas women with endometrial cancer have higher bone mineral density (BMD) than control subjects, possibly due to the prevalence of high body-fat mass. The aim of this study was to compare BMD in patients with cervical cancer, endometrial cancer, and controls.
Methods: We analysed and compared spinal and femoral BMD in 130 patients with cervical cancer, 68 with endometrial cancer, and 140 age-matched menopausal female control subjects. We also compared serum calcium, phosphorus, total alkaline phosphatase, osteocalcin, and urinary deoxypyridinoline levels.

Results: Compared with the control group, T-scores for some lumbar vertebrae (L4), the femoral neck, and Ward’s triangle were lower in patients with cervical cancer, whereas only L4 T-scores were significantly lower in patients with endometrial cancer. Deoxypyridinoline levels were significantly lower in women with endometrial cancer ($P < 0.002$) than in women with cervical cancer, but no other biochemical variable differed among groups.

Conclusions: Cervical cancer was associated with lower BMD and may be a risk factor for secondary osteoporosis. However, endometrial cancer generally seemed to have no damaging effect on bone. A larger follow-up study is required to clarify these findings.

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P041

Up-regulation of inhibitors of DNA binding/differentiation gene during alendronate-induced osteoblast differentiation

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Objective: Patients with cervical cancer have lower bone mass than women without cancer, whereas women with endometrial cancer have higher bone mineral density (BMD) than control subjects, possibly due to the prevalence of high body-fat mass. The aim of this study was to compare BMD in patients with cervical cancer, endometrial cancer, and controls.

Methods: We analysed and compared spinal and femoral BMD in 130 patients with cervical cancer, 68 with endometrial cancer, and 140 age-matched menopausal female control subjects. We also compared serum calcium, phosphorus, total alkaline phosphatase, osteocalcin, and urinary deoxypyridinoline levels.

Results: Compared with the control group, T-scores for some lumbar vertebrae (L4), the femoral neck, and Ward’s triangle were lower in patients with cervical cancer, whereas only L4 T-scores were significantly lower in patients with endometrial cancer. Deoxypyridinoline levels were significantly lower in women with endometrial cancer ($P < 0.002$) than in women with cervical cancer, but no other biochemical variable differed among groups.

Conclusions: Cervical cancer was associated with lower BMD and may be a risk factor for secondary osteoporosis. However, endometrial cancer generally seemed to have no damaging effect on bone. A larger follow-up study is required to clarify these findings.

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P042

A monthly combined agent of ibandronate and cholecalciferol is effective in bone metabolism but not in muscle strength and bone mineral density in Korean 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 150 mg and cholecalciferol 24,000 IU on muscle strength and bone metabolism in postmenopausal osteoporosis.

Study design: 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 combination 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.

Keywords: Osteoporosis, Muscle strength, Bone mineral density, Ibandronate, Cholecalciferol

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P043

Dose laparoscopy-assisted vaginal hysterectomy with ovarian preservation affect ovarian reserve in early postoperative period?

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Objectives: The aim of this study was to assess the impact of laparoscopy-assisted vaginal hysterectomy (LAVH) with ovarian preservation on ovarian reserve in early postoperative period.

Materials and methods: Sixty premenopausal women aged 31–48 years with regular menstruation who underwent scheduled
LAVH with conservation of both ovaries were included in this study. None of those who underwent additional adnexal surgery were included in the present study. Serum samples were collected preoperatively and 3–days postoperatively and assayed for anti-Müllerian hormone (AMH) levels, and the changes between the two samples were analyzed.

Results: Postoperative Day 3 serum AMH levels (2.28 ± 2.00 ng/ml) significantly reduced compared with preoperative AMH levels (2.72 ± 2.13 ng/ml). The mean value of the rate of decline of AMH levels after LAVH was 20.90 ± 24.77%.

Conclusion: Our results suggest that LAVH may have an influence on ovarian reserve in early postoperative period.

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P044

Age-specific serum AMH (Antimullerien Hormone) levels in women with and without polycystic ovary syndrome

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AMH is considered as a reliable marker of ovarian reserve. Further, patients with PCOS have 3 times higher serum AMH levels than women without PCOS, yielding AMH to be a significant marker in the diagnosis of PCOS.

This cross-sectional study was conducted on a cohort of 1325 women admitted to the Istanbul University Cerrahpasa School of Medicine, Dept. of Ob&Gyn, between 2012 and 2016. We examined 475 women with PCOS and 850 women without PCOS. The serum AMH levels were categorized by age using 3-years-periods.

In our population, serum AMH levels showed a plateau until the age of 25. From the age of 25 years onward, AMH levels started to decrease and correlate inversely with age. The data also divided into percentiles for each age category. The mean AMH levels were 2.40 ng/mL, 4.27 ng/mL and 8.81 ng/mL (in 25th, 50th and 75th percentile) for ages between 21 and 23 years. The mean AMH levels were 1.98 ng/mL, 3.97 ng/mL and 7.48 ng/mL (in 25th, 50th and 75th percentile) for ages between 27 and 29 years. The mean AMH levels were 1 ng/mL, 2.15 ng/mL and 3.89 ng/mL (in 25th, 50th and 75th percentile) for ages between 33 and 35 years. The observed higher values were due to presence of PCOS and therefore, we split data into PCOS and non-PCOS for each age category. The mean AMH levels were 8.27 ng/mL in the PCOS group and 2.21 ng/mL in the control group for the 21–23-years-age group. The mean AMH levels were 8.37 ng/mL vs. 2.21 ng/mL for the 27–29-years-age group whereas those were 5.93 ng/mL vs. 1.79 ng/mL for the 33–35-years-age group, respectively.

Our results showed that ovarian aging is slower and later in women with PCOS than women without PCOS. Therefore, in the evaluation of ovarian reserve and serum AMH levels, the presence of PCOS should be considered. In turn, Straw stages during menopausal period should be regarded, if the woman has previously had PCOS in her life. Otherwise, this may easily cause an inaccurate or incomplete diagnosis or even treatment of patients.

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P045

Early reduction of ovarian reserve – How should we empower them with fertility?

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The number of human oocytes in a female is fixed and peaks at 6–7 mil during fetal life. At birth, a baby girl is born with 1–2 million oocytes, and at puberty she’s left with around 3–5 lakh oocytes.

Genetics, lifestyle, ethnicity, environment, ovarian surgeries, medical conditions like genital tuberculosis, cancer and cancer treatment, uterine artery embolization all affect the quality and quantity of oocytes. Ovarian reserve tests which include a basal FSH, Estradiol, Anti-mullerian hormone (AMH), inhibit B, ovarian volume and antral follicle count, can predict the IVF outcomes like oocytes retrieved, fertilization and implantation rates.

POR in young women occurs due to diverse etiological factors and majority of such women need to undergo in vitro fertilization (IVF) to achieve pregnancy. Nevertheless, pregnancy rates remain low in such women despite aggressive fertility treatments. Such women should be encouraged to attempt to conceive sooner rather than later.

Ovarian reserve tests can identify women at risk of reduced ovarian reserve, and aggressive fertility treatment may help such women to get pregnant is shorter than normal.

The key points in treating such women include avoiding prolonged, profound pituitary suppression, controlled ovarian stimulation and prevention of a premature LH surge.

Intrauterine insemination with COS yields very few pregnancies and should not be advocated in such cases. Addition to LH in the early follicular phase to the conventional high doses of FSH (450–600 IU/d) has a beneficial effect on oocyte and embryo quality. Pure HMG may be used for ovarian stimulation instead, and has been shown to improve oocyte yield. Short agonist protocols, is one of the most widely used agonist protocols in poor responders. Micro dose flare and ultrashort protocols have not been shown to improve the clinical outcomes in POR patients. Antagonist protocols have been found to deliver same pregnancy rates in women with POR as short agonist protocols.

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P046

The differences between the tibolone and transdermal estrogen in Korean symptomatic menopausal women

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Objective: To compare the efficacy between tibolone and transdermal estrogen for the menopausal symptoms in Korean menopausal women.

Methods: At Korea University Anam hospital obstetrics and gynecology department, 44 patients were recruited as tibolone group, who started tibolone as their first HRT and 49 as transdermal
Fibroid recurrence women aged 40 and older

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Objective: To evaluate the association between route of surgery, myoma weight, age and recurrence of leiomyomas following myomectomy in women aged 40 and above.

Design: A retrospective chart review.

Setting: Academic affiliated community hospital: Henry Ford Health System Patients: 64 women above the age of 40 who underwent uterine myomectomy, regardless of route, between 2003 and 2013.

Interventions: Uterine myomectomy, regardless of route (open, robotic, laparoscopic, hysteroscopic).

Measurements and main results: A total of 64 patients age above 40 were evaluated. 23 were open surgeries, 22 were laparoscopic/robotically, 10 hysteroscopically and 9 vaginally. A logistic regression model using route was used to predict recurrence. The open route was used as reference and the recurrence in other routes was compared. There was no association of route of surgery with recurrence (p 0.438). These women were followed for over a 10 year period. Recurrence was evaluated based on leiomyoma weight. Binary logistic regression model using myoma weight to predict recurrence was used. Odds ratio was scaled to 100 g increase in myoma weight. In this patient population followed over a 10-year period, we noted that for every 100 grams increase in myoma weight, the odds of having a recurrence increased by 25% (OR 1.25, p 0.028). Age was protective against in these older women with OR 0.90 (0.82, 0.98) and p = 0.023.

Conclusion: Fibroid recurrence is associated with increasing fibroid weight. This would play a role in preoperative counseling those patient with large or multiple uterine fibroids. Recurrence is not associated with route of myomectomy in women aged 40 and older.

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P048

Thyroid disorders associated with chronic liver disease

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Interest in the effect of thyroid gland functioning on other organs has grown in recent years due to increased recognition that its disorders have a significant impact on health and quality of life. Thyroid hormones regulate the basal metabolism of cells, including hepatocytes, thereby affecting the functioning of the liver, which in turn metabolizes thyroid hormones, regulating their systemic effects.

The aim of the study was to establish the prevalence of thyroid dysfunction in female patients with chronic liver disease and correlate this with the severity of the hepatic disease.

Materials and methods: 80 patients were randomly selected according to the following criteria: women of reproductive age with chronic liver disease (cirrhosis or hepatitis) of non-alcoholic origin, absence of organic disease of the pelvic organs, and absence of autoimmune diseases of the liver and thyroid. Severity of hepatic disease was established on the basis of clinical symptoms, blood biochemistry, ultrasound and scintigraphy of liver and thyroid, and the level of thyroid hormones (total T3, T4, fT3, fT4, TSH). Patients were divided into two groups, depending on the type of liver disease.

Results: Among the 40 patients with cirrhosis, thyroid gland volume was increased by 19.0% avg. (×2.4%), reduced T3 and fT3, and increased rT3, compared to the control group (changes similar to those of euthyroid syndrome disease). The T3/rT3 ratio was negatively correlated with the severity of cirrhosis. Among the 40 patients with chronic hepatitis B, levels of T4, T3 and thyroxine-binding globulin were elevated by 63.4% avg. (×1.6%) but levels of TSH and fT4 were in normal range, so they were euthyroid.

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The perimenopausal period starts with climacteric symptoms and lasts until the end of the first postmenopausal year. Clinical, terminological and laboratory variations make this period difficult to diagnose. Most of the patients undergo unnecessary and early hormone therapy when only laboratory findings are taken into consideration. Evaluation of the perimenopausal patients mainly with gestagen response was aimed in our study regardless of the laboratory findings.

Prospective, one-armed study was conducted from 2010 until 2016. Ninety-seven perimenopausal women with ages between 45 and 55 years were enrolled in the study. All women were assessed for AMH, FSH, E2, Prolactin, TSH levels parallel to ultrasonographic endometrial thickness assessment. Norethisterone acetate 5 mg b.i.d. was admitted to all patients for 7 days and response to the gestagen test was positive in 96.8% of cases, while vasomotor fibrous changes, six fibroadenomas (2.5–3 cm), four large simple breasts surveillance by US scan is performed if the US scan detected an anomaly. During surveillance, 22 cases of fibrous changes, six fibroadenomas (2.5–3 cm), four large simple cysts (3–5 cm) and one incipient breast cancer.

In conclusion, hormone levels are insufficient to diagnose the perimenopausal period and are meaningless in these perimenopausal patients, however, they may be used for research purposes. Treatment should be planned according to symptoms and contraception should be taken into account during perimenopausal period. Cyclic gestagen treatment should be considered as the first choice.

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delivered in group sessions has proven to be effective in alleviating treatment-induced menopausal symptoms in women with breast cancer. However, in-person CBT is inconvenient for some women and can result in low levels of program compliance. Accessibility and feasibility of the CBT program could be increased by offering the program via the Internet. The objective of this study was to evaluate the feasibility and to generate preliminary data on the efficacy of a guided, Internet-based CBT program.

**Methods:** Breast cancer survivors with treatment-induced menopausal symptoms were recruited. Self-report questionnaires were completed at baseline (pre-treatment) and 10 weeks (post-treatment). Counselors’ evaluations were obtained via interviews. Primary outcomes were program usage, compliance rates and patient and counselor satisfaction. Secondary outcomes were overall levels of endocrine symptoms and hot flush/night sweats (HF/NS) problem rating.

**Results:** Of the 21 women who participated in the pilot study, 90% completed the online CBT program. Satisfaction rates were high among both patients and counselors. Minor revisions to the program were advised. There was a significant decrease over time observed for overall levels of endocrine symptoms and HF/NS problem rating.

**Conclusion:** These findings suggest that an Internet-based CBT program for women with treatment-induced menopausal symptoms is feasible and promising in terms of efficacy. The efficacy of the CBT program is currently being investigated in a larger randomized controlled trial. If demonstrated to be efficacious and cost-effective, the availability of such a structured supportive intervention program will be a welcome addition to standard medical treatment offered to breast cancer survivors.

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**P053**


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**Objective:** To evaluate the epidemiological characteristics of 92 registered cases of patients affected on POF and to describe basal information of bone mineral density (BMD).

**Methods:**

- **Inclusion criteria:** High gonadotropin and low oestrogen before age 39.
- **Basal evaluation:** Medical history, hormonal determination (FSH, LH, E2, PRL and TSH) and biochemical profile.
- **Complementary studies:** Immunological study including antithyroid, antiphospholipidid and antinuclear (ANA) antibodies; karyotyping and determination of FMRI premutations to detect molecular changes related to X-Fragile Syndrome. Finally, measure of bone mineral density (BMD) by dual energy X-ray (DEXA).

**Results:** 92 cases were evaluated, mean age of POF diagnosis was 33.17 years old and mean patients Body Mass Index (BMI) was 25.16 kg/m².

In 10.8% of cases, an active autoimmune disease was detected and 13.04% had positive antibodies non-related to a clinically active disease. Furthermore in 15.3% of patients an oncological history was recorded, including 11% of them chemotherapy, 3.6% radiotherapy and 5.43% ovarian surgery.

Family history of POF was present in 29.3% of patients. The genetic evaluation disclosed 3.3% cases of chromosomal alteration and 6.5% cases of abnormal count of Fragile X pre-mutations. 52 cases were considered as idiopathic.

BMD was determined in 48 cases and analysed in respect to BMI: 41.6% presented a normal study and mean BMI of 27 kg/m²; whereas 58.3% shown an alteration on BMI and mean BMI of 23 kg/m², determining a SD in this outcome (p = 0.024).

More than 90% of patients treated with hormonal therapy.

**Conclusions:** In our results, previous oncologic treatments remain the best-known and frequent cause of POF. Familiar association also stand out in epidemiology, even though as in the literature, the cause of POF persists mainly undetected. It is necessary to take into account effects of decreased BMD, among others, to preserve the health of our study population.

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**P054**

**Detection of genome wide causal genes of premature ovarian failure by whole exome sequencing**

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Premature ovarian failure (POF) is defined by amenorrhea before the age of 40 along with hypergonadotropic hypogonadism. It is a genetically heterogeneous disease that mutations in over 50 genes are discovered as candidate causal genes and a lot of other genes and pathways seem to implicate. Therefore, genome wide screening is necessary to elucidate underlying causal genes and pathways related with POF. In this study, we identified novel coding variants by analyzing exome sequences of 37 Korean POF patients. Among 37 POF patients, two patients with Y chromosome and one patient with X chromosomal abnormality were filtered out. To prioritize candidate genes, recurrently mutated genes which have more than 3 missense mutations were considered. Genes harboring loss of function variants which are predicted nonsense and splice site mutation were also selected. Total 188 genes were selected and there was only one previously reported POF gene, DIAPH2. Enriched GO term and pathway of the genes were active transmembrane transporter activity (GO:0022804) and ATP binding cassette (ABC) family protein mediated transport which is known to be related with reproduction. We identified mutated ABC transporter genes in ten of 34 (29%) POF patients and GO:0022804 related genes in 15 of 34 (44%) patients. Taken together, these findings suggest that whole exome sequencing and bioinformatics analyses are effective strategies for the detection of genetic variants likely to identify causal candidate genes of POF.

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P055

Genetic causes of premature ovarian failure
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Among known causes of premature ovarian failure are included chromosomal defects, exposure to radiation, certain drugs and autoimmune diseases. Even if medicine progresses daily, approximately 75–90% of cases of premature ovarian failure remains etiologically undiagnosed. Discovery on human genome enlarged greatly the list of mutation that can cause ovarian failure. We studied the incidence of the most common chromosomal defects related to primary ovarian insufficiency; 100 patients with unknown cause of premature ovarian failure have undergone genetic testing. No case lack of a second X chromosome (Turner syndrome) or X chromosome deletion was registered. The FMR1 gene premutations, carriers of X fragile syndrome, was positive in 9% percent of cases. In our studied group 3 cases of asymptomatic galactosemia were discovered. The percentage of fragile X syndrome premutation carriers in our studied group corresponded with the results published by other studies. Considering the fact that fragile X premutation carriers present a relative infertility this may implicitly signify that the patient can be a carrier for a mental retardation allele, we consider that the screening for FMR1 premutation in women with premature ovarian insufficiency should be recommended.

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P056

Diminished ovarian reserve and primary ovarian insufficiency in two women with celiac disease. Is there a link?
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Introduction: Celiac disease (CD) is the most common life-long food sensitive enteropathy in humans, characterized by malabsorption, chronic inflammation of small intestine mucosa, villous atrophy and, crypt hyperplasia. CD occurs as a consequence of the ingestion of wheat gluten or related rye and barley proteins. Celiac disease may be associated with a wide range of diseases, including infertility and miscarriages.

Aim: We report two young women with CD and abnormal ovarian function.

Materials and methods: We present a 33 year-old woman with CD and diminished ovarian reserve and a 39 year-old woman with CD and primary ovarian insufficiency, both non drinkers and non smokers.

Results: Both patients had bowel disorders from childhood and mild anemia. Diagnosis of celiac disease was made by small bowel biopsy. A gluten free diet has improved bowel symptoms, without improvement of ovarian function.

Conclusion: Diminished ovarian reserve and primary ovarian insufficiency represent impaired ovarian function. The possible impact of celiac disease in the ovarian function requires further investigation.

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P057

The effect of treatment on work ability in women with severe menopausal symptoms
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Background: Women experiencing severe menopausal symptoms report serious problems dealing with the physical and mental demands of their work resulting in low work ability. Treatment of menopausal symptoms has been a major subject of study. Hormonal replacement therapy (HRT) is the most effective in reducing symptoms, but several non-hormonal management options have also shown to be effective. However little is known about the effect of alleviation of menopausal symptoms on perceived work ability.

Objective: To evaluate the effect of treatment on work ability in women with severe menopausal symptoms.

Study design: This longitudinal study investigated the effect of treatment of menopausal symptoms on self-reported work ability. Attendees of a menopause clinic (n = 31) filled out self-reported questionnaires assessing work ability (Work Ability Index; WAI) and menopausal symptoms (Greene Climacteric Scale; GCS) at their first visit and at their follow-up appointment 3–6 months thereafter.

Main outcome measures: The paired-samples t-test was used to compare the mean difference between the work ability and menopausal symptoms reported at the first visit and at follow-up.

Results: Self-reported menopausal symptoms were significantly reduced at follow-up (mean total GCS-score 26.57 vs 14.73 t(30) = 8.02, P < 0.001). Work ability at follow-up was significantly improved (M = 34.85, SE = 1.08), compared to the first visit (M = 30.73, SE = 1.15). This difference in WAI outcome, −4.13, BCa 95% CI [−5.89, −2.23], was significant t(30) = −4.82, P < 0.001. Within this group 21 women were treated with hormonal replacement therapy.

Conclusions: Alleviation of menopausal symptoms leads to improvement of work ability over a relative short time period.

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Factors associated to three menopause symptoms in Afro-Colombians with the 10-items Cervantes Scale

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Objective: Identify factors associated to hot flushes (HF), aching in muscles and/or joints, vaginal discomfort and dryness in Afro-Colombians with 10-items Cervantes Scale (CS-10).

Methods: Cross-sectional study of the project CAVIMEC (Calidad de Vida en la Menopausia y Étnicas Colombianas), support for the ethics committee of the Universidad de Cartagena, Colombia. Black-skinned women, daughters of black mother and father and who recognize themself as Afro-Colombian, were included. Participation voluntarily, anonymous, with informed consent. We used sociodemographic questionnaire and CS-10, adaptation from the 10-items Cervantes Scale (CS).

Results: Were studied 646 women, mean age 48.7 ± 5.7 years, a premenopausal 41.9% premenopausal, 17.4% perimenopausal and 40.5% postmenopausal. Cronbach’s alpha 0.82. The 73.1% reported HF, 71.3% aching in muscles and/or joints and 25.5% vaginal discomfort and dryness. Risk factors associated to HF: age group 50–54 years OR: 3.8 [2.2–6.6], overweight OR: 3.2 [2.1–5.0] and work activity outside home OR: 1.4 [1.0–2.1]. Obesity-II OR: 4.1 [1.5–11.0], age group 50–54 years OR: 4.6 [2.6–8.1], currently attached OR: 1.9 [1.3–2.7], postmenopausal for more than 5 years OR: 2.2 [1.1–4.2], were associated with aching in muscles and/or joints. Vaginal discomfort and dryness had risk factors: smoking now OR: 3.3 [1.9–5.7], perimenopause OR: 2.7 [1.6–4.6], postmenopause OR: 3.4 [2.2–5.2]. The protective factors for this symptom: the use of hormonal therapy OR: 0.2 [0.1–0.5], work activity outside home OR: 0.4 [0.3–0.6] and postmenopausal after 45 years OR: 0.4 [0.2–0.7].

Conclusions: Different risk and protective factors are associated to HF, aching in muscles and/or joints, vaginal discomfort and dryness.

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Comparison of the quality of life of climacterics belonging to two Colombian ethnics. Evaluation with Cervantes Scale

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Objective: To compare the quality of life of climacterics Colombian belonging to two different ethnics groups with Cervantes Scale (CS).

Methods: Cross-sectional study is part to project CAVIMEC (Calidad de Vida en la Menopausia y Étnicas Colombianas). We included age 40–59 years’ women, mestizas and afro descendents, residents to Caribbean Colombian. We employed sociodemographic questionnaire and CS, specific instrument with 31 questions that assess symptoms, domains and quality of life in climacteric. The higher score has worse result. Participation anonymous, voluntarily, with informed consent. EPI-INFO-7 was used to statistical analysis. p < 0.05 was considered statistically significant.

Results: Were participated 1894 women. 646 (34.1%) afro descendents and 1248 (65.9%) mestizas, age mean 48.7 ± 5.7 and 48.2 ± 5.8, respectively. The afro descendents group had more prevalent than mestizas in hot flashes suddenly, effortless hot flashes, more fluids retention and hot flashes at all times (p < 0.05). The mestizas had more presence than afro-descendent in headache every day, considered herself nothing happy with couple, they felt the couple role none important, do not have a good health and sexual life any important (p < 0.05). In other 22 questions of the CS did not watch significant difference. The mestizas had significantly greater psychic, sexual, relationship impairment, health and aging deterioration, as well as less impairment of vasomotor symptoms than afro descendents. Global score of the CS was 39.2 ± 22.6 afro descendents and 43.7 ± 25.0 mestizas, p = 0.0003. There was greater and severe deterioration of sexuality and the relationship of mestizo couples (p < 0.001).

Conclusions: Were observed differences in the asses of some symptoms, impairment of domains and quality of life, to compare mestizas and afro descendents Colombians.

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Characterization of the 10-item Cervantes Scale (CS-10) and lifestyle in a sample of Brazilian women

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Aim: To characterize a Brazilian women sample, considering lifestyle and quality of life.

Methods: A cross-sectional study from Brazilian southern cities included 420 mid-aged women (40–61 years), which completed the 10-item Cervantes Scale (CS-10) and a socio-demographic questionnaire. Questions about lifestyle and habits were analysed using SPSS, version 21.0, considering menopausal status. Lifestyle descriptive analysis was carried out. Categorical variables were expressed as relative frequencies (% ) and continuous variables as median [25–75 percentiles].

Results: Most women were married (70%), multiparous (64%), employed (67%), non-smokers (68%), had a sexual partner (88%),
had similar educational level (11.76 [11.41–12.47]), and family income (in minimum wages, 3.20 [2.13–6.40]). They moderately to never consume hot beverages (60%) or alcohol (68%), but frequently drink coffee (82%) and exercise (52%). They were categorized in pre (n = 154), peri (n = 53) or postmenopausal (n = 213) women, and the median age of menopause was 48.00 [46.16–47.41] years. CS-10 analysis revealed that women self-reported, from a moderated to a severe manner: anxiety and mood changes (70%); joint stiffness, aches and pains (66%); skin alterations (e.g. texture, color) (59%); sleeping difficulties (53%), tiredness (51%), hot flushes and night sweats (49%), palpitations (38%), vaginal dryness complaints (39%), depression (34%), and urinary incontinence (14%).

**Conclusion:** Main complaints were related to mood, osteoarticular system, skin, sleep, tiredness and hot flushes, although most of Brazilian women have presented a healthy lifestyle, configuring climaterium as a period whose manifestations involve a complex biopsychosocial mechanism.

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P061

**Menopause Rating Scale (MRS) and Brazilian women lifestyle characterization**

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**Aim:** To verify factors associated with quality of life in a sample of Brazilian women.

**Methods:** A cross-sectional study from Brazilian southern cities included 420 mid-aged women (40–61 years), which completed the Brazilian Portuguese version of the 10-item Cervantes Scale (CS-10) and a socio-demographic questionnaire. Questions about lifestyle and habits were analysed using SPSS, version 21.0, considering menopausal status. Comparisons between status, by Kruskal–Wallis test, and correlations among all variables were carried out. Categorical variables were expressed as relative frequencies (n%) and continuous variables as median [25–75 percentiles].

**Results:** Most women were married (70%), multiparous (64%), employed (67%), non-smokers (68%), had a sexual partner (88%), had similar educational level (11.76 [11.41–12.47]), and family income (in minimum wages, 3.20 [2.13–6.40]). They moderately to never consume hot beverages (60%) or alcohol (68%), but frequently drink coffee (82%) and exercise (52%). They were categorized in pre (n = 154), peri (n = 53) or postmenopausal (n = 213) women, and the median age of menopause was 48.00 [46.16–47.41] years. MRS analysis revealed that women self-reported, from a moderated to a severe manner: joint stiffness, aches and pains (59%); irritability and mood changes (52%); problems with memory and concentration (52%); anxiety (51%) and depressive mood (41%); sleeping difficulties (51%); hot flushes and night sweats (41%); reduced libido (41%), heart palpitations (30%), vaginal dryness complaints (29%), and urinary dysfunctions (17%).

**Conclusion:** Most of women have presented a healthy lifestyle such as non-smoking and regular physical exercise; however, there was an apparent influence of the menopause in the osteoarticular system, mood and sleep, possible due to regulation by estrogen, which affects quality of life.

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Besides, premenopausal women reported greater vaginal lubrication with aging and marital status had a great influence in women's postmenopausal group, suggesting that this condition, together with family income and physical activity, and negatively related to being married and menopausal status.

**Conclusion:** A greater intensity of symptoms was related to postmenopausal women, suggesting that this condition, together with aging and marital status had a great influence in women's quality of life.

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P063

Factors associated with Brazilian Portuguese 6-item Female Sexual Function Index (FSFI-6) in a sample of Brazilian women

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**Aim:** To verify factors associated with sexual function in a sample of Brazilian women.

**Methods:** A cross-sectional study from Brazilian southern cities included 420 mid-aged women (40–61 years), which completed the Brazilian Portuguese version of the 6-item Female Sexual Function Index (FSFI-6) and a socio-demographic questionnaire. Questions about lifestyle and habits were analysed using SPSS, version 21.0, considering menopausal status. Comparisons between status, by Kruskal–Wallis test, and correlations among all variables were carried out. Categorical variables were expressed as relative frequencies (n%) and continuous variables as median (25–75 percentiles).

**Results:** Most women were married (70%), multiparous (64%), employed (67%), non-smokers (68%), had a sexual partner (88%), had similar educational level (11.76 [11.41–12.47]), and family income (in minimum wages, 3.20 [2.13–6.40]). They moderately to never consume hot beverages (60%) or alcohol (68%), but frequently drink coffee (82%) and exercise (52%). They were categorized in pre (n = 154), peri (n = 53) or postmenopausal (n = 213) women, and the median age of menopause was 48.00 [46.16–47.41] years. Premenopausal women displayed higher sexual desire, when compared to post (p = 0.035) and perimenopause (p = 0.031) groups. Besides, premenopausal women reported greater vaginal lubrication, when compared to post menopause group (p = 0.032). The female sexual function index was higher in premenopausal women, when compared to postmenopausal group (p = 0.018). Both desire, vaginal lubrication and female sexual function index were positively related to family income and physical activity, and negatively related to being married and menopausal status.

**Conclusion:** Our data suggest that postmenopausal women displayed low libido and sexual function, probably due to low hormone enrolled in this life stage, while physical activity seems to reverse this reduction.

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P064

Investigation of quality of life in menopausal women in Iran

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**Background and objectives:** Menopause is sensitive and critical period, and the implications and complications associated with that women with problems facing new difficulties and these problems may cause disruption in the health and quality of life process. Given that the quality of life is an important health issue of postmenopausal women, an interest in various communities and is one of the fundamental objectives of the health care in this era. The present study was to evaluate the quality of life of menopausal women in Hamadan in 1394.

**Methods:** This is a descriptive cross-sectional study. In which 103 postmenopausal women aged 60–40 in Hamadan were randomly selected and studied. The instrument for collecting demographic questionnaire and quality of life during menopause.

**Results:** The results showed that overall quality of life was medium in 68% of the cases. Quality of life score associated with education level (p = 0.027), economic status (p = 0.044) and job status (p = 0.045).

**Conclusion:** The results of this study showed that menopause causes a change in the quality of life women. Therefore, designing and implementing appropriate educational programs are necessary to promote the quality of life in menopausal women.

**Keywords:** Menopause, The quality of life, Women
P066
Effect of group counseling on quality of life of menopausal women in Iran
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Objective: Menopause is a critical period of life for women. During this phase many women face with problems that can cause health problems and disturb their quality of life. This study aimed to investigate the effect of counseling on quality of life in postmenopausal women conducted in 2015 in Hamadan, Iran.

Methods: In this quasi-experimental study, 80 postmenopausal women were randomly selected and allocated to case and control group (40 per group). Data collection tool included questionnaires of demographic information and quality of life during menopause, which were completed by the samples before the intervention. In the case group, training program was run during 4 sessions in the form of weekly consulting sessions for 45–60 min. Training program included familiarity with menopause symptoms, confrontation and self-care during this period. In control group, only routine care affairs were conducted. Three months after interven-

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P067
Quality of life of women postmenopausal in a municipality, São Paulo, Brazil
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Introduction: Menopause is a physiological process of physical change and emotional. The quality of life has been increasingly recognized in terms of satisfaction and well-being in relation to expectations and goals achieved and reflect the intensity of symptoms and level of physical and emotional losses.

Objective: To evaluate quality of life of Brazilian women after menopause, residents in the city of Caçapava.

Methodology: Cross-sectional study with 80 postmenopausal women treated at a health care, assessed by the validated instrument by WHO WHOQOL Bref in the physical, psychological, social relationships and environment.

Results: The physical domain had mean (52.49 ± 9.10), the social relationships domain (64.09 ± 12.45), psychological (51.12 ± 12.59), environmental revealed (55.1 ± 10.72).

Conclusion: We found scores compatible with satisfactory quality of life. The married had a higher chance of being among the best scores in the Social Relations domains. Difficulties in moving, transportation, access to information and little leisure seem to be considerable factors affecting the QoL in postmenopausal women.

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P068
The impact of anthropometrical changes of corpulence and weight gain on self esteem of the menopausal women in the region of Nador
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Menopause is a period of transition where women are confronted to many physical and psychological changes that can affect...
their life style, she endures many classical unpleasant symptoms including menopausal weight gain and corpulence changes. The bodily changes and the image that the woman perceives on herself during this period can play an important role on her well-being, self-esteem and psychological health.

The purpose of this study was to investigate the impact of anthropometrical changes of corpulence and weight gain on self esteem of the menopausal women in the region of Nador, also how can these changes affect their body image and increase the risks of psychological problems. A total of 250 women aged between 40 and 59 years took part in this study. The data were collected using a questionnaire on their lifestyle, feelings and psychological experiences of women also we used the anthropometric measurements and scale for body image.

It was observed that the majority of menopausal women suffer from gain weight with a high percentage of body fat which has a negative impact on their self-perception and affects their femininity. Very few studies have been addressed in this subject particularly in Morocco, although it seems important to highlight the impact of menopausal transition on the psychological health, body image and well being of women.

**Keywords:** Self esteem, Menopause, Gain weight, Psychological health

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**P069**

**Performance of the 21-item “Vulvovaginal Symptoms Questionnaire” in postmenopausal Spanish women**

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**Background:** Vulvovaginal symptoms (VVS) are highly prevalent after the menopause, however, not accurately assessed with the ordinary quality of life tools. Hence, appropriate evaluation is mandatory to provide correct treatment.

**Aim:** To assess VVS in postmenopausal Spanish women.

**Methods:** In this pilot cross-sectional study the Spanish language version of the 21-item Vulvovaginal Symptoms Questionnaire (VSQ) was applied to postmenopausal women seeking routine gynecological care in order to assess VVS. Confirmatory factor analysis was performed to verify the four a priori sub-scales by evaluating the goodness of fit of the final model. The internal consistency of the scale and that of its subscales was assessed by calculating Cronbach’s alpha coefficients.

**Results:** One hundred fifty postmenopausal women aged 45–75 years participated in the psychometric validation of the VSQ. Mean age was 58.9 ± 5.7 years, the majority were Caucasian (92.7%), 91.3% were naturally menopausal, 10% used phytoestrogens, 64% lived in rural areas and 10% smoked. Calculated Cronbach’s alpha coefficients were 0.88, 0.69, 0.73, 0.57, and 0.81 for the whole VSQ scale and the symptoms, emotions, life impact and sexual impact subscales respectively. Median [IQR] VSQ scores were higher among women with vulvar symptoms, 4.0 [6.0] as compared to those without, 0.0 [0.5] (p < 0.0001). Among women who were currently sexually VSQ were higher among symptomatic ones 7.0 [6.0] as compared to asymptomatic ones, 0.0 [0.1] (p < 0.0001). Results were similar among non-sexually active women (3.0 [3.0] vs.0.0 [0.25]; p < 0.001). Vulvar symptoms increase with age in sexually active women, and with the use the phytoestrogens (possibly a confounding factor). However, in non-sexually active ones it was related antidepressant use.

**Conclusions:** Internal consistency of the VSQ in this postmenopausal Spanish sample, in which age and psychotropic drug treatment were important covariates.

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**P070**

**The impact on self-regard of menopausal atrophic vaginitis**

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The hypoestrogenic state that characterize menopausal period, involve vaginal atrophy and various symptoms related to it: dryness, burning, dyspareunia with postcoital bleeding and sexual dysfunction. This is one of the problems that is usually ignored, not discussed with the clinician and by not knowing the treatment possibilities the patients prefer to make lifestyle changing, such as stopping sexual activity and get used to the idea of aging. We intended to assess from a subjective point of view the importance of an active sexual life in the prevention of vaginal atrophy and on a better self-regard. In this study 43 postmenopausal women with symptoms of vaginal atrophy were included. A questionnaire with 10 questions was applied at first visit, after a half a year and after a year. The questionnaire targeted the intensity of vaginal atrophy symptoms, the social impact, the sexual activity and the impact on personal life. All patients included in the study were asked to respect a sexual intercourse frequency of at least four times per month. After half year, more than 50% of investigated women declared that experienced an improvement of symptoms, with a progressive betterment of the sexual life and a real positive change regarding their self-regard as a woman. A year later by the inclusion in the study the percentage grew to 73%. According to other study the impact of a sexual active life consist in a grown level of androgens and gonadotropins.

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P071

The effect of chronic vulvar dystrophy on urinary continence in patients at climacterium

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Chronic dystrophy is the growth of abnormal skin on the vulva, its causes being lichen sclerosus, with thin vulvar skin lesions and squamous hyperplasia with thick tegument. Lichen appears as discolored, translucent irregular areas of skin on/around the labia especially in women at climacterium. It can cause from lack of clinical manifestations to intense itching and progressive vulvar pain. Squamous hyperplasia transforms vulvar skin thick with white elevations causing intense itching. We examined a number of 22 climacteric patients, aged between 52 and 73 diagnosed with vulvar dystrophy in the interval 2014–2016. Urinary incontinence was diagnosed in 90% of them: 36% presented stress urinary incontinence, 40% mixed incontinence (vulvar dystrophy being a factor in the continence impairment), while in 22% of the cases the main etiology of the disease was the severe alteration of the vulvar anatomy. The 5 cases presenting important distortion of the external genital organ anatomy included partial labial adhesion or complete labial fusion caused by chronic dystrophy and required surgical intervention. The etiology in the appearance of labial adhesions is thought to be inflammation of the labia with denudation of the superficial layer which heals by fibrosis causing adhesions. Labial fusion in menopause is a rare condition which in addition to chronic dystrophy has other two risk factors: relative hyperandrogenism associated with lack of estrogens and chronic urinary tract infections (UTI). Regarding recurrent UTIs, they represent both a risk factor and a consequence of labial fusion, the urine dribbling through the labial adherence over the external urethral orifice and draining through the vagina. Labial fusion affecting urinary continence is an uncommon phenomenon in postmenopausal women. The prognosis is good with surgical treatment, while estrogen and corticosteroid topic application should be used as prophylaxis for recurrence.

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P074

Comparison chemical, clinical pregnancy rate, live birth rate and obstetric outcome in fresh versus frozen embryo transfer in in vitro fertilization cycles

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Introduction: There is inadequate investigation about results of two methods of IVF via fresh or freeze thawed embryo transfer so this study was done to compare pregnancy rate, live birth rate, obstetrics and prenatal complications in singleton pregnancies after these two methods.

Material and methods: In this retrospective cohort study 559 women who were referred to infertility clinic of Shahid Behshhti hospital in Isfahan and another private clinic were recruited. According to patient situation they received fresh or freeze thawed embryos. Obstetrical outcomes were assessed by calling and interviewing patients who became pregnant.

Results: The results showed that in 303 frozen cycles there were 70 alive pregnancy in compare with 256 fresh embryo transfer who had 46 alive pregnancy (p = 0.04).

Singleton pregnancy after transfer of frozen thawed embryo was associated with more preterm labor in compare with fresh embryo transfer (p = 0.03).

Data analysis showed that other obstetrics outcome such as gestational hypertension, gestational diabetes, ante partum hemorrhage, I UGR, LBW, admission to NICU was the same in both groups.

Conclusion: Although the fresh embryo transfer is the commonest way in IVF cycles, Results of our study showed that rate of live birth with freeze thawed embryo transfer was more and rate of pregnancy complication and prenatal outcomes were the same.

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Keywords: IVF, Fresh embryo, Freeze thawed embryo, Infertility, Obstetrics outcome

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P075

Relative importance of the different components of the Bologna criteria for predicting poor ovarian response in assisted reproduction

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Introduction: The Bologna criteria published in 2011 defined poor ovarian response (POR) in women undergoing in-vitro fertilisation (IVF) treatment by 2 out of the 3 criteria: advanced maternal age and/or other clinical risk factor for POR (Bologna 1), 3 or less oocytes retrieved in a previous IVF cycle with conventional stimulation protocol (Bologna 2) and abnormal ovarian reserve test (Bologna 3). This retrospective analysis aims at evaluating the relative importance of the three criteria in prediction of POR and live-birth outcome.

Methods: Data on 132 women undergoing the second IVF treatment cycle in Queen Mary Hospital, Hong Kong, between January 2012 and June 2013, who fulfilled the Bologna criteria for POR, were retrieved and analysed. In this study, women aged ≥40 years and/or having history of endometriosis or ovarian surgery were classified as Bologna 1; those having 3 or less oocytes retrieved in the previous IVF cycle with conventional stimulation protocol (Bologna 2) and abnormal ovarian reserve test (Bologna 3). This retrospective analysis aimed at evaluating the relative importance of the three criteria in prediction of POR and live-birth outcome.

Results: Subjects with Bologna 1+2 (n=12) had significantly more retrieved oocytes and utilizable embryos compared to those with Bologna 2+3 (n=49) or Bologna 1+2+3 (=26) (p<0.05), but not Bologna 1+3 (n=45). There was no significant between-group difference in pregnancy rate. However, those with Bologna 1+2+3 had significantly worse live-birth rate (0%) compared to those with Bologna 1+2 (33.3%, p<0.05) or Bologna 1+3 (15.6%, p<0.05).

Conclusions: Poor ovarian responders fulfilling different combinations of the Bologna criteria had different IVF outcomes. The best ovarian response and live-birth rate were observed in those with Bologna 1+2 with normal antral follicle count, and the worse in those fulfilling all three criteria.

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P076

The association between interleukin-10 (IL-10) -592C/A, -819T/C, -1082G/A promoter polymorphisms and endometriosis

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Purpose: Endometriosis has an incidence reaching up to 50% in infertile women. Cytokine-mediated immune responses seem to play an important role in endometriosis pathogenesis, but still the etiology and pathophysiology remain unclear. In the current study we tried to investigate whether there is a relationship between IL-10 genetic polymorphism, serum levels of IL-10 and the presence of advanced endometriosis.

Methods: The presence of IL-10 592C/A, 819T/C, 1082G/A promoter polymorphisms and IL-10 serum levels were investigated in advanced endometriosis patients compared to healthy controls. Genomic DNA was extracted from peripheral blood leukocytes and further analyzed by PCR.

Results: IL-10 serum levels were significantly higher in endometriosis group compared to controls (1.48, 0.68, p<0.001). We observed a significant association between IL-10 592C/C and 8199C/C genotypes, presence of C alleles and an increased risk of endometriosis. No difference was observed in IL-10 serum levels corresponding to different alleles or genotypes.

Conclusion: Our results suggest that IL-10 592C/A and 819T/C promoter polymorphisms confer susceptibility to endometriosis. No associations were found between the IL-10 1082A/G polymorphism and susceptibility to endometriosis.

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P077

Abdominal wall endometriosis: Prevalence and clinical spectrum

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The purpose of our study was to evaluate the prevalence and clinical findings including radiologic features of abdominal wall endometriosis. A retrospective search of our institution’s database over a 10-year period was performed. We found 68 surgically proven cases of abdominal wall endometriosis. All patients had undergone sonography including power Doppler examination. Additional CT was performed in 54 patient. The clinical data were analyzed, and the imaging studies were reviewed by radiologists. All patients had a history of at least one prior cesarean section. All presented with focal pain near the surgical scar, which was cyclic in three patients. 61 patients presented with a palpable mass near the scar. Sonography detected 65 lesions within the abdominal wall, with a mean diameter of 28 mm. All lesions were hypoechoic, vascular, and solid, with some cystic changes in one. The calculated frequency of abdominal wall endometriosis is approximately 0.9% of all women who had a cesarean delivery. Abdominal wall endometriosis frequently presents with non-cyclic symptoms. Imaging findings of a solid mass near a cesarean section scar strongly suggest its diagnosis.

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P078

Submucosal fibroids, intracavitary fibroid – A case report

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Introduction: The vast majority of women with fibroids go through life, have their children without knowing they harbor fibroids in their wombs. Women, who do have symptoms, it includes pain and heavy menstrual bleeding. Fibroids are classified according to their location within the uterine wall—intramural fibroids; subserosal fibroids; submucosal fibroids. A pedunculated lesion within the cavity is termed an intracavitary fibroid and can be passed through the cervix. Cervical fibroids.

Case presentation: A 43 years old lady having two kids came with the chief complaint of excessive bleeding with clots, pelvic pain, incontinence, painful sexual intercourse and prolonged monthly periods. On per speculum examination, it was noted – fibroid extend trough the cervix. A provisional diagnosis of intracavitary fibroid was made. All routine investigations were normal. Urine routine examination and microscopic examination: Normal specific gravity. Ultrasound was done in full bladder showing normal size uterus, endometrial cavity was filled by a hypoechoic solid mass of 33 × 28 mm, with polype or pedunculated lesion, which is projected from the inner lining the uterus and extended through the cervix. No intra mass degeneration or calcification was seen and diagnosed as submucosal fibroid. Bilateral ovaries were enlarged and cystic degenerated. Total abdominal hysterectomy with bilateral salpingo-oophorectomy was done. Histopathological report confirmed intracavitary fibroid. Her recovery was smooth.

Conclusion: Fibroids are the most common benign tumors in females and typically found during the middle and later reproductive years. The most fibroids are asymptomatic, they can grow and cause heavy bleeding, painful sexual intercourse, urinary frequency. Menstrual cycle may last for more than seven days and may notice large blood clot formations. Symptoms caused by uterine fibroids are a very frequent indication for hysterectomy.

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P079

Submucosal myomas vaporisation using laser diode in outpatient with paracervical anesthesia

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Background: Uterine fibroids are the most common pathology in uterus. A large part of the fibroids are submucosal. Hysteroscopic myomectomy is considered the approach technique of choice for patients with symptomatic submucous fibroids who produce, in particular, heavy uterine bleeding, infertility or repeat abortions. There are different techniques for outpatient hysteroscopic myomectomy (miniresectoscopy, versapoint or laser).

Objective: Describe the outpatient hysteroscopic resection of submucosal myomas using laser diode and the advantages of this procedure against the other techniques.

Methods: Outpatient resection of fibroids is now possible using the technique of vaporization with diode laser or with electric energy with a bipolar electrode called Versapoint or with a bipolar miniresectoscope. We describe the technique with laser diode using a 5.8 mm hysteroscope of external diameter. The MyoTwister fiber has a curvature that allows to work ideally in the uterine cavity. Patients with a high degree of anxiety would not be good candidates to the procedure. The advantage with regard to the resectoscope is that it is done outpatient, with no income, without general or spinal anesthesia, very good tolerance for the patient and allows immediate patient recovery.

Results: The efficacy of the technique is assessed by % of resected fibroids and degree of tolerance for the patient. Many studies show that after the intervention, the rate of myoma resected is more than 90%, high percentage of patients’ tolerability and recovering normal menstruations.

Conclusions: According to all published data, the results obtained are encouraging, with a high percentage of complete resection of the myoma and with great tolerability by the patients.

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P081

Pretreatment vitamin D deficiency is associated with poor breast cancer prognostic features in postmenopausal women

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Objective: To evaluate the association between pretreatment vitamin D (VD) deficiency with breast cancer (BC) prognostic features in postmenopausal women.

Methods: An analytical cross sectional study was conducted with 192 women, aged 45–75 years. Women with recent diagnosis of BC, in amenorrhea >12 months and age ≥45 years were included. Serum level of 25-hydroxyvitamin-D [25(OH)D] was measured in all patients 20–30 days after BC diagnosis, and values of 25(OH)D < 30 ng/mL were considered as VD deficiency. Data on BC (type, grade, tumor stage, lymph node status), estrogen receptor (ER), progesterone receptor (PR), HER2 and epithelial proliferative activity (Ki-67) were collected. For statistical analysis, t-Student test, chi-square test and logistic regression (OR-odds ratio) were used.

Results: The median 25(OH)D level was 25.8 ng/ml (range 12.0–59.2 ng/ml). Sufficient VD levels were detected in 65 patients (33.8%), while deficient levels in 127 cases (66.2%). Participants with deficient 25(OH)D levels had a higher proportion of tumors with a high grade and locally advanced and metastatic disease, more positive lymph node, a lower proportion of ER, PR positives tumors and higher Ki-67 (p < 0.05). Patients with normal VD had a higher frequency of luminal A and luminal B (80%) when compared to patients with VD deficiency (65.2%) (p < 0.05). Further, all cases of triple negative were detected in VD deficient women. Multivariate analysis, after adjusting for age, time since menopause and BMI, showed that a deficient level of VD was an independent prognostic indicator of positive axillary lymph node status (OR 2.26, CI
95% 1.10–5.16, \( p = 0.043 \), negative ER (OR 4.18, CI 95% 1.17–15.87, \( p = 0.034 \)), and high Ki-67 (OR 2.78, CI 95% 1.34–66.65, \( p = 0.005 \)).

**Conclusions:** In postmenopausal women with BC, there was an association between VD deficiency and tumors with worse prognostic features. VD deficiency was shown to be a risk factor for ER negative tumors, with positive axilla and a higher rate of cell proliferation.

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**P082**

**Membrane-bound progesterone receptor1 (PGRMC1) can mediate breast cancer proliferation significantly stronger with E2/norethisterone compared to E2/progesterone – A xenograft model**

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**Objective:** To investigate the importance of the membrane-bound progesterone receptor1 (PGRMC1) in the development of breast cancer comparing two different progestogens in a xenograft model.

**Methods:** MCF7 cells were stably transfected with PGRMC1 expression plasmid or empty vector (pcDNA-3HA). Nude mice were inoculated with Estradiol (E2) pellets before the injection of tumor cells into both flanks (n = 6 each group), a norethisterone (NET), progesterone or placebo pellet was implanted at 12th day after tumor cells injection, and tumor volumes were monitored for 6–7 weeks. Tumor tissue was analyzed by immunohistochemistry. The experiment was repeated in a second xenograft model with T47D cells.

**Results:** Progesterone and NET did not increase the E2-induced tumor proliferation in MCF7 and T47D-implants without PGRMC1 transfection in the mice, whereas the MCF7/PGRMC1 and T47D/PGRMC1 tumor volumes were increased, significantly stronger induced by sequential E2/NET compared with the sequential E2/progesterone regimen.

**Conclusion:** Tumor growth of breast cancer may need certain cell components like PGRMC1 which mediate proliferating effects especially of synthetic progestins like NET. Xenograft models cannot replace clinical studies but may suggest effects which may have consequences for clinical practice.

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**P083**

**Increased expression of PGRMC1 is associated with poor prognosis of breast cancer patients**

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**Objective:** We previously have shown that certain progestogens strongly stimulate proliferation of breast cancer cells overexpressing Progesterone Receptor Membrane Component1 (PGRMC1) and therefore hypothesized that PGRMC1 may play a critical role in breast cancer progression. Since until now no information was available if expression of PGRMC1 is also associated with worse prognosis of breast cancer patients, we investigated the clinicopathologic significance of PGRMC1 expression in the cancer tissue of patients with breast cancer.

**Methods:** Expression of PGRMC1 was analyzed by immune histochemical staining of primary tumor tissues obtained from 69 breast cancer patients. A labeling score was developed and results were correlated with tumor size, lymph node metastasis and clinical outcome.

**Results:** Overexpression of PGRMC1 is correlated with larger tumor size and higher lymph node metastasis. Kaplan-Meier survival curves indicate that patients with high expression of PGRMC1 in the tumors have poorer disease-free and overall-survival than that with low PGRMC1 expression, independent of the estrogen-receptor status, and that PGRMC1 may be even better predictive compared to proliferation markers like Ki67.

**Conclusions:** Our findings suggest that the expression of PGRMC1 may be important for predicting the prognosis of patients with breast cancer.

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**P085**

**Ovarian function after gonadotropin-releasing hormone agonist during chemotherapy in young breast cancer patients**

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**Objective:** This study was performed to investigate recovery of ovarian function after gonadotropin-releasing hormone (GnRH) agonist co-treatment with chemotherapy in young breast cancer patients.

**Methods:** This prospective study included 105 reproductive-aged women who were diagnosed with breast cancer and received GnRH agonist during chemotherapy for ovarian protection. Changes in follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol and anti-Müllerian hormone (AMH) were measured and recovery of ovarian function (defined either resumption of menstruation or serum AMH level ≤ 1 ng/mL) were assessed for 12 months after completion of chemotherapy.

**Results:** Mean age was 32 years. After 12 months of follow-up, resumption of menstruation was observed in 94 (89.5%) women, and mean time until resumption was 5.4 months. Seventy-five women (71.4%) had AMH ≥ 1 ng/mL at 12 months. Therefore, nineteen (18.1%) women experienced resumption of menstruation, but had still low AMH. Although most women had experienced men-
and education of RF and president fellowship SP-273.2015.4.

Conclusion: GnRH agonist co-treatment is effective for ovarian protection in young breast cancer patients who undergo chemotherapy. Serum FSH and AMH levels, rather than chemotherapy-related amenorrhea, may be better markers for evaluating recovery of ovarian function.

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P086

Change of hair microstructure for breast cancer presence
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Biotissues and somatic cells are widespread objects for the optical biomedical diagnostics but their significant heterogeneity together with high scattering light significantly complicate obtaining statistically reliable data. That's why new research objects need.

The object of the research was hair of two groups of volunteers. The first group contains healthy women which no official cancer diagnosis is. Women with breast cancer disease were in the second group of volunteers. For model experiments wool of mice (line BYRB) with spontaneous tumors of mammary gland was used. Wool had been cut from all skin surfaces of healthy mice and mice with malignant tumor(s) of same line. Hair microstructure was investigated by optical microscope Altami invert 3 working in phase contrast mode. The nitrogen and oxygen distribution within hair external layer was researched by electronic microscope JEOLE-6000. The cells size of the external hair layer was measured by “Photocor compact” and laser devices.

It is experimentally shown that hair of healthy mice and women has dense structure. At the time, hair structure has destroyed for breast cancer present. Parts of the external layer are absent. Pathological process development leads to the hair cell size decreasing.

The investigation of nitrogen and oxygen distribution within cell can be also used for biomedical diagnostics. The experiments have shown that concentration of nitrogen in healthy mice is more then in hair of cancer carrier. The mean of oxygen concentration rises in women with malignant tumor(s) of mammary gland. At the time, hair structure has destroyed for breast cancer present. Parts of the external layer are absent. Pathological process development leads to the hair cell size decreasing.

The represented data about hair and wool structure can be used to improve techniques for non-invasive diagnostics of cancer diseases.

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P087

The contraceptive trend in Korea
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Background: To assess the knowledge, attitude, practice and preferences on contraceptive methods among the Korean female population, to determine the association between knowledge and attitude on contraceptive methods with the variables.

Objective: The purpose of this study was to test and validate a model to predict contraception behavior in Korean premenopausal women.

Methods: A descriptive survey of 2532 females among 20-50 year old women who underwent myomectomy was done using a structured knowledge questionnaire on practice and preference at University Hospital, Bucheon, South Korea.

Result: Of the 2532 women, 2066 women (81.6%) used contraception but 466 women (18.4%) did not use it. As a result of comparing contraceptive methods by age, the rates of male-based contraceptive method use were higher in the 20–30 age group (p = 0.025), whereas the rates of female-based contraceptive method use were higher in the 31–40 age group (p = 0.007). The contraceptive failure rates were higher in younger age groups (40.26%) and the emergency contraception rate was more than 30% in women aged 20–40 years and it was higher than the rate in women aged 41–50 (28.72%). Condom use was most frequent in Korean women and oral contraceptive use was less than 3%. Most women were aware of the need for contraception (90%). Women aged 20–30 and 31–40 mainly obtained information from the Internet, whereas women aged 41–50 used many different ways such as searching the Internet, asking their friends and visiting a hospital.

Conclusions: The contraceptive use rates were more than 80% and men were more actively involved in contraception in their young age of 20s and 30s. Condoms and calendar-based contraceptive methods, male-based contraceptive methods, were more likely to be used, whereas oral contraceptive pills accounted for less than 3% of total method use. Taking into account contraceptive failure rates, more education on contraceptive methods is thought to be needed in Korea.

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P088

Pregnancy outcomes in women undergoing myomectomy aged 40 and older
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Objective: To evaluate the effectiveness of myomectomy in women desiring fertility above age 40.

Background: More women in the recent years desire to preserve their uterus in the presence of symptomatic uterine fibroids. Myomectomy has become an increasingly common gynecological procedure. Age of childbearing has increased the demand for less aggressive management of uterine fibroids. Scarce data on the surgical management of fibroids in women above age 40.

Methods: Retrospective chart review of 139 women above the age 40 who underwent myomectomy, regardless of route, between 2005 and 2016 at our institution. To ensure no loss of follow up, we contacted all patients by phone with a questionnaire about their symptoms, recurrence if any, and pregnancy outcomes (including miscarriages, abortions, fetal losses, etc.). Statistical analysis was done using linear regression models, binary regression models, ANOVA, and Kaplan Meier analysis.

Results: The mean age was 44.32 years (SD 4.15). Of all the 139 women, 124 (11.1%) became pregnant. 48 patients had myomectomy done specifically to conserve fertility. 50% of these needed a reproductive endocrinology and infertility consult and 31% became pregnant. Of these 15 patients, 7 (53.3%) had a live birth.
Conclusion: Myomectomy to conserve fertility is a reasonable option for women aged 40 and older.

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P089

Considerations regarding psychiatric implications of contraception in premenopause

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Introduction: Contraception in premenopause is one problem little studied in the literature of speciality. It is considered probability that the risk of pregnancy in premenopause is low and so is not necessary the contraception, although its absence is a factor that can lead to depression.

Aims and methods: Were studied two groups of women with age between 40 and 49 years (in Romania the most frequent age for the beginning of menopause is 49). This study was made in the period 2012–2016.

The first group was formed by 139 women which refused to use none method of contraception.

The second group formed by 108 women: 51 of them used HRT for hormonal deficiency in premenopause or for early menopause; other 57 used contraceptive methods (natural, etc.).

I evaluated in what measure, the risk to become pregnant is a stress factor or even a risk for psychiatric disorders.

Results: At the first group of women which did not use any methods of contraception in the period 2012–2013 recorded three pregnancies which were solved by medical abortions.

At the second group of women who used hormonal therapy for any diseases or used one contraceptive method did not record any pregnancy. Though the hormonal therapy administered was not given for contraception we considered that this hormonal treatment had contraceptive effect too. At this group of women observed another phenomenon. They were not stressed by the risk of a pregnancy and this thing had as result the growth of life quality and to avoid some possible psychiatric disorders.

Conclusions: The contraception in premenopause represents an insufficient known problem as medical point of view that social point of view.

Absence of contraception in premenopause represents a stress factor and sometimes can get to anxiety and even to depression.

In that problem one aspect is sure: it cannot be ignored.

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P091

Does cardiovascular risk vary according to the criteria for the diagnosis of PCOS?

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Aim: The risk of cardiovascular disease (CVD) is higher in females with PCOS compared to healthy individuals. Chronic inflammation, insulin resistance, hyperandrogenemia, hyperlipidemia and increased oxidative stress are known to have a role in the formation of atherosclerosis and CVD. The aim of our study is to evaluate if cardiovascular risk vary according to the different criteria’s of polycystic ovary syndrome (PCOS) by using carotid intima-media thickness (CIMT), which is an important marker of major cardiovascular events in the later stages of life.

Material and methods: The study group was formed of 69 women aged 18–35 years diagnosed with PCOS and the control group comprised 54 age-matched healthy women. Body mass index, CIMT, oral glucose tolerance test, hormonal and lipid profile were compared between the groups.

Results: There was no significant difference in CIMT levels between the groups. The CIMT levels in the PCOS group did not differ whether or not hyperandrogenism, polycystic ovary like appearance on ultrasound or oligo/anovulation status were present. Furthermore when all the cases were divided into subgroups according to the BMI values, the CIMT values were similar between the groups. CRP, total cholesterol and LDL levels were positively correlated with mean CIMT values.

Conclusion: Since PCOS and atherosclerosis both have a complex nature, it is likely that the evaluation of CIMT alone may not be...
The purpose of this work was to study the therapeutic effect of hormone therapy in women with menstrual dysfunctions caused by chronic viral hepatitis.

**Materials and methods:** The controlled randomized study evaluated the treatment results of 80 patients with menstrual dysfunctions in association with liver pathology, randomly picked out from 319 women suffering from chronic viral hepatitis. The selection of the hormonal therapy was made depending on the menstrual irregularities, hormonal profile and results of the genitals sonography: 1st group (26 patients) - hepatoprotectors, 2nd group (23 patients) – Didrogesteron 10 mg (Duphaston) + hepatoprotectors, 3rd group (31 patients) – Estradiol 2 mg + Didrogesteron 10 mg (Femoston) + hepatoprotectors. The control group included 15 healthy women of reproductive age with normal menstrual cycle.

**Results:** In the 1st group a gradual normalization of hepatic function after 3 months of traditional treatment was observed, a full recuperation of the menstrual function using only hepatoprotectors is not possible. Duphaston is a selected treatment for correcting the menstrual function at women with the minimum and moderate hepatitis activity degree, contributed to menstrual cycle adjustment, thus decreasing menstrual cycle dysfunction’s incidence with 52% compared with 1st group (RR = 0.246; IC = 0.52 ± 0.098; \( p < 0.001 \)). Femoston is recommended for the recovery of serious hormonal dysfunctions, caused by viral the mixed hepatitis, moderate or severe forms. The high efficiency of the Femoston therapy was observed in 67.74% of cases (RR = 0.51, IC = 0.34 ± 0.098 \( p < 0.05 \)). The clinical researches showed the lack of adverse effects of the Femoston and Duphaston therapies over the hepatic function.

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**P094 Prevalence of cardiometabolic risk factors in subfertile women with different polycystic ovary syndrome (PCOS) phenotypes in Croatia**

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This cross-sectional study aimed to estimate the prevalence of cardiometabolic risk factors in ethnically homogeneous women with different PCOS phenotypes undergoing IVF treatment. The study included 157 controls, 135 asymptomatic women with polycystic ovarian morphology (PCOM) and 236 women diagnosed with PCOS and phenotyped according to the Rotterdam criteria. Anthropometric measurements, transvaginal ultrasound scan and blood sampling for biochemistry analyses were performed on the same day in a single clinical center. Metabolic profiles and prevalence of cardiometabolic risk factors such as obesity, dyslipidemia and insulin resistance assessed by clinical-setting specific threshold were compared among the groups. Women with PCOS A were younger, more insulin resistant and had higher body mass index and larger waist circumference than other women. PCOS C and PCOS D women were similar in metabolic profile. Likewise, there was no difference in metabolic profiles between controls and PCOM. No difference in lipid profile was found between different PCOS phenotypes. Women with PCOS A phenotype had higher prevalence of obesity, insulin resistance and hypertriglyceridemia than other PCOS phenotypes. The prevalence of insulin resistance...
and hypertriglyceridemia in PCOS D (30% and 23.9%) was found to be intermediate between that of PCOS C (24.5% and 18.4%) and PCOS A (47.3% and 27%). The high prevalence of hypercholesterolemia (around 50%) was common feature of all groups. In conclusion, in women with PCOS, the presence of oligomenorrhea was associated with higher prevalence of metabolic disturbances compared with the presence of hyperandrogenism in both lean and obese women with PCOS. Obesity is more prevalent in hyperandrogenic PCOS phenotypes than in non-hyperandrogenic PCOS phenotype and controls. In obese controls, asymptomatic PCOM and PCOS showed low reactivity in the patient group, indicating severe grade differentiation. These findings suggested secondary amenorrhea due to abeta apolipoprotenaemia.

Conclusions: We report a rare case of secondary amenorrhea due to abeta apolipoprotenaemia.

Case report: A 28 year-old woman presented with secondary amenorrhea in the last 11-month period. She had menarche on the age of 13 with normal development of secondary female characteristics. Her BMI was low. A progesterone challenge test was performed and was positive. Her gonadotropin levels at baseline were FSH = 26 mIU/mL and LH = 22 mIU/mL. Her lipidaemic profile showed very low cholesterol values and non-detective levels of apo-B. Her spinal Dexa scan showed a T-score = −3.47. Furthermore, she had vision disorders, especially on night vision and on colours differentiation. These findings suggested secondary amenorrhea due to abeta apolipoprotenaemia.

Conclusion: Abeta apolipoprotenaemia is a very rare cause of amenorrhea. Total cholesterol is used for steroid hormone synthesis. Especially LDL is used for corpus luteum progesterone synthesis. Lipoprotein disorders with low lipid production may impair ovarian steroidogenesis.

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P097

Androgen excess in women – A life long problem

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Introduction: Hyperandrogenism in women leads to skin and hair disorders, metabolic disturbances and can increase cardiovascular and neoplastic risk. There are different treatment options including local and endocrine treatment.

Objective: Defining the importance of the AEiW by summarizing the prevalence of Hyperandrogenic Skin Disorders and PCO.

Perform a narrative review of studies about the efficacy, health risks, tolerability, and possible health benefits of different treatment options.

Results:

Prevalence

Acne: 80–95% in adolescents and 5% in women beyond 40

Hirsutism: 5–15% with regional differences
PCO: 15% (most prevalent endocrine disorder)
Local therapies have low and medium efficacy.
The combination of estrogen with an antiandrogenic progesto-
gen is the most effective treatment targeting symptoms and
endocrine dysregulation. The individual cardiovascular risk has to
be assessed and balanced with the benefit.

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P098
Analysis of Codon 72 polymorphism in the p53
tumor suppressor gene in women with idiopathic recurrent pregnancy loss
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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).

Study design: 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 χ² 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 (≥2 and ≥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.

Keywords: Codon 72 polymorphism; p53 tumor suppressor gene; Recurrent pregnancy loss

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P099
Application of robotic single-site surgery for early stage cervical cancer: A pilot study
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Aims: Recent reports propose that robotic single-site (RSS) surgery is feasible in treating a benign condition of gynecologic process. The aim of this study is to evaluate the feasibility and safety of RSS surgery for the surgical treatment of early stage cervical cancer (carcinoma in situ of cervix & cervical cancer Ia1).

Method: Patients with preoperative diagnosis of CIS and cer-
vical cancer Ia1 by loop electrosurgical excision procedure were selected. 12 patients (10 patients: CIS, 2 patients: cervical cancer Ia1) who underwent RSS surgery from March 2014 to August 2015, at Dongsan medical center, were included in this study. All surgical procedures were performed by robotic single-site instruments (da Vinci Si® surgical System, Sunnyvale, CA) via a single umbilical incision. All patients underwent type 1 hysterectomy with or without salpingo-oophorectomy according to the grossly ovarian pathology.

Results: The median patient age and body mass index were 42.5 years (range, 33–61 years) and 22.2 kg/m² (range, 18.6–26.4 kg/m²). The median console time and total operative time was 52.5 min (range, 36–185 min) and 125 min (range, 90–280 min), respectively. There was no case of conversion to laparoscopy or laparotomy. There was only one wound disruption and dehiscence of umbilical skin. Patients were repaired at post-operative 1month.

Conclusion: RSS surgery is feasible and safe in selected patients with early stage cervical cancer. Operative times were reasonable and surgical procedure was well tolerated by patients. Large-scaled studies comparing laparoscopic single site surgery in patients should be performed to confirm the safety and benefits of RSS surgery.

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P100
Asymptomatic high grade endometrial cancer
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Most women with endometrial cancer (EC) have abnormal uter-
inine bleeding. However, there is a small percentage of patients who are asymptomatic at the time of diagnosis. The objective of the study is to analyze the epidemiological characteristics and risk fac-
tors of asymptomatic high grade EC.

Material and methods: Retrospective multicentric cohort study in 3 Spanish hospitals: Hospital Universitario Miguel Servet in Zaragoza, Hospital Clinico San Carlos in Madrid and Hospital Virgen del Rocio in Sevilla. We studied the epidemiological characteristics and the presence of risk factors associated with high grade EC depending on the presence of symptoms at the time of diagnosis. We included all subtypes of high grade EC: G3 endometrioid (G3EC), serous carcinoma (SC), clear cell carcinoma (CCC) and malignant mixed mesodermal tumors (MMMT). A total of 373 cases of high-grade EC were included (135 G3EC, 96 SC, 64 CCC and 78 MMMT).

Results: 90% of all patients (n = 335), had uterine bleeding at the time of EC diagnosis. All patients with asymptomatic EC (n = 37) were postmenopausal; of them, 24.3% (n = 9) were nulligest, 45.9% (n = 17) hypertensive, 45.9% (n = 17) were obese and 2.7% (n = 1) were under hormonal treatment. There were no significant differences between patients with asymptomatic high-grade carci-
noma and those who present clinic in these factors: hypertension (p = 0.433), diabetes (p = 0.577), obesity (p = 0.825), use of hormone

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therapy \(p = 1.000\), nulliparity \(p = 0.459\) and menopausal status \(p = 0.237\).

**Conclusions:** Risk and epidemiological factors associated with high-grade EC are similar depending on the presence or absence of symptoms.

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**P101**

**Correlation between hysteroscopic image and anatomopathological result in the diagnosis of endometrial cancer in menopausal patients**

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**Objective:** Before the appearance of bleeding in a menopausal patient, hysteroscopy is a test that allows us to visualize and evaluate the endometrial cavity in its entirety, which is extremely important in menopausal patients.

According to the existing literature, hysteroscopy has a sensitivity of 75–86% and a specificity of 96–99% for the detection of endometrial cancer. Our objective was to evaluate the effectiveness of hysteroscopy in the diagnosis of malignant endometrial disease in menopausal patients in our unit in the last 5 years.

**Method:** Between 2011 and 2016 we performed 761 hysteroscopies on suspicion of benign or malignant endometrial pathology in menopausal patients, and a targeted biopsy was performed in cases of suspected malignant endometrial disease. Twenty-five biopsies were taken on suspicion of endometrial carcinoma in the hysteroscopic image. All pathological anatomies diagnosed with endometrial cancer were analyzed in the referred period, obtaining 207 positive biopsies. The pathological anatomy was taken as Gold Standard for the diagnosis of endometrial cancer, and it was compared with the hysteroscopic diagnosis by calculating the indices of sensitivity, specificity, positive and negative predictive value. The degree of non-random concordance between the hysteroscopic image and the anatomopathological result was also assessed using the Cohen Kappa coefficient.

**Results:** Hysteroscopy had a sensitivity of 86% and a specificity of 99%, with a positive predictive value of 91% and a negative predictive value of 99%. The concordance observed between the two diagnostic tests was very high, with an almost perfect agreement between the hysteroscopist and the pathologist: Kappa index of 0.88 (95% CI 0.84–0.91) and \(p < 0.0001\).

**Conclusions:** Hysteroscopy and guided biopsy are corroborated as the most efficient methods for the diagnosis of malignant endometrial pathology in menopausal patients.

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**P102**

**Different features of histopathological subtypes of ovarian tumor in pre- and post-menopausal women**

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**Objective:** To date, epidemiological evidence has supported a link between ovarian cancer risk and menopause. However, little is known about the menopausal status affects the risk of specific histopathological subtypes of ovarian tumor. We aimed to analyze the differences in various histopathological subtypes of ovarian tumor between pre- and post-menopausal women.

**Methods:** We reviewed the medical records of patients who underwent surgery for a suspected ovarian neoplasm and histopathologically confirmed at Busan Paik hospital between 1997 and 2016. These tumors were regrouped according to 2014 World Health Organization (WHO) classification.

**Results:** A total of 4683 cases (3404 with pre- and 1279 with post-menopausal) were included for analysis. Epithelial tumors account for 52.6% of the total cases, germ cell tumors for 27.1%, sex cord–stromal tumors (SCSTs) for 4.1%, tumor–like lesions for 14.0%, and secondary tumors for 0.8%. In epithelial tumors, epithelial ovarian carcinoma was predominantly seen in post-menopausal women (5.4% vs. 22.1%, \(P < 0.0001\)), whereas benign epithelial tumors were significantly associated with pre-menopausal women (40.5% vs. 31.9%, \(P < 0.0001\)). Germ cell tumors were noted more frequently in pre-menopausal women than post-menopausal women (31.3% vs. 16.1%, \(P < 0.0001\)). The majority of SCSTs were predominantly occurred in post-menopausal women (21.1% vs. 9.5%, \(P < 0.0001\)). Tumor–like ovarian lesions were significantly associated with pre-menopausal women (15.2% vs. 10.7%, \(P < 0.0001\)).

**Conclusions:** We have demonstrated the differences in diverse histopathological subtypes of ovarian tumor according to menopausal status based on the new WHO classification in Korean women.

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**P103**

**Increasing accuracy of histopathological samples by hysteroscopic biopsy in postmenopausal bleeding**

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**Material and methods:** The study evaluated the results from 244 postmenopausal women in hospitalized in the gynaecology department of the “Dr. I. Cantacuzino” Hospital, with the principal admitted diagnosis of metorrhagia in postmenopause.

**Results:** The women were admitted for bleeding in post-menopause, either in acute bleeding or for investing a recent
episode of bleeding in postmenopause. All women undergone biopsy and had a histology result, with blind curettage, hysteroscopy followed by curettage or biopsy by hysteroscopy, and some of them hysteroscopy and resectoscopy. In 40 cases the biopsy revealed neoplasia of endometrium, 38 cases with different types of adenocarcinoma, and in 2 cases adenosarcoma. The hysteroscopy had a positive predictive value of 51% and a negative predictive value of 87.7% in diagnostic the malignancy in this study group.

The age of patients with endometrial carcinoma it was significant higher than the other patients with non-malignant reasons of bleeding ($p < 0.0001$, CI 95%; 7.01–12.58), the difference between the two median ages in these group is almost 10 years.

**Conclusion:** Hysteroscopy is the golden standard in evaluation of the uterine cavity in postmenopausal bleeding. New techniques and diagnostic devices help in evaluating the cavity even in advance age. The importance of correct diagnosis and sampling is equal important at advance ages were the risk of endometrial neoplasia is increase and also in the groups with risks for endometrium transformation is increased (obesity, diabetes, hypertension, tamoxifen treatment) and for endometrium surveillance.

**Keywords:** Metrorragia in postmenopause; Bleeding in postmenopause; Endometrial biopsy; Adenocarcinoma of endometrium; Hysteroscopy

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**P104**

**The hypoechoic image inside the endometrial cavity during menopause**

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**Introduction:** In several asymptomatic menopausal patients, in which routine annual transvaginal screening is performed, we may observe a small hypoechoic image inside the endometrial cavity, with an atrophic endometrium nearby. On the other hand, some patients with several minor complaints-like vaginal uncolored or pink-colored discharge, may have the same endometrial image.

**Method:** We prospectively observed 37 asymptomatic routine screened menopausal patients and 19 patients with some minor complaints (discharge, unspecific lower abdominal pain), in which atrophic endometrium was described, beneath a hypoechoic endometrial image (2–6 mm). Vaginal cultures and cervical cytology were negative. MRI was performed in 14 out of the 19 symptomatic patients, due to small follicular images in the ovaries, all of them were negative.

**Results:** We suggested a follow up for the next twelve months, performing ultrasound examinations and vaginal cultures every three months. In four of the symptomatic patients we observed a growing endometrium (over 5 mm) and we performed endometrial aspiration (Pippelle) – in two cases early stage endometrial adenocarcinoma was diagnosed.

**Conclusion:** Although a hypoechoic image associated with an atrophic endometrium is in most cases irrelevant, being related to an isolated secretion of the endometrial glands, our experience suggests that follow-up is valuable especially in symptomatic patients.

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**P105**

**High grade endometrial cancer. The same risk factors?**

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Endometrial carcinoma (EC) has classically been divided into two groups: type I (good prognosis and estrogen dependent) and type II (worst prognosis and independent estrogen). The aim of the study is to analyze the risk factors associated with all types of high-grade EC.

**Methods:** Retrospective multicentre cohort study in three Spanish hospitals (Hospital Miguel Servet in Zaragoza, Hospital Clínico San Carlos in Madrid and Hospital Virgen del Rocío in Sevilla). We studied the risk factors associated with high grade EC: endometroid G3 (CEG3), serous (CS), clear cells (CCC) and mixed mesodermal tumors (TMMM). Differences between subtypes were analyzed and depending on whether it was EC type I/II.

**Results:** Diabetes, obesity, nulliparity and use of hormonal replacement therapy showed no significant difference between all subtypes. TMMM was less frequently associated with hypertension and conversely it showed greater association with the use of tamoxifen in patients with breast cancer.

**Conclusions:** Risk factors associated with high-grade CE are similar in types I and II. Tamoxifen is especially associated with TMMM.

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**P106**

**Synchronous endometrial and tube cancer**

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Synchronous tumors of the endometrium and ovary are a well-known and well described entity, but the series with cases of endometrial cancer (EC) and fallopian tubes cancer (TC) are much more limited. It is important to exclude it from metastatic disease because it implies therapeutic and prognostic implications. We report two patients with concurrent endometrial and tube cancer and how the diagnosis was made that one of them was synchronous tumors and metastases in the other. Size, deep myometrial invasion, lymphovascular space affection and the presence of lymphatic metastasis were important factors in the differential diagnosis.

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P107

Immunohistochemical hormone receptors expression in high grade endometrial cancer

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Hormone receptors expression is a characteristic of type I endometrial cancer (EC), especially in low and intermediate histological grade, which is associated with excess estrogenic stimulation of the endometrium. The aim of the study is to analyze the immunohistochemical hormone receptors expression in high-grade EC.

Material and methods: Retrospective multicentric cohort study in 3 Spanish reference hospitals: Hospital Universitario Miguel Servet in Zaragoza, Hospital Clínico San Carlos in Madrid and Hospital Virgen del Rocío in Sevilla. We studied the estrogen and progesterone expression in 130 high grade EC surgical specimen: EC: 51 G3 endometrioid (G3EC), 36 serous carcinoma (SC), 15 clear cell carcinoma (CCC) and 28 malignant mixed mesodermal tumors (MMMT).

Results: Overexpression of estrogenic hormone receptors was observed in 77 patients (59.2%) and progesterone receptors in 78 (60%). G3EC was more likely to have estrogen receptor overexpression (82.4%; n = 42). These differences were significant (p < 0.001). The same results were obtained in overexpression of progesterone receptors study, with the highest percentage of positive study for ECG3 (80.4%; n = 41) (p < 0.001). In the multivariate analysis they showed no independent prognostic factor in survival analysis.

Conclusions: In high grade EC, hormone receptors expression is a characteristic of G3EC, which is associated with excess estrogenic stimulation of the endometrium. It is not an independent prognostic factor of relapse or death.

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P108

High grade endometrial cancer and menopausal status

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Endometrial carcinoma (EC) is the most common malignant neoplasm in developed countries. Only 20% and 25% are diagnosed before menopause. The aim of the study is to analyse the menopausal status of patients with high-grade endometrial cancer.

Material and methods: Retrospective multicentre cohort study in 3 Spanish reference hospitals: Hospital Universitario Miguel Servet in Zaragoza, Hospital Clínico San Carlos in Madrid and Hospital Virgen del Rocío in Sevilla. We studied the menopausal status in women with high grade EC diagnostic: G3 endometrioid (G3EC), serous carcinoma (SC), clear cell carcinoma (CCC) and malignant mixed mesodermal tumours (MMMT). A total of 373 cases of high-grade EC were included, of which 135 were G3EC or type I and 238 were type II (96 SC, 64 CCC and 78 MMMT).

Results: 371 patients (95.1%) were postmenopausal at the time of EC diagnosis; 10 patients (2.7%) were perimenopausal and 8 (2.2%) had normal cycles and were considered premenopausal. There were no significant differences between groups (p = 0.694).

Conclusions: Menopause status in women with high-grade EC diagnostic are similar in all subtypes.

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P109

Malignant diseases of the female genital organs on the territory the Grocka municipality for the period 2002–2014: Good preventive measures

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About 10 million people in the world die of malignant ailments. At the same time, in Europe more than 60,000 women get ill of Ca PVU.

The purpose of the work is the establishment of the total number and structure of malignancies, of female population living in the Municipality of Grocka for the 13th period (2002–2014) [1].


Conclusion: If we analyze the results, number of women suffering from the Ca PVU not significantly change. But, the increase of the Ca corporis uteri et Ca ovarii show that we still do not have and appropriate medical check-up (like PAP and colposcopy for PVU) in order to detect the premalignant et malignant changes of the uterus body and ovary. The worst results appear with cancer of the breast. The obligation of the introduction that every women must pass the PAP test, colposcopy and the ultrasound examination once a year, women older than 45 must pass mammography test and continue with self-inspection, with the aid of media, will help to stop this negative trend, or at lest to minimise it.

Reference


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P110

Levonorgestrel intrauterine device and preservation of fertility in endometrial cancer grade I

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Endometrial cancer is the most frequent gynecologic cancer. Although it mainly occurs in menopausal women, it can hit younger patients as well. Hysterectomy is considered the standard treatment and it could represent a problem for those young women who desire to preserve fertility. A conservative management can be offered to these patients when the tumor is well differentiated and advanced stage is excluded. Several studies are available in literature about fertility-sparing approach. Progestin treatment, seem to be the most validated conservative management. We report the case of a patient 43 years old, nulliparous, diagnosed by directed biopsy by hysteroscopy of endometrial cancer FIGO stage IA grade I. After the conservative treatment (levonorgestrel-releasing IUD Mirena®), the patient entered in complete remission. She conceived by IVF treatment and delivered at 31 weeks gestation by caesarean section for obstetrical indication. Laparoscopic total hysterectomy with bilateral salpingectomy was performed five months after delivery.

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P111

Immunohistochemical analysis of collagen types I, III, matrix metalloproteinases-1, -9, and gonadal steroid receptors alterations on the pathophysiology of female pelvic organ prolapse and urinary incontinence

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Introduction: The aim of this study was to investigate the potential effect of alterations in the expression of collagen types I, III, matrix metalloproteinases (MMPs) -1, -9, estrogen (ERα and ERβ) and progesterone (PR) receptors of the pubocervical fascia on the pathophysiology of pelvic organ prolapse (POP) and urodynamic stress urinary incontinence (USUI) after menopause.

Materials and methods: This was a prospective clinicopathological study based on immunohistochemical methods. Forty samples were obtained from postmenopausal women with synchronous POP and USUI (Group A), forty specimens were collected from postmenopausal patients with POP only (Group B), while forty postmenopausal women without POP or USUI who underwent gynecological surgery for another benign indication formed control group (Group C). Immunohistochemistry for collagen types I, III, MMPs -1, -9, ERα, ERβ and PR receptors was performed on formaline fixed and paraffin embedded sections.

Results: There were no statistically significant differences among the three groups in terms of age, parity, or body mass index. Collagen type III as well as ERα and ERβ receptors were found significantly reduced among samples of Group A. Collagen type I was significantly reduced in Group B when compared to the control Group, while further reduction was observed in Group A. MMPs were significantly increased among patients with pelvic organ prolapse, in comparison with the control Group. The higher levels of MMPs expression were observed in Group A.

Conclusions: It seems that lower expression of collagen type III and estrogen receptors in the vaginal wall and around the urethra of postmenopausal women with POP is potentially involved in the pathophysiological pathways of USUI. In addition, alterations in connective tissue such as decrease of collagen type I and increase of the expression of MMP-1, -9 may play an important role on the pathophysiology of both POP and USUI.

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P112

Resilience and urinary incontinence symptoms in postmenopausal women

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Background: Bio-, psycho- and social changes take place during the menopausal transition; which affect female health. Resilience is the capacity to overcome stress imposed by life adversity.

Objective: To assess and correlate resilience and urinary incontinence (UI) symptoms in postmenopausal women.

Methods: In this cross-sectional study, 150 postmenopausal women (45–75 years) were requested to fill out the 10-item Connor-Davidson Resilience Scale (CD-RISC), the 4-item International Consultation on Incontinence Questionnaire (ICIQ-SF) and a questionnaire containing personal data.

Results: Mean age of all surveyed women was 58.9 ± 5.7 years, the majority were Caucasian (92.7%), 91.3% had natural menopause, 10% used phytoestrogens, 64% lived in rural areas and 10% smoked. Calculated Cronbach’s alpha coefficients for the CD-RISC and the ICIQ-SF were high (indicating good reliability) (0.89 and 0.91, respectively). For the entire sample, median [interquartile range] total CD-RISC and ICIQ-SF scores were 35.0 [9.0] and 3.0 [8.0], respectively. An 18.0% of women had severe UI according to item 1 of the ICIQ-SF (scores 3–5). There was an inverse correlation between item 1 ICIQ-SF scores and CD-RISC scores (Rho = −0.24; p = 0.003). Women with severe UI had a higher median total ICIQ-SF scores (sum of items 1 to 3) and lower total CD-RISC scores as compared to those with nil or mild UI (15.0 [4.0] vs. 0.0 [5.0]; and 31.0 [6.0] vs. 35.0 [9.0], respectively, p < 0.05 for both). Multiple linear regression analysis determined that higher total CD-RISC scores (better resilience) positively correlated with exercising regularly and inversely correlated with economic problems; whereas ICIQ-SF scores positively correlated with age and phytoestrogen use.
**Conclusions:** In this postmenopausal sample, resilience correlated with economic problems, regular exercise and severity of UI. However, due to the relatively small and convenient sample, our findings do not allow generalizations.

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**P113**

**Vaginal pessary is the best option for some women**

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**Introduction:** Pelvic organ prolapse (POP) means that uterus, bladder or urethra are protruded toward or through the introitus of the vagina. Due to changes in the position, function of these organs is disturbed. About 50% of women experience some degree of POP during their lifetime.

POP can be treated by conservative and surgical treatment. The main conservative treatment is vaginal support device. It is generally safe, non invasive and inexpensive way of POP treating.

**Material and methods:** Over a 3 years period, we tracked 79 patients with POP grade II–IV. In terms of age, we divided them into 2 groups: aged 63–74 and 75–85 years. The first group consisted of 36 patients, mean age of 69.5 years, with POP grade II–IV; the second group consisted of 43 patients, mean age of 80 years, with POP grade III–IV degree.

In the first group, 15 patients (41%), immediately decided to undergo operative treatment. These were patients with urinary incontinence and medium levels of POP (II–III). To the remaining patients of the first group, vaginal support device was placed. Because of the discomfort and inadequate relief of symptoms, another 5 women underwent surgical treatment. Other patients were satisfied with vaginal pessary.

To all patients of the second group a vaginal pessary was applied. This was older women, with some concomitant diseases, and the possibility of serious operative complications. The satisfaction of these patients was 75%. In 11 patients (25%) problems related to POP were not resolved. Two patients underwent to colpocleisis for unresolved POP problems. None of the patients with vaginal pessary had serious complications.

**Conclusion:** Treatment of POP and urinary incontinence should be adapted to the actual health condition (physical and mental) of the particular patient. Vaginal pessary is a good option for managing POP in older patients, and patients with some chronic concomitant disease with major operative risk.

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**P114**

**The relationship and the seasonal variation between vitamin D and total testosterone**

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**Background:** There is evidence on a possible association of vitamin D and testosterone level. But there is inconsistent evidence in Korea. And, in Korea, there are insufficient evidences on association of seasonal variation and vitamin D, testosterone. We therefore aim to investigate the association of vitamin D and testosterone in Korean men. Also aim to investigate the vitamin D and testosterone have seasonal variation in Korean men.

**Methods:** This study was cross-sectional study including 1559 men, aged 25–86 years, taken medical examination. We measured serum 25(OH)D level, total testosterone level, other labs and patients’ lifestyle characters. We categorized patients by 4 seasons, analyze seasonal variability in 25(OH)D and total testosterone.

**Results:** The average age of the subjects was 53.3 ± 8.8 years, and the mean serum 25(OH)D, total testosterone levels were 15.9 ± 7.0 ng/ml, 5.1 ± 1.6 ng/ml, respectively. In the ANOVA model, 25(OH)D and testosterone were not have association ($p = 0.51$). And we analyze seasonal variation in mean of 25(OH)D level by ANOVA, there are relationship with seasonal variation and 25(OH)D ($p$ for trend <0.001). In total testosterone, there are no significant association with seasonal variation and total testosterone level, just has trend ($p = 0.06$). But after adjustment, total testosterone and 25(OH)D are has significant association with seasonal variability ($p = 0.007, p < 0.001$).

**Conclusion:** We find the serum 25(OH)D and total testosterone level had not correlation in Korean men. And the serum 25(OH)D and total testosterone level was affected by seasonal variation in Korean men.

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**P115**

**Andropause symptoms severity inventory (ASSI): Preliminary study with a Portuguese sample**

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**Introduction:** The Andropause Symptoms Severity Inventory (ASSI) is a new measure that assesses both intensity and frequency of symptoms of late-onset hypogonadism (LOH), as part of a longitudinal project about LOH (EVISA; Pimenta et al., 2014). The initial pool of 42 symptoms was developed based on a previous validated measure of menopausal symptoms (MSSI-38; Pimenta et al., 2012), and with the input of experts in psychology and endocrinology. The aim of the present study is to present the preliminary analysis of the ASSI with a Portuguese sample.

**Methods:** A community sample of 631 Portuguese men aged between 40 and 91 years ($M = 52.14; SD = 8.33$) completed the ASSI. Factor exploratory analysis was performed to test the proposed theoretical dimensions. Factorial adequacy was assessed through inter-item correlations and internal reliability (Cronbach’s alpha).

**Results:** Overall inter-item correlations and internal reliability supported the theoretical dimensions proposed; the 42 symptoms
Sexual activity in patients with coronary artery disease

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Erectile dysfunction (ED) is a clinical syndrome of generalized vascular disease. In 80% of men with ED have a vascular disease. The fear of patients with coronary artery disease (CAD) during sexual activity (SA) and their partners about death is a common psychological problem. Physiological responses during SA: increase in heart rate (HR), blood pressure (BP), respiratory rate – can be interpreted as symptoms of cardiovascular events.

Objective: To estimate the effect of Sildenafil on tolerance psycho-emotional and physical stress due to SA in patients with CAD.

Results: We examined 30 men with CAD and ED – aged 35–68 years old (mediana – 48.4 years). These patients had a diagnosis of stable angina II–III FC, and 1 and 2, the level of risk at Princeton classification. This patient had monitoring of electrocardiogram (ECG) and BP during wakefulness, including episodes of SA without medical support, and on the background of Sildenafil. A positive result was considered an effective SA based on the quality of sexual life questionnaire “LIEF.” Examination was carried out in a familiar environment for patients, with regular sexual partner. On the background of Sildenafil during the SA we recorded significantly smaller acute stress reaction and degree of emotional load was significantly less than in patients without prescribe of Sildenafil.

Conclusions: The use of Sildenafil in patients with CAD and ED indicate the possibility of the treatment of ED and significant increase tolerance to the psycho-emotional and physical coital stress.
Lactation is associated with a lower risk of subclinical vascular disease after the menopause

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Background: Breastfeeding has been associated with a beneficial metabolic profile. We aimed to evaluate the association between a personal history of breastfeeding and the extent of subclinical atherosclerosis in a sample of healthy postmenopausal women.

Methods: This cross-sectional study included 283 postmenopausal women, hormone therapy naive, and without overt cardiovascular disease. Fasting venous blood samples were obtained for biochemical and hormonal evaluation. Subclinical vascular disease was defined as increased carotid and femoral intima-media thickness (IMT > 0.9 mm) and/or increased carotid-femoral pulse wave velocity (PWV > 75th percentile, i.e. 9.5 m/s) or the presence of atheromatous plaques in either carotid or femoral arteries. The absence of all was defined as healthy vascular structure and function.

Results: The median number of births was 2 (0–4) and the median duration of lactation was 3 months (0–80 months). Subclinical vascular disease was prevalent in 42.7% (121/283) of women. Subclinical vascular disease was less prevalent in women who breastfed for a shorter period compared to women who breastfed for a longer period compared to women who breastfed for a shorter period or not at all (≥3 months vs <3 months: 35.7% vs 48.9%, p = 0.036, Fisher’s exact test). Subclinical vascular disease was predicted by the total duration of lactation (OR = 0.960; 95% CI: 0.922–0.999; p = 0.015), age, BMI and blood pressure, in the multivariate approach. Moreover, lactation for ≥3 months was associated with lower odds of subclinical atherosclerosis after menopause compared to women who breastfeed their infants for a shorter duration (OR = 0.457; 95% CI: 0.254–0.823; p = 0.009), in a model adjusted for age, menopausal age, BMI, blood lipids, blood pressure and smoking.

Conclusion: Breastfeeding for at least 3 months is associated with lower odds for subclinical vascular disease. This effect is independent of traditional cardiovascular risk factors. Larger studies are necessary to confirm these findings.

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Cutoff value of pericardial adipose tissues in association with metabolic syndrome in aging Koreans

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Purpose: Metabolic syndrome (MS) is well known for the risk of cardiovascular disease, which is focused on central obesity. Recent studies reported the association of pericardial adipose tissue (PAT) and MS. However, there was no study to demonstrate the cutoff value between the PAT and MS in aging Koreans.

Methods: The data of three hundred seventy four subjects were analyzed to compare the PAT, which was measured by the coronary MDCT, and various metabolic parameters according the MS, cross-sectionally. After the PAT was divided into tertiles, various metabolic parameters were compared and, furthermore, the odds ratio of having MS was calculated. Finally, we tried to demonstrate the cutoff value representing the best association between PAT and MS using ROC curve.

Results: 27.5% of all subjects were MS and mean PAT was 123.9 cm³. PAT showed significant positive correlation with body mass index, waist circumference, glucose, triglyceride, hsCRP, uric acid, homocysteine, and negative correlation with HDL. Furthermore, after divided into tertiles, PAT was also significantly associated with various metabolic parameters. The odds ratio of having MS was 4.19 (2.27–7.74) in the top tertile of PAT after adjusting age, sex, and smoking. The cutoff value to represent the best association between PAT and MS was found at the point 142.2 cm³ of PAT.

Conclusion: PAT was significantly associated with MS and various metabolic parameters. The cutoff value was 142.2 cm³ of PAT to show the best association with MS in aging Koreans.

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Association of vitamin D with the components of metabolic syndrome and coronary artery calcium score

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Background: Metabolic syndrome (Mets) is classically an important risk factor of cardiovascular disease (CVD). Several studies investigating the relationship between vitamin D and variables related to extraskeletal health, such as glucose metabolism, hypertension and coronary artery disease have been reported, but inconclusive. The aim of this study is to assess the association of vitamin D level with the components of Mets and coronary artery calcium score (CACS).

Methods: A total of 410 adults participated in the study between September 2009 and November 2011 in health promotion center of CHA hospital. Sociodemographic data were assessed by questionnaires. Body composition, blood pressures as well as metabolic components including glucose, and lipid profile were assessed and analyzed in relation to 25-hydroxyvitamin D(25(OH)D) levels.
Participants performed scanning for coronary calcium by computer tomography. CACS was compared between the two 25(OH)D groups (a. >30 ng/mL, b. <30 ng/mL). The association of 25(OH)D levels and metabolic components and CACS was examined by multiple logistic regression analysis after adjustment for other confounders.

**Results:** There was a significant difference of CACS between the two 25(OH)D groups (p = 0.046, 95% CI: 0.23–0.44, p < 0.01). Neck circumference (NC) was high positively correlated with triglyceride (TG) (r = 0.19, p < 0.01). Other biochemical laboratory parameters; fasting blood glucose (FBG) (r = 0.23, p = 0.04) and triglyceride (TG) (r = 0.31, p < 0.01) were also positively correlated. But negatively correlated with high-density lipoprotein cholesterol (HDL-C) (r = −0.44, p < 0.01).

**Conclusion:** Neck circumference is simple, noninvasive and time saving screening measure that can be used instead traditional anthropometric parameters to identify cardio-metabolic risk in perimenopausal and menopausal women.

**Keywords:** Neck circumference; Anthropometry; Cardio-metabolic risk; Exercise capacity; Perimenopausal women; Menopausal women

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**P123**

Noninvasive risk markers of Asian Body Shape Index for screening early atherosclerosis in perimenopausal/ menopausal women

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**Background:** Asian body shape index (ABSI) was introduced as novel noninvasive risk marker that predictors for cardiovascular diseases (CVD) and may better reflect health status. The body mass index (BMI), waist circumference (WC) and waist–hip ratio (WHR) are well-used anthropometric but their validity is regularly questioned.

**Objective:** To evaluate the association between ABSI and traditional anthropometric parameters to screening early atherosclerosis using carotid intima media thickness (CIMT).

**Material and method:** The cross-sectional hospital based study was conducted in 40-80 years perimenopausal/ menopausal women, Suranaree University of Technology Hospital, Thailand. CIMTs were measured using B-mode ultrasonography. The novel ABSI, Asian formula and traditional anthropometric parameters (BMI, WC and WHR) were measured. All lipid parameters were assessed in the entire participants.

**Results:** Total of 114 participants with age of 53.75 ± 9.92 years and mean CIMT of 0.70 ± 0.15 mm. The prevalence of early atherosclerosis in perimenopausal/ menopausal women was 22.30%. ABSI and BMI were significantly different between normal and atherosclerotic which CIMT ≥ 0.90 mm (p < 0.01), ABSI was correlated with atherosclerosis (r = 0.19, p = 0.04) but there was no correlation with mean CIMT. Both WC and WHR were correlated with mean CIMT, however they had no correlation with atherosclerosis. Only the traditional anthropometrics BMI was not correlated with CIMT or atherosclerosis.

**Conclusions:** ABSI appears to be a clinically useful measure for screening early atherosclerosis, perhaps better than traditional anthropometry in perimenopausal/ menopausal women.

**Keywords:** Asian body shape index; Carotid intima media thickness; Early atherosclerosis; Perimenopausal women; Menopausal women

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**P124**

Association between vitamin D deficiency and the risk factors for metabolic syndrome in postmenopausal women

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**Objective:** To evaluate the association between vitamin D (VD) deficiency and risk markers for metabolic syndrome (MetS) in postmenopausal women.

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Methods: An analytical cross-sectional study was conducted with 466 women, aged 45–75 years. Women in menorrhagia >12 months and age >45 years, without VD supplementation, and without cardiovascular disease were included. Clinical and anthropometric data were collected. Laboratory parameters, including total cholesterol (TC), HDL, LDL, triglycerides (TG), glucose, insulin and 25-hydroxyvitamin-D [25(OH)D] were measured. Women showing three or more diagnostic criteria were diagnosed as having MetS: waist circumference >88 cm, TC ≥150 mg/dL, HDL <50 mg/dL, blood pressure ≥130/85 mmHg, glucose ≥100 mg/dL. Serum values of 25(OH)D <30 ng/mL were considered as VD deficiency. For statistical analysis, t-Student test, chi-square test and logistic regression (OR–odds ratio) were used.

Results: Sufficient VD values were detected in 148 patients (31.8%) and deficiency in 318 patients (68.2%). Women with low serum 25(OH)D levels were older, with a longer time since menopause, and had higher TC, TG, insulin and HOMA-IR levels (p < 0.05). MetS was detected in 57.9% (184/318) of women with VD deficiency and in 39.8% (59/148) of those with sufficient VD (p = 0.003). In the multivariate logistic regression analysis, the lowest 25(OH)D level (<30 ng/mL) was significantly associated with MetS (OR=1.90, 95% CI 1.26–2.85), high triglycerides (OR=1.55, 95% CI 1.13–2.35) and low HDL (OR=1.60, 95% CI 1.19–2.40) (p < 0.05), compared with 25(OH)D levels ≥30 ng/mL after adjusting for age, time since menopause and BMI. It was observed that the mean concentration of 25(OH)D decreased according to the increase in the number of components of MetS (p = 0.016).

Conclusions: VD deficiency in postmenopausal women was associated with higher prevalence of MetS. Compared to women with adequate VD levels, those with deficiency had a higher risk of MetS, hypertriglyceridemia and low HDL values.

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P125

Relationship between health literacy and hypertension knowledge among women in Isfahan Province, Iran

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Background: Hypertension is usually symptomless and is not seriously considered until it causes some chronic complications. If hypertension is not appropriately controlled, consequences such as heart attacks, heart failures, brain strokes, chronic kidney diseases, vision loss, and vascular diseases are quite likely to occur. Among the reasons for not controlling the blood pressure, a lack of hypertension knowledge and patients health literacy stands remarkable.

Objectives: Thus, the present study was conducted to determine the relationship between health literacy and Hypertension knowledge among hypertensive women in Isfahan Province, Iran.

Materials and Methods: This descriptive cross-sectional study was conducted on 700 patients with hypertension selected according to a multistage random and quota types. Data collection tools included Health Literacy for Iranian Adults (HELIA) and Hypertension Knowledge Level Scale (HK-LS) that were completed by patients. Data were analyzed using Pearson’s correlation, one way ANOVA, independent T test.

Results: The mean age of participants was 60.58 years. Results showed that the relation between age and health literacy and knowledge was statistically significant. More than a half of participants (75.5%) are inadequate and partially adequate of health literacy. There was a significant correlation between the hypertension knowledge and the mean score of health literacy.

Conclusion: Highlighting patients with hypertension who suffered insufficient health literacy, designing and implementing training programs in accordance with patients’ age, literacy level, and cultural class, and increasing patients’ accessibility to health data through different methods can be effective in promoting individuals’ health literacy and, consequently, overall wellness.

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P127

The effect of education intervention in Iranian postmenopausal women’s lifestyle with hypertension

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Objective: Cardiovascular disease is the leading cause of morbidity and mortality in postmenopausal women and hypertension is a major risk factor for cardiovascular disease. The aim of this study was to assess the effect of education intervention on the lifestyle in Iranian postmenopausal women with hypertension.

Method: This study is a randomized controlled trial that examined the impact of intervention (an educational program to increase self-care including: reduce salt consumption, increase regular exercise, increase ability to coping with stress, decrease cigarette and other drug use) on self-care behaviors by health workers in women over 50 years old, suffering hypertension in Isfahan city. A sample size of 947 was selected through multi-stage random sampling method. The data collection instrument was a questionnaire based on the health belief model structures which was measured as Likert scale. The SPSS 23 software as well as the statistical tests t-paired and independent t test were used to analyze the data.

Results: The participants’ average age in this study was 60.1 ± 8. The results indicated a change of HBM structures in the treatment group before and after the intervention (P < 0.05) while they remained unchanged in the control group (P ≥ 0.05).

Conclusion: The results of this study showed that education based on the health belief model was effective in self-care behaviors. Besides, the important role of the health workers in teaching preventive behaviors should be taken into account.

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P128

Relationship between self-care behaviors and health literacy among hypertensive patients in Isfahan

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Introduction: Adherence to self-care behaviors among hypertensive patients is a major factor in hypertension management.
Moreover, health literacy has a considerable role in controlling this condition. Hence, this study aimed to determine the self-care behaviors and their relationship to health literacy in patients with hypertension in Isfahan.

Materials and methods: This cross-sectional study was performed on 210 hypertensive patients referred to selected health centers in Isfahan. Multistage random sampling was applied. The questionnaires employed were H-SCALE (Hypertension Self-Care Activity Level Effects) and S-TOFHLA (Short Test of Functional Health Literacy in Adults). The data were analyzed using the independent t-test, Pearson’s correlation test, Spearman’s correlation test, and multiple regression analysis through the SPSS software, version 20.

Results: In this study, the mean age of the subjects was 57.3 ± 8.9. The mean scores of their self-care behaviors and health literacy were 150.02 ± 12.01 and 75.83 ± 14.73, respectively. A low percentage of the patients (7.1%) were on a low salt-diet and 39% of them measured their blood pressure regularly. Furthermore, 74.3% of the patients had adequate health literacy and there was no significant relation between the self-care behaviors and health literacy (p = 0.631).

Conclusion: In this research, the patients’ self-care behaviors were at an acceptable level and a high percentage of them had adequate health literacy. Nevertheless, there was no relationship between the self-care behaviors and health literacy.

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P129
Circulating sex hormones are associated with memory performance in postmenopausal women
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Background: The association between memory disorders and sex hormones has not been clearly defined. We aimed to evaluate the association of circulating sex hormones with memory function in postmenopausal women.

Methods: This cross-sectional study included 39 women with subjective memory complaints. Fasting venous blood samples were obtained for biochemical and hormonal assessment. Demographic and anthropometric parameters were recorded. We evaluated verbal memory, using the Hopkins Verbal Learning test (HVLT), visuospatial memory, using the Brief Visuospatial learning test as well as working memory performance, using the verbal digits backwards test (VSPAN).

Results: Scores of verbal memory performance correlated with free estrogen index (FEI: HVLT delayed recall & retained percentage: r = 0.564, p-value = 0.015 and r = 0.543, p-value = 0.020, respectively). Moreover, working memory scores correlated with levels of FEI (VSPAN: r = 0.519, p-value = 0.027). Multivariate analysis showed that working memory scores were predicted independently by:

(i) free androgen index (log FAI: b = 0.766, p-value = 0.013);
(ii) testosterone (b = 0.881, p-value = 0.001);
(iii) free estrogen index (FEI: b = 0.533, p-value = 0.039).

All models were adjusted for age, menopausal age and years of education. No other significant correlations were observed between levels of sex hormones and scores of neurological scales.

Conclusion: Circulating sex hormones are associated with memory performance after menopause. This association is mainly evident on the domain of working memory, however, bioavailable estrogens are also associated with verbal memory performance scores. Larger studies are necessary to evaluate the significance of our findings.

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P130
Vasomotor symptoms are associated with episodic memory in postmenopausal women
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Background: The adaptation of the adult brain to aging is influenced by co-morbidities, genetic and environmental factors as well as psychological variables. We aimed to determine the association of climacteric symptomatology with episodic memory in a sample of Greek postmenopausal women.

Methods: A total of 39 postmenopausal women with subjective memory complaints were recruited for this cross-sectional study. We evaluated verbal and visuospatial episodic memory, using the Hopkins Verbal Learning Test (HVLT) and the revised Brief Visuospatial Memory Test (BVMT). Greene’s Climacteric scale was used for the assessment of menopausal symptoms.

Results: Verbal memory scores correlated with the intensity of vasomotor and overall climacteric symptoms. Visuospatial memory correlated with the intensity of psychological, psychosomatic and overall climacteric symptoms. Verbal memory scores were predicted by:

(i) vasomotor symptoms (HVLT retained percentage & delayed recall: b = −0.568, p-value = 0.009 and b = −0.563, p-value = 0.012);
(ii) psychological symptoms (HVLT discrimination index: \( b = -0.390, p\text{-value} = 0.023 \)), in combination with free estrogen index (log FEI);

(iii) combined symptomatology (HVLT total: \( b = -0.557, p\text{-value} = 0.034 \)).

Visuospatial memory performance scores were predicted by log FEI in combination with psychological symptoms (BVMT total & delayed recall: \( b = -0.558, p\text{-value} = 0.001 \) and \( b = -0.474, p\text{-value} = 0.005 \)) or combined climacteric symptoms (BVMT & delayed recall: \( b = -0.593, p < 0.001 \) and \( b = -0.492, p\text{-value} = 0.002 \)). Psychosomatic and sexual symptoms were not associated with verbal memory.

**Conclusion:** The intensity of climacteric symptoms is associated with memory performance in this sample of postmenopausal women. Among the spectrum of climacteric symptoms, vasomotor and psychological symptoms are associated with verbal and visuospatial memory, while psychosomatic and sexual symptoms showed no association.

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**P131**

**Options of hormone replacement therapy effect on female’s self-rating at perimenopause**

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Nowadays, various aspects of estrogen’s influence on cognitive (gnostical) function are the subject of focused attention from researchers’ point of view.

**The purpose of research:** An assessment of hormone replacement therapy’s (HRT) effect on ability to memorize and reproduce a verbal material in women at the period of perimenopause.

**Material and methods of research:** Have provided a study of 100 women at age from 45 to 52 years old. The average age had amounted 47.5 ± 1.2 years. The cognitive function have been studied by means of tests for visual and oral–aural memory, test Memorize ten words (MTW), Clock painting test (CPT), test for digits distribution (DD), and test for attention – Schulte Table. There was a medication containing 2 mg of estradiol valerate and 10 mg of dydrogesterone used as HRT.

**Results:** When the capabilities of patients to memorize and reproduce the verbal material were studied with help of MTW method, we found, that at short-term reproduction the number of correct answers at the background of HRT has increased since 3rd month of the therapy from 7.8 ± 0.9 score to 8.45 ± 0.8. By contrast, the number of correctly reproduced words, when remembering was postponed, did not change.

During DD test at the background of therapy by medication containing 2 mg estradiol valerate and 10 mg dydrogesterone noted valid decrease of time spent by patients to pass test. Thus, the study proved the optimizing effect of the 2 mg estradiol valerate and 10 mg dydrogesterone on attention and mind. This is testified by that at the background of the therapy of medication containing 2 mg estradiol valerate and 10 mg dydrogesterone the total time spent on DD test and number of errors were reduced, and also short-term memory been improved (MTW).

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**P132**

**Association between patient depression level and hysterectomy satisfaction in the United States**

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**Background:** In the U.S., hysterectomy is the most common non-obstetrical surgery for women. However, there have been few investigations into understanding factors, such as depression, related to procedure satisfaction.

**Methods:** Women who had planned to have a hysterectomy at Henry Ford health System in Detroit for non-cancer reasons, were recruited via telephone for longitudinal study. These are data from 121 women who had their surgery ≥6 months ago. Women reported procedure satisfaction (response of “agreed” or “strongly agreed” vs. “neither agree nor disagree”, “disagree” or “strongly disagree”) with the following:

“I was satisfied with my decision.” within 14 days prior to surgery and at 1, 4, and 6-weeks, and 3 and 6-months post-surgery. The Patient Health Questionnaire-9 (PHQ-9) was used to measure depression severity. Wilcoxon signed-rank tests were used to assess associations between PHQ-9 scores and satisfaction at each time-point.

**Results:** Average participant age was 46.7 years (SD = 8.4, range = 30–64 years) and 49.6% self-identified as Black. Mean ± SD PHQ-9 scores at each time point were: 6.2 ± 6.0, 4.0 ± 4.4, 3.4 ± 3.9, 3.2 ± 3.7, 3.7 ± 5.0, and 3.4 ± 4.9. Percentages of women who reported being satisfied at each time point are: 95%, 77.7%, 72.7%, 76.0%, 76.0% and 76.9%. PHQ-9 depression scores were associated with post-surgical satisfaction only at 1-week and 3-months post-surgery (\( p < 0.001 \)). Mean depression scores for “satisfied” versus “unsatisfied” participants were: 1 week, 3.6 (SD = 4.4) versus 6.0 (SD = 4.7); and 3 months, 3.18 (SD = 4.6) and 6.3 (SD = 5.4).

**Conclusion:** These data suggest depression may be associated with procedural satisfaction in the early post–hysterectomy period. Patients with lesser depression scores reported more satisfaction at 1 week and then at 3 months.

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**P133**

**The effects of vitamin B in mental health and cognition**

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**Objective:** Vitamin B deficiency could influence memory function, cognitive impairment and dementia. In particular, vitamins B1, B3, B6, B9 and B12 are essential for neuronal function and deficiencies have been linked to depression, dementia and Alzheimer’s disease (AD). We discuss the neurochemical pathways in cognition and mental health and provide evidence that vitamin B contributes to the complexity of depressive symptoms and cognitive decline.

**Methodology:** Using PubMed searches with key terms related to dementia, cognitive decline and mental health.

**Results:** Cognitive decline is one of the major causes of disability in older people leading to poor quality of life. Cognitive decline during ageing is multi-factorial. Ageing results in impaired neurotransmitter synthesis, signaling and overall diminished neuronal
function. Over time, symptoms include forgetfulness, inability to focus and decreased problem solving skills and may progress to anxiety, depression, dementia and AD. Currently there are no drugs or other treatments specifically approved to treat cognitive impairment or prevent its progression. Vitamin B complex plays an important role in homocysteine synthesis. Low levels of vitamin B1, B2, B6, B9 and B12 result in elevated homocysteine levels linked to brain atrophy, a precursor to cognitive decline leading to dementia and AD. It is postulated that increased homocysteine levels and deficiency of certain B vitamins contribute significantly to the pathophysiology and onset of the disease and its progression. Low level of vitamin B is often noted in patients with dementia and AD and its supplementation has been shown to improve memory and slow the progress of brain atrophy.

Conclusion: This knowledge may aid in the use of vitamin B as a preventative measure of severe cognitive decline, and thus reduce the onset of conditions such as, dementia and AD.

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P134

Shattering the mirror

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Create Some Buzz, Novi, United States

What do you think of when you hear the word menopause? Old? Over the hill? Crone? Hag?

Society has given us an image of what menopause looks like and it overlays whatever our eyes show us when we look in the mirror. It is not pretty. We see ourselves as worn out, dried up, useless. It robs us of our self-esteem and robs society of our wisdom.

But, what if we’ve got it wrong? What if menopause actually opens the way for women to claim their highest self?

In this talk, Jeanne Andrus, The Menopause Guru, examines the development of the menopause myth through a series of iconic images, from Sarah of the Bible to the Little Mermaid’s Ursula, and then, turns it on its head, asking the question, “What if menopause is really a gift? What if it gives us more than it could ever take?”

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P135

The effects of Pueraria thomsonii flower extract on estrogenic activity, osteoblast differentiation and osteoclast formation in vitro

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Pueraria is the predominant source of isoflavones considered to be phytoestrogens that mimic the hormone 17β-estradiol (E2). Due to the risks associated with hormone replacement therapy, there is a growing need for alternative sources of estrogenic formulations for the treatment of menopausal symptoms. Therefore, we examined the effects of Pueraria thomsonii flower extract on estrogenic activity using an estrogen-dependent MCF-7 human breast cell proliferation assay and HEK 293 cells co-transfected with human estrogen receptor (ER a and/or b) and ERE-luciferase reporter genes. To investigate the changes in osteoblast differentiation and osteoclast formation by Pueraria thomsonii flower extract, human osteoblastic MG-63 cells and rat primary osteoclast cells were measured by Alizarin Red S, ALP and TRAP staining reactions. As a result, we observed that proliferation of MCF-7 cells was increased by Pueraria thomsonii flower extract treatment. Furthermore, the estrogenic activities of Pueraria thomsonii flower extract, measured by ER dependent luciferase activities, were increased by up to 115 fold in dose dependent manners, preferentially through ER b (b/a = 2.8 fold). Also, treatment of Pueraria thomsonii flower extract significantly enhanced ALP enzyme activity and Alizarin Red S stained cells in osteoblastic MG-63 cells. On the other hand, in the osteoclast formation assay using primary osteoclast cells, the formation of tartrate resistant acid phosphatase (TRAP)-positive multi-nucleated cells was dramatically reduced by Pueraria thomsonii flower extract treatment. These results suggest that Pueraria thomsonii flower extract could provide strong estrogen-like effects in estrogen receptor positive cells and its phytoestrogens could be developed as a dietary supplement against post-menopausal symptoms including hot flush and osteoporosis.

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P136

Intake of Withania somenifera enhance the antioxidant property of aged mice

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The brain and neurological system are amongst the greater accumulators of oxidative damage with aging. The reason is a consequence of oxygen consumption, number of mitochondria, abundant nitric acid, rich in PUFA and lower levels of antioxidant enzymes such as GPX, catalase, etc. Associated condition accelerating the process of brain aging include vitamin B group deficiencies, high C-reactive protein and deficiency of antioxidants like acetyl-L-carnitine.

Method: 30 mice, Mus musculus, are divided into 5 groups (6 each). Experimental groups are treated with 100 mg/kgbw and 200 mg/kgbw with Withania somenifera extract for 30 days orally.

Result and conclusion: Treated group (supplement with extract) show significantly low LPO at p ≥ 0.01 than the control one and increase in GSH, CAT value in brain. It is concluded that after supplemented with the Withania somenifera mice show enhance value of antioxidant enzymes in treated mice brain than control.

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P137

Critical role of testosterone in both sexes

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The location of androgen receptors and the physiologic effect of testosterone is described.

Nervous: Neuroprotective, immunomodulator, improves sleep, dry eyes, hot flashes and depression. Enhances verbal learning,
memory and focus. Regulates β amyloid and dendritic growth. Therapeutic in MS, Parkinson’s and Alzheimer’s diseases.

**Cardiovascular:** Cardiac protective, vasodilator, augments cardiac output, strengthens cardiac muscle, inhibits plaque development, modulates cardiac adaptive hypertrophy, angiogenic, and improves O2 consumption in CHF.

**Breast:** Inhibits proliferation and cancer growth, proapoptotic, reduces ER α, increases ER β and chemotherapy responsiveness.

**Pulmonary:** Bronchorelaxation, pulmonary vasodilation, anti-inflammatory, immunosuppressant, and depressing sensitivity to histamine substances.

**GI tract:** Improves glycemic control, glucose tolerance and insulin sensitivity. Beneficial role in lipid homeostasis, alcohol excretion, steatosis, viral hepatitis, and cirrhosis. Stimulates peri-stalsis.

**Uterus, vagina, bladder:** Strengthens the bladder, improves incontinence and urgency. Increases vaginal blood flow, strength and lubrication. Prevents proliferation of endometrium.

**Sexual organs:** Stimulates ovulation and follicular development, increases sex drive/libido, erectile function and spermatogenesis. Prostate tumor suppressor and proliferator.

**Muscle, joints:** Increases lean muscle mass and strength. Anti-inflammatory, relieves pain and is effective therapy for arthritis and autoimmune disease.

**Bone, marrow:** Enhances immune function, stimulates erythropoiesis, increases nitric oxide and inhibits platelet aggregation. Reduces bone turnover and increases bone density.

**Fat:** Decreases visceral fat. Aromatizes to estradiol with a secondary effect via the ER.

Testosterone induces clinical effects in every organ system and has a critical role in human development, health, anti-aging and disease prevention.

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**P138**

**Early age at menopause: How should we empower them with health?**

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According to the WHO's health statistics for 2015, in India the average female life expectancy in 2015 is 69.9 years and is projected to increase to 73 years by 2021.

Age of menopause is a very important biomarker of not only the loss of fertility but also an increased risk for various midlife diseases and problems leading to decreased quality of life. There is much epidemiological observational, clinical and randomized controlled trial data to support that early menopause accelerates the development of chronic diseases. Hence, the average age of menopause is a vital determinant to develop protocols for preventive health care for women in the community. The earlier age at menopause has several implications for India.

Various studies done to identify the average age at menopause and the age of maximum prevalence of chronic disorders in India. The average age of menopause in the samples studied is 46 years. Chronic diseases (CVD, Osteoporosis, Diabetes, Cerebrovascular incidences and other NCD’s) in India present themselves almost a decade earlier than in Caucasians with an increase in overall morbidity and mortality. The findings provided a basis for further research and also help to understand the health status and health needs of women in India and thereby guidelines are formulated for screening and managing Indian Menopausal Women.

This talk aims to highlight various studies done to determine the age at menopause and factors associated with the health at menopause in the urban & rural population of Indian women. There is an urgent need to empower these women with good health at midlife and to develop age-specific preventive measures, such as screening tests, counselling, and health education, especially lifestyle management for healthy and active aging.

The Indian Menopause Society has taken various initiatives aimed at improving awareness and individualized management methods, thereby working towards the slogan 'Fit at 40, Strong at 60, Independent at 80'.

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**P139**

**Improvement of NYHA in multimorbidity patients with heart failure treated with Entresto® (Sacubitril/Valsartan)**

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**Objectives:** Heart failure (HF) is a chronic condition with an increasing prevalence in developed countries. In addition, it is typical that it manifests itself in elderly patients with multimorbidity. Entresto® (Sacubitril/Valsartan) is a new therapy for patients with chronic HF.

The aim of the study is to evaluate the improvement of the clinic and the decrease in hospital admissions after treatment.

**Methods:** Observational study. Patients in follow-up in the Multimorbidity Chronic Unit with diagnosis of HF.

For the analysis of the data, t-student was used to determine the differences between two sample means of hospital admissions.

**Results:** Nineteen patients were included in the study (M/W 53/47) with a mean age of 82 years ± 1.3 SD, with a diagnosis of chronic HF with NYHA III-IV. Seventy nine percent of patients had a reduced ejection fraction (HFrEF). Doses of 24/26 mg were indicated in 84% of patients.

At weeks of treatment initiation there was an improvement in NYHA in 78% of cases. After initiation of treatment, patients had a lower incidence of HF decompensation with a significant reduction in admissions (46 vs 9, t 1.94, p = 0.0004, 95% CI 1.004–2.89).

As a side effect, 17% had hypotension with doses of 24/26 mg, specifying the suspension of the drug. There were no other side effects or death of any of the patients.

**Conclusions:** In our experience Entresto® (Sacubitril/Valsartan) improves symptomatology and reduces hospital admissions of multimorbidity patients with chronic HF.

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P140

Investigating the financial status and social care of Iranian elderly

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The increasing life expectancy phenomenon forces the people to have enough money to meet their needs in old age. Therefore the finance matter and social care are vital for the elderly. This study aims to investigate the financial status and social care of Iranian elderly and their associations with demographic characteristics and financial behavior. This study employed a secondary data. The data was analyzed using Statistical Package of Social Science (SPSS) version 20. The procedures were descriptive statistics, t-test, chi-square test, ANOVA and multiple regression analysis. The study found that majority of the respondents had limited income and assets. About sixty percent of elderly had negative net worth. A significant positive correlation was found between net worth and good financial behaviour. Most of them have not appropriate social cares. More than half of them suffered from chronic disease. Since most of the elderly has low income, social care and moderate financial behaviour, financial education should be addressed to this population in managing their money in old age, which leads to a better quality of life among the Iranian elderly.

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P141

Women with the metabolic syndrome have evidence of subclinical arterial disease early after menopause

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Background and aim: The menopause transition has been associated with subclinical vascular disease. High-resolution ultrasound is a reliable, non-invasive method to detect early structural and functional atherosclerotic changes in the arterial wall. The present study aimed to examine features of the metabolic syndrome with indices of vascular structure and function in a population of postmenopausal women.

Methods: We screened 473 informed-consenting, postmenopausal women, retrieved from the Menopause Clinic of the Aretaieio Hospital, University of Athens. Mean age was 56 ± 6.7 and mean menopausal age was 7.9 ± 6.3 years. Metabolic syndrome (MS) was defined according to the Joint Definition. The individual features of the metabolic syndrome as well as the presence of the syndrome per se were tested for association with sonographically evaluated carotid artery intima-media thickness (CIMT), flow-mediated dilation of the brachial artery (FMD), pulse wave velocity (PWV) and central pressures (CP).

Results: MS was present in 17.3% of our postmenopausal women. Mean values of PWV increased linearly with the accumulation of MS features. Furthermore, the presence of the MS was an independent predictor of increased CIMT (b: 0.16, p < 0.001) and increased PWV (b: 0.114, p = 0.012). Among the individual features of the MS, fasting hyperglycemia was the strongest predictor of both subclinical atherosclerosis (IMT) and arterial stiffness (PWV).

Conclusions: Women with metabolic syndrome have evidence of subclinical arterial disease early in the course of their postmenopausal life. Fasting hyperglycemia appears to be the strongest determinant of the increased risk.

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P142

Low levels of adiponectin predicts the incident non-alcoholic fatty liver disease in middle-aged Korean men and women

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Objectives: Only a few studies evaluated whether adipokines influence the incidence of non-alcoholic fatty liver disease (NAFLD). We investigated the prevalence and incidence of NAFLD according to the levels of adiponectin, high molecular weighted (HMW) adiponectin, and leptin.

Methods: A total of 374 men aged 45 years and older and 342 postmenopausal women were enrolled. Adipokine assays and liver sonography were conducted at baseline. The subjects were followed up for a maximum of 8 years. At every visit, fatty liver was assessed by liver sonography.

Results: At baseline, 215 (30.0%) had NAFLD. The subjects with NAFLD had lower levels of adiponectin, HMW adiponectin, and higher levels of leptin than those without fatty liver. After adjusting for age, sex, waist circumference, triglyceride, HOMA-IR, and potential confounders, the odds ratio of 1SD increase in the level of each adipokine for NAFLD was 0.572 (0.436–0.750), 0.571 (0.425–0.767), and 1.183 (0.893–1.566) in adiponectin, HMW adiponectin, and leptin, respectively. Among the subjects without baseline NAFLD, 1011.5 person-years were followed up. The incidence of NAFLD was 67.2 in 1000 person-years. While leptin did not influence the incidence of NAFLD, comparing to higher levels (third tertile), low levels (first and second tertiles) of adiponectin (hazard ratio 2.316, 1.149–4.667) and HMW adiponectin (hazard ratio 3.749, 1.694–8.297) significantly raised the risk of incident NAFLD.

Conclusions: Low levels of adiponectin and HMW adiponectin were the independent risk factors for prevalent and incident NAFLD in middle-aged Korean men and women.

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P143

The rs8135828 polymorphism of the THO complex subunit 5 (THOC-5) gene and its correlation to lipid and metabolic profile in mid-aged women

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Background: THO (suppressors of the transcriptional defects of hpr1delta by overexpression) complex, sub-unit 5 (THOC-5), is part of the mRNA TREX complex (TRanscription-EXport); important for transcription, mRNA packaging and nuclear exportation. Reports have correlated specific polymorphic variations of the gene coding for this complex with abnormal HDL-C metabolism.

Objective: To analyze lipid and metabolic values in relation to genetic variants of the rs8135828 polymorphism of THOC-5 gene in mid-aged women.

Methods: DNA was extracted from the whole blood of 183 women aged 40–65 and tested for the rs8135828 polymorphism of TOCH-5 gene using real-time PCR. HDL-C, LCD-C, triglyceride and total cholesterol levels as well as metabolic parameters were correlated to polymorphism genotypes.

Results: Mean age of all surveyed women was 50.6 ± 6.3 years, a 54.6% were postmenopausal and 16.4% had the metabolic syndrome (METS, ATP III modified criteria). Genotype GG was the most frequently determined (62.3%). There were no differences in lipid levels according to genotypes; however women with the AG genotype displayed significantly higher glycaemia levels with a trend toward a higher METS prevalence and increased abdominal perimeters.

Conclusions: In this preliminary study, women with AG genotypes of the rs8135828 polymorphism of THOC-5 gene presented higher glycaemia levels; there is a need for more research in this regard.

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P144

Ovary hormone deficiency exacerbated high fat and high sugar diet – induced overactive bladder in a rat model

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Objective: The pathophysiology mechanism of menopause in the metabolic syndrome associated bladder dysfunction is still not clear. The major aims of the present study were to examine high-fat-high-sugar diet and surgical menopause – induced metabolic syndrome by elucidating the critical role of oxidative stress in over-active bladder.

Methods: Female Sprague–Dawley rats were fed with high-fat-high-sugar diet with/without ovariectomy surgery to mimic menopause and to induce metabolic syndrome. At six months after high-fat-high-sugar feeding, cystometrogram, physical indicator, urine and serum biochemistry parameters were measured. The terminal deoxynucleotidyl transferase nick-end labeling assay was performed to evaluate the distribution of apoptotic cells. Immunofluorescence studies and Western blots were carried out to examine the expressions of muscarinic and purinergic receptors, fibrosis-associated proteins, mitochondria stress markers, apoptosis-associated proteins and mitochondrial respiratory sub-units enzymes.

Results: Bladder hyperactivity was induced accompanied by bladder interstitial fibrosis after 6 months of high-fat-high-sugar feeding, while surgical menopause exacerbated these bladder damages. In addition, surgical menopause enhanced the generation of oxidative stress mediated by mitochondria-dependent pathways, and consequently attributed to bladder apoptosis. Such oxidative stress-enhanced bladder cell apoptosis and urothelial barrier defects were potential factors that might play crucial role in bladder over-activity and interstitial fibrosis. Ovary hormone deficiency with high-fat-high-sugar feeding also induced bladder dysfunction via over-expression of muscarinic and purinergic receptors.

Conclusions: High-fat-high-sugar feeding enhanced the generation of oxidative stress mediated by mitochondria, while ovary hormone deficiency enhanced bladder apoptosis and interstitial fibrosis, exacerbated overactive bladder syndrome.

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P145

Abdominal obesity as risk factor for deterioration of the quality of life in Afro-Colombian women

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Objective: To identify if abdominal obesity (AO) is risk factor to deterioration of quality of life in Afro-Colombian women.

Methods: Cross-sectional study, part of the CAVIMEC (Calidad de Vida en la Menopausia y Etnias Colombianas) research project, carried out in Afro-descendant women with ages between 40 and 59 years. Pollsters of the health area did door-to-door visits and applied a socio-demographic questionnaire, the Menopause Rating Scale (MRS) and took anthropometric measurements. AO was defined as presence of abdominal circumference higher to 88 cm, which was taken of foot and to umbilical level. The highest scores of items, domains and total punctuation of the MRS define greatest severity of symptoms, domain deterioration and worse quality of life. A bivariate and a stepwise logistic regression analysis were done. Data analysis was carried out with Epi-Info-7 and MedCalc. There was not impact in the integrity of participants.

Results: 461 women with age of 50.2 ± 5.4 years were included. Body mass index 27.6 ± 4.5 kg/m², 50.5% were in overweight and 23.9% had obesity. 35.5% were in premenopause, 15.4% in perimenopause and 49.1% in postmenopause. The average of waist circumference was 83.0 ± 10.4 cm and 161 (34.9%) presented AO. There were not significant differences in the score of symptoms, domains and total score when comparing women according to the
presence of AO. AO had OR: 1.85 (1.03–3.32) for severe somatic symptoms, OR: 2.0 [1.08–3.70] for severe psychological symptoms, OR: 1.13 [0.74–1.70] for severe urogenital symptoms and OR: 2.0 [1.24–3.21] for severe deterioration of the quality of life. In the adjusted models, according to number of children, arterial hypertension and to have sexual partner, the ao had OR: 1.98 [1.18–3.31] for severe deterioration of quality of life.

**Conclusion:** The AO was associated two times more with high deterioration of the quality of life in Afro-Columbian women.

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P146

Are individual or work-related factors associated with work outcomes in menopausal women?

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Many women are now in employment during their menopause. Evidence suggests that although most women do not take absence or perceive their job performance to be affected by their menopause, some women do. It is therefore important to understand what factors might be associated with such outcomes. This paper explores individual and work-related factors and their associations with menopause-related work absence and perceived work performance impact. 896 menopausal, working women from 10 organisations completed an electronic survey. Data included individual-related factors (sociodemographic: age, education level, dependents, level of physical activity, psychological distress; menopausal symptoms: perceived bothersomeness, duration and frequency of hot flushes), work-related factors (physical and psychosocial work environment, line manager factors: age, gender, symptom disclosure; and job satisfaction), menopause-related absence and self-perceived job performance impairment (dependent variables). Univariate and multivariate logistic and linear regression analyses were performed to examine the extent these variables significantly predicted the dependent variables of interest. Results showed the factors significantly associated with menopause-related absence were largely work-related than individual-related (accounting for 35% and 13% of variance respectively). In contrast, the factors that predicted performance detriments were largely individual-related rather than work-related (accounting for 16% and 19% of variance respectively). These findings suggest that both individual and work-related factors may be associated with work outcomes and that researchers, employers and policy makers should take a multi-perspective approach. This may be more effective in helping those women who find menopausal transition impacts negatively on their working life.

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P147

Bone mineral density and trabecular bone score in men with vertebral fractures

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The aim of this study is to evaluate the trabecular bone score (TBS) and bone mineral density (BMD) in men with osteoporotic vertebral fractures.

**Materials and methods:** We’ve examined 197 men aged 45–89 years, divided according to the gerontologic classification: 45–59 yrs (n = 83), 60–74 yrs (n = 86), 75–89 yrs (n = 28). Group A – consists of 44 men with vertebral fractures (mean age = 63.7 ± 10.8 yrs; mean height – 1.73 ± 0.72 m; mean weight – 79.4 ± 14.9 kg) and group B – 153 men without fractures (mean age = 62.3 ± 10.2 yrs; mean height – 1.73 ± 0.62 m; mean weight – 76.3 ± 8.9 kg). The BMD of lumbar spine L1–L4, femoral neck and total body were measured by DXA (Prodigy, GEHC Lunar, Madison, WI, USA). The TBS L1–L4 was assessed by the TBS iNsight software package installed on our DXA machine (Med-Imaps, Pessac, France).

**Results:** In total group we found that men with osteoporotic vertebral fractures have significantly lower TBS L1–L4 (A – 1.027 ± 0.210, B – 1.185 ± 0.170; F = 25.54; p < 0.001) and BMD of lumbar spine (A – 1.009 ± 0.172 g/cm², B – 1.150 ± 0.130 g/cm²; F = 33.74; p < 0.001), femoral neck (A – 0.821 ± 0.143 g/cm², B – 0.908 ± 0.135 g/cm²; F = 13.62; p < 0.001), total body (A – 1.110 ± 0.117 g/cm², B – 1.183 ± 0.094 g/cm²; F = 17.80; p < 0.001) compared with men without fractures. When we analyzed BMD depending on age, we found the significantly differences in group A: TBS L1–L4 – 45–59 yrs – 1.025 ± 0.248 vs 1.226 ± 0.156 (p < 0.001), 60–74 yrs – 1.083 ± 0.170 vs 1.150 ± 0.175 (p = 0.195), 75–89 yrs – 0.951 ± 0.170 vs 1.183 ± 0.174 (p = 0.002) and BMD of lumbar spine – 45–59 yrs – 1.027 ± 0.18 vs 1.154 ± 0.13 (p = 0.001), 60–74 yrs – 1.014 ± 0.16 vs 1.148 ± 0.14 (p = 0.002), 75–89 yrs – 0.950 ± 0.17 vs 1.182 ± 0.17 (p = 0.003); total body – 45–59 yrs – 1.141 ± 0.11 vs 1.203 ± 0.09 (p = 0.02), 60–74 yrs – 1.121 ± 0.11 vs 1.179 ± 0.09 (p = 0.04), 75–89 yrs – 1.040 ± 0.11 vs 1.128 ± 0.08 (p = 0.02).

**Conclusion:** Subjects with vertebral fractures have significantly lower TBS and BMD parameters than the healthy men.

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P148

Prevention of postmenopausal osteoporosis in Chinese women: A 5-year double-blind, randomized, parallel placebo control study

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**Objectives:** To observe the effectiveness and safety of menopause-related hormone therapy (MHT) to prevent bone loss in Chinese women during their menopausal transition and early menopause as well as to evaluate the effects of 5-year MHT on overall health to add Level I evidence for the prevention of osteoporosis using MHT.

**Design:** This clinical study was a prospective, double-blind, randomized, parallel placebo control study. Two groups were
higher proportion of women in the OG (78.7%) consumed inadequate amounts of protein.

**Methods:** Patients ($n=274$; age 53–91 yo) were assessed regarding their PI and eating behavior; meals, feeding schedule, snacking and appetite. Sample was divided into groups according to PI and the presence of osteoporosis (OG) and those with osteopenia and normal densitometry (OsNG). Comparisons tests were performed using SPSS software.

**Results:** None differences were found regarding eating behavior. It highlighted that 41.8% of women in OsNG do not have regular schedules to eat vs 39% in OsNG ($\chi^2 = 0.160; p = 0.689$). 30.1% of the women included consume inadequate amounts of protein. The mean PI was $1.30 \pm 0.47$ g/kg/day. Women with osteopenia reported the lowest PI in comparison with osteoporosis and normal ($1.2 \pm 0.4$ vs $1.4 \pm 0.5$ and $1.3 \pm 0.4$ g/kg/day, respectively; $F = 4.770; p = 0.009$). A higher proportion of women in the OG (78.7%) consume more than 1 g/kg/day meanwhile only 67.2% of OsNG reached this recommendation ($\chi^2 = 2.93; p = 0.086$), independently of age or eating behavior factors.

**Conclusion:** A higher protein intake and proportion of women who attended the PI recommendation was observed in the OG. Similar patterns of eating behavior were observed and they seem not to be related to the presence of osteopenia nor osteoporosis, suggesting that PI is related to other factors [1,2].

**Reference**


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**P150**

**Osteoporosis and osteopenia treatments in a Mexican female population older than 50 years, recording medical experience**

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Osteopenia decreases bone mass below the normal indices which precedes osteoporosis a major deficiency. When bone density is ±1 standard deviation (SD) is normal. Osteopenia is diagnosed between 1 and 2.5 SD, while osteoporosis is >2.5 and severe osteoporosis when fractures have occurred. Risk increases for developing osteoporosis with calcium and vitamin D deficiency, smoking, alcohol consumption and sedentary lifestyle. The purpose of the present study is to describe the management of treatment in patients with osteopenia or osteoporosis in Mexican women (>50 yo).

**Methods:** 277 patients with densitometry studies were evaluated for osteopenia or osteoporosis.

**Results:** Surveillance measures, lifestyle modification, nutritional adjustments and physical activity were established (3%). 69% was osteopenia, treated with combination Calcium and Vit D (17%), only Calcium (5%,) and Vit D (1%). Alendronate alone or with Vit D, or combined with calcium (<1%). Estrogens, strontium ranelate, zoledronic acid alone or combined with calcium and Vit D (<1% each). 19% was Osteoporosis and treatment was combination Calcium-Vit D (62%), and others such as Alendronate, Diacerein, Denosumab, Teriparatide and Zoledronic Acid (<2% each). This patients present chronic comorbidities, then osteopenia and osteoporosis medication is additional to diabetes and hypertension (15%), treated with hypoglycemic and beta blockers and vasodilators.

**Conclusions:** Treatments of osteopenia and osteoporosis were above 65%. Early diagnosis and mild intensity were 3% with surveillance status. Treatments focused on Calcium-Vit D, and depending on comorbidities, treatment is adjusted with Alendronate, Diacerein, Denosumab, Teriparatide and Zoledronic Acid, which are indicated alone or in combination. 15% of comorbidities as diabetes and hypertension are treated [1,2].
Skeletal muscle and hormonal status in postmenopausal women

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The aim of the present research was to study the correlation between skeletal muscles and growth hormone, total and free testosterone level in postmenopausal women.

Materials and methods: The study involved 42 healthy women aged 60–86 years (mean age – 70.62 ± 6.97 yrs). Lean mass of the total body, upper and lower extremities was evaluated using Dual X-ray absorptiometry (Prodigy, GEHC Lunar, Madison, WI, USA). Strength of skeletal muscle was evaluated using springy carpal dynamometer. To determine the functional capacity of skeletal muscle, we used a “4-meter” test. To measure the level of growth hormone, total and free testosterone, Immulite 2000 analyzer-based electrochemiluminescent method was used (Siemens DPC, USA).

Results: For the purpose of quartile analysis, women were divided into 4 groups depending on their growth hormone values: Q1 – growth hormone <1.12 ng/ml (n = 11), Q2 – growth hormone being 1.13–1.98 ng/ml (n = 10), Q3 – growth hormone being 1.99–2.60 ng/ml (n = 11), Q4 – growth hormone >2.61–3.19 ng/ml (n = 10). Women with the lowest growth hormone values are also marked with the lowest lean mass of upper (p = 0.01) and lower (p < 0.05) extremities, as well as appendicular lean mass (p = 0.03). We found a significant correlation between appendicular lean mass and level of growth hormone (women aged 60–74 yrs: r = 0.36; women aged 60–89 yrs: r = 0.31), between strength of skeletal muscle and level of total testosterone (women aged 75–89 yrs: r = 0.55; women aged 60–89 yrs: r = 0.32), free testosterone (women aged 75–89 yrs: r = 0.31), growth hormone (women aged 75–89 yrs: r = 0.35; women aged 60–89 yrs: r = 0.32), between function of skeletal muscle and level of total testosterone (women aged 75–89 yrs: r = 0.40), free testosterone (women aged 75–89 yrs: r = 0.48).

Conclusion: Significant correlation between parameters of lean mass, skeletal muscle strength, functionality and level of growth hormone and androgens was determined in postmenopausal women.

Reference

The clinical manifestation of the gynecologic emergency in postmenopausal women through the emergency room

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Objectives: The purpose of this study was to assess the clinical characteristics of postmenopausal women who were admitted to the emergency room.

Methods: This retrospective study was conducted by using medical records of 44 patients who were admitted to the emergency room in a university hospital in Cheonan in 2016.

Results: Medical records of 41 patients aged 51–93 years were included in this study. Most frequent symptom was abdominal pain, followed by fever, vaginal bleeding, dyspnea, and diarrhea, etc. The major diagnosis was cancer, and patients underwent treatment under the diagnosis of uterine leiomyoma, pelvic inflammation, ovarian cyst, etc. 17 out of 41 menopausal patients underwent surgical operation, and 24 did not undergo surgery.

Conclusion: In accordance with the increased post-menopausal distress incidence, the number of postmenopausal women being admitted to the emergency room is increasing as well. Therefore, further management and efforts are required for postmenopausal women in the future.

This research was supported by High Value-added Food Technology development program, Ministry of agriculture, Food and Rural Affairs, Republic of Korea (114025-03-1-HD030).

Impact of pedometer-based walking on menopausal women’s sleep quality: A randomized controlled trial

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Objective: Sleep disturbances are one of the most common psycho-physiological issues among postmenopausal women. This study was designed to evaluate the impact of walking with a pedometer on the sleep quality of postmenopausal Iranian women.

Methods: This randomized, controlled trial was conducted on 112 women who were randomly assigned to two groups. The women in the intervention group (n = 1/4 56) were asked to walk with a pedometer each day for 12 weeks and to increase their walking distance by 500 steps per week.

A sociodemographic instrument and the Pittsburgh Sleep Quality Index were used to collect data.

Sleep quality was measured at baseline, 4, 8, and 12 weeks after intervention. The control group: (n = 1/4 56) did not receive any intervention.

Results: After 12 weeks, subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction improved to a significantly greater extent in the intervention group than in the control group (p < 0.05). The total sleep quality score was significantly higher in the intervention group than in the control group (0.64 vs. 0.98, p = 1/4 0.001).

Conclusion: This study showed that walking with a pedometer is an easy and cost-effective way to improve the quality of sleep among postmenopausal women. Use of this method in public health centers is recommended.

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upregulation of ovarian aromatase and p-PKB expression without stimulating the growth of breast cancer cells.

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P156

Assessment of the effects of *Tribulus terrestris* and Tibolone on sexuality in post-menopausal women

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**Objective:** Assessment of the effects of *Tribulus terrestris* and Tibolone in women with hypoactive sexual desire dysfunction after menopause.

**Method:** A prospective, randomized, double-blind trial involving 66 postmenopausal women with hypoactive sexual desire dysfunction was carried out. Women were allocated into three groups: Control group (n = 30) received placebo; *Tribulus terrestris* group (n = 30) received 750 mg *Tribulus terrestris* daily; and Tibolona group (n = 24) received 1.25 mg Tibolone daily. Sexual function was assessed with the Sexual Quotient – Female Version questionnaire (QS-F) at baseline and at the end of the 90 days period.

**Results:** All women in Control and *Tribulus* groups completed the study; in Tibolona group four women did not complete it, three for side effects. *Tribulus* and Tibolone treatments significantly improved the scores of all subscales with respect to baseline. In the control group was found a significant increase in women’s desire and sexual interest; and excitability capacity. Total sexual function score decreased significantly in the Control group. At baseline all groups showed an unfavorable-regular pattern, and after 90 days treatment the Control Group kept the same pattern, *Tribulus* changed to a regular-good pattern and Tibolona, to a good-excellent pattern.

**Conclusion:** *Tribulus terrestris* and Tibolone may be evaluated as a good therapeutic option for women with decreased sexual desire after menopause. Considering that phytomedications have fewer disadvantages, and translational validity of various animal models, and functional assays used in menopausal research. We discuss the advantages, disadvantages, and translational validity of various animal models used in basic menopausal studies reported in the literature, including ovary-intact, ovariectomy, 4-vinylcylohexene diepoxide-treated, and β-galactose-treated rodent models. These in vivo and in vitro menopause models were evaluated for their ability to mimic ovarian aging and estrogen deficiency, and for their ability to screen and assess potential drug candidates for alleviating the main menopausal symptoms, including hot flashes, vaginal dryness, perimenopausal cognitive impairment, postmenopausal osteoporosis, and skin aging. This review will help in future research to develop novel and safe therapeutic approaches to relieve menopausal symptoms of aged women.

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P157

Use of rodent models in the study of menopausal symptoms: A review of experimental studies

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Menopause is defined as the cessation of menstruation for more than 1 year due to the loss of ovarian follicles and estrogen depletion. Menopausal symptoms can adversely affect the quality of life of modern people and impose a considerable public health burden. The main treatment for menopausal symptoms is hormone therapy, but this has various side effects. Therefore, basic research on menopausal symptoms is necessary to find alternative treatments for the effective relief of menopausal symptoms. However, due to the complex pathophysiology of menopause and differences between humans and other species in terms of the transition of reproductive senescence, there is currently no ideal experimental model for menopause. This review explores the application of the currently available in vitro and in vivo models, and functional assays used in menopausal research. We discuss the advantages, disadvantages, and translational validity of various animal models used in basic menopausal studies reported in the literature, including ovary-intact, ovariectomy, 4-vinylcylohexene diepoxide-treated, and β-galactose-treated rodent models. These in vivo and in vitro menopause models were evaluated for their ability to mimic ovarian aging and estrogen deficiency, and for their ability to screen and assess potential drug candidates for alleviating the main menopausal symptoms, including hot flashes, vaginal dryness, perimenopausal cognitive impairment, postmenopausal osteoporosis, and skin aging. This review will help in future research to develop novel and safe therapeutic approaches to relieve menopausal symptoms of aged women.

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P158

The experimental and theoretical investigation of diffusion of compound in blood flow

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In the work the created experimental setup modeling human circulation and results of the numerical simulation of these processes are represented for investigations of diffusion of the injected compound in blood flow.

The experimental setup was created for investigation of photosensitizer diffusion in blood flow and its fluorescence dynamics. The principal scheme of the device includes network of silicon tubes and peristaltic pump which does not contact with liquid directly.
Thus, the chemical cleanliness of the investigated liquid is achieved. Tubes diameter is from 2 to 8 mm for blood vessel modeling. Pump power corresponds to rate of blood flow with regulation possibility. Pressure sensors are also connected on tube system for registration of pressure changing within its. Each sensor has connected on computer and can registers pressure dynamics. Its scheme let to use tubes for modeling different blood flow path.

For numerical simulation rose bengal was used as a photosensitizer injected into blood vessel. It is shown that the curves of its fluorescence intensity have non-monotonic nature. There is a sharp curves decline in the first few seconds. It is especially pronounced for 590 and 580 nm (near the “transparency window” of biological tissues). However, difference between curves for different viscosity is a little. Cells concentration has the most influence to the curves. At 560 nm fluorescence increase is weakly expressed. The greatest fluorescence increasing is observed at 590 nm.

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P159

Vaginal Microbiota in postmenopausal women treated with pulsed CO2 laser for genitourinary syndrome of menopause (GSM)

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Introduction: Pulsed CO2 laser is a novel treatment for GSM. Different papers have reported a significant improvement in vulvo-vaginal atrophy (VVA) after 3 laser sessions. Changes in the vaginal flora were also reported with an increase in Lactobacillus and a reduction in E. coli, E. faecalis and other bacteria. The aim of this pilot study is to evaluate the effect of pulsed CO2 laser in the vaginal microbiota of postmenopausal women with symptoms of VVA.

Methods: We prospectively recruited postmenopausal women with GSM who agreed in participating in the study. All women were submitted to 3 laser treatments with an interval of one month in between. A vaginal swab was taken for vaginal microbiota evaluation at baseline and one month after the last laser treatment.

Results: Fourteen women with a mean age of 60.2 were recruited. Alpha diversity (using the Chao 1 and the Shannon index), was irrelevant when comparing pre and post laser evaluation, showing a stability in the vaginal microbiota. No statistically significant difference was observed at baseline compared to the end of the lase cycle. However we observed a decrease in Coriobacteriaceae (−5.40%), a decrease in Clostridiales (−3.44%), a reduction in Enterobacteriaceae (2.74%) and an increase in Lactobacillae (3.17%).

Conclusion: Vaginal microbiota in postmenopausal women with GSM is maintained stable by a cycle of pulsed CO2 laser therapy. Despite the absence of a significant difference, we observed the stabilizing effect of CO2 laser on vaginal microbiota with trend towards a decrease in Coriobacteriaceae, Clostridiales and Enterobacteriaceae. On the contrary Lactobacilli tended to increase. Further study with bigger numbers would help in better understanding the interaction between pulsed CO2 laser and vaginal microbiota in postmenopausal women.

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Identification of pre and post hysterectomy patient centered preferences in the United States: Results of a focus group methodology

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Study objective: To identify patient-centered preferences before hysterectomy, and to assess women’s overall experience post-surgery.

Design and setting: Focus groups at Henry Ford Hospital (Detroit, Michigan, USA).

Patients and interventions: All English-speaking Henry Ford Health System patients having undergone hysterectomy and within three time periods post hysterectomy: 0–6 months, 6–12 months, 12 months and greater post hysterectomy. Focus groups were conducted to identify women’s expectations and degree to which patient-centered preferences were discussed before their hysterectomy surgeries, and to assess women’s outcomes and overall experience post-surgery.

Measurements and results: 25 women participated. Questions also addressed experiences and resources that helped to inform women’s decisions to move forward with surgery, their reflections post-surgery, and advice participants had for women who might be facing a decision about hysterectomy.

The only expectation that persisted during recovery, regardless of the complications experienced, was that women thought they would heal faster and be back to their normal energy level than the doctor predicted.

Women brought up the following topics that they feel could have been discussed: Mood change/depression, weight gain/loss, unexpected issues such as constipation, extended healing time and other complications (shoulder, back pain), emotionally coping during recovery.

Conclusion: Various themes identified included not only physical aspects but also social consequence of hysterectomy, personal feelings of being broken or changed self-image, frustrations, consequences related to sexual intimacy, regrets and depression. Providers should be aware that clearly undergoing hysterectomy is also an emotional experience for most women.

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P161

Functional ability: An effective biomarker of healthy ageing independently of multimorbidity

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Introduction: The aim of the present study was to explore what functional and conditioning tests could be more strongly related to healthy ageing in community-dwelling older adults.
Methods: Thirty-one subjects (16 females; age: 76 \( \pm \) 5 yrs; SPPB: 10 \( \pm \) 2) took part in this study. Healthy ageing was assessed through a self-reported health status scale [1]. Physical functioning was measured by the 4-m habitual gait speed (GS), 3-m timed up-and-go (TUG), chair-rising (CR) and stair-climbing (SC) tests. One repetition maximum (1RM) and maximal muscle power (Pmax) tests were conducted in the leg press exercise using a linear encoder. DXA analysis and 7 days-accelerometry were used to assess body composition and physical activity, respectively. Bivariate correlations and multiple linear regression models were performed for the prediction of healthy ageing, adjusting by sex, age, cognitive function, medication and multimorbidity.

Results: Healthy ageing showed a significant correlation with GS (r = 0.62), TUG (r = –0.63), CR (r = –0.46), SC (r = –0.55), Pmax (r = 0.40), lean mass (LM) (r = 0.38) and 1RM (r = 0.38) (all p < 0.05). According to multiple linear regression analysis, only TUG independently predicted healthy ageing (\( \beta = −5.225 \), 95% CI –7.976 to –2.474, p < 0.001). Additionally, Pmax but not 1RM or LM values, was associated with TUG performance (p < 0.05).

Discussion: Functional ability was related with healthy ageing independently of multimorbidity. These findings highlight the role of functional status assessment in the management of healthy ageing of older people [2]. Finally, power training has been demonstrated to improve TUG in a previous intervention [3] and could be the most effective strategy to improve healthy aging.

Reference


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P163

Androgen excess and the menopause

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Many studies have investigated the role of estrogens during menopause. The dramatic decline of estrogen concentrations during the perimenopausal period results in vasomotor symptoms, bone loss, alterations in lipid profiles and reduction of insulin sensitivity.

On the other hand, less attention has been paid to the role of androgens during menopause. The classic concept is that the circulating concentrations of the main androgens [testosterone (T), \( \Delta_4 \) -androstenedione (\( \Delta_4 A \)) and dehydroepiandrosterone sulfate (DHEA-S)] gradually decrease in perimenopausal women, although at a lesser degree compared to estrogens. Nevertheless, data from the Study of Women’s Health Across the Nation (SWAN) indicate that transient increases may occur during the menopausal transition.

It is known that estrogens and androgens may have opposite effects on cardiovascular disease (CVD) risk. Thus, it has been hypothesized that the relative androgen excess described during the menopausal period may better predict the risk of CVD than estrogen concentrations alone. The strongest association has been described between T concentrations and increased risk of CVD, triglyceride, insulin resistance and breast cancer.

Post-menopausal hyperandrogenism originates from the adrenals or the ovaries. Clinically, it is characterized by terminal hair growth and/or signs of virilization. Up to date, there is no consensus regarding specific clinical, hormonal and imaging criteria for the diagnosis of post-menopausal hyperandrogenism. In any case, health care professionals have to evaluate post-menopausal women in order to exclude rare but potentially life-threatening diseases, such as adrenal tumours.

Adrenal and ovarian androgen production plays a much more complex role during the menopausal period than previously recognized. Further epidemiologic and clinical research is needed for establishing the initiation and duration of estrogen and androgen replacement therapy, as a means to prevent CVD.

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P164

Timely diagnosis is vital: The effect of delayed diagnosis on bone mineral density in women with premature ovarian insufficiency

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Background: The long-term effect of Premature Ovarian Insufficiency (POI) on bone mineral density (BMD) is well recognised. Little is known about the early effects of POI on the rate of bone loss or the consequences of delayed diagnosis. The aim of this study...
was to explore the effect of aetiology and time to diagnosis on BMD in POI.

**Methods:** Retrospective database analysis of 563 patients from the West London Menopause and PMS Centre, where data is recorded in the International POI Registry.

**Results:** 563 patients were included in the analysis. Aetiology was classified as idiopathic (60.4%), genetic (2.1%) or iatrogenic following treatment for malignancy (25.6%) or benign conditions (11.9%).

Overall, at the time of diagnosis 32.3% had osteopenia and 4.3% had osteoporosis.

Mean T score in patients with idiopathic POI was significantly lower at both the spine ($p = 0.001$) and hip ($p = 0.02$) than in patients with iatrogenic POI.

Time to diagnosis was significantly longer in women with idiopathic POI (median 12 months) compared to iatrogenic POI (median 0 months) ($p = 0.001$).

Longer time to diagnosis was associated with lower BMD. For every 1 month increase in time to diagnosis the BMD measured decreased by 0.026 at the spine ($p = 0.001$) and 0.018 at the femur ($p = 0.013$).

Women with an underlying genetic cause had high rates of osteopenia (25%) and osteoporosis (25%). This may be because they are diagnosed at a significantly younger age (mean 23.7 years) compared to other aetiologies (idiopathic mean 33.2 years, benign 32.6 years, cancer 31.1 years) ($p < 0.0001$).

**Conclusions:** Delayed diagnosis is common in women with POI and has a detrimental effect on BMD. The NICE Guidelines now include clear diagnostic criteria for POI. Early diagnosis is essential to ensure timely treatment and prevention of bone loss.

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**P165**

**Body mass index and obesity-related cancer risk in men and women with type 2 diabetes (ZODIAC-56)**

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**Objective:** Aim was to investigate the relationship between BMI and obesity-related cancers in men and women with type 2 diabetes.

**Research design and methods:** A dataset of patients with T2D who participated in the ZODIAC study between 1998 and 2012 was linked to the Netherlands Cancer Registry. Cox proportional hazards models were used to investigate cancer risk, adjusting for selected confounders. Analyses were performed for the total group of obesity-related cancers and for non sex-specific and sex-specific obesity-related cancers (in men: advanced prostate cancer, in women: ovarian, endometrial and postmenopausal breast cancer).

**Results:** A total of 52,044 patients was included (49% women). During follow-up from inclusion in the ZODIAC study, 689 men and 914 women were diagnosed with an obesity-related cancer. In men, BMI was associated with a higher risk of the total group of obesity-related cancers and non sex-specific obesity-related cancers (HR (per 5 kg/m² increase) 1.12 (95%CI 1.02–1.23) and HR 1.18 (95%CI 1.06–1.31)). No association was found with prostate cancer. In women, an association between BMI and all obesity-related cancers combined and sex-specific obesity-related cancers was present (HR 1.15 (95%CI 1.08–1.22) and HR 1.22 (95%CI 1.14–1.32)). No association with non sex-specific cancers was found in women.

**Conclusions:** BMI is a risk factor for obesity-related cancers in men with T2D, except for advanced prostate cancer. The results of this study provide reason to reconsider the classification of advanced prostate cancer as an obesity-related cancer, at least in T2D. In women with T2D, BMI is a risk factor for the total group of obesity-related cancers and for sex-specific obesity-related cancers.

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**P166**

**Loss of muscle mass in elderly with hip fracture: importance of Body Mass Index and functional capacity. Prospective observational study: PREFISSARC study**

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**Background and aims:** In hospitalized elderly patients, prolonged bedding is associated with loss of muscle mass, a fact that negatively influences functional recovery. The objective is to study the factors that influence the loss of muscle mass in the elderly with hip fracture.

**Methods:** Observational study, conducted in two post-acute rehabilitation facilities. Patients have been heavy on admission and discharge. Body mass index (BMI) has been calculated. Autonomy in Basic Activities of Daily Living (ADL) has been measured with the Barthel Index (BI), gait ability with Functional Ambulation Categories (FAC), and cognitive status with the Mini Mental State Examination (MMSE). The study of body composition has been performed by BIA (Akern, Florence), on admission and discharge. The cut-off points proposed by the EWGSOP, ≤5.67 kg/m² for women, and ≤7.25 kg/m² for men, were considered as reduced appendicular lean mass (aLM).
Subjects with BMI < 29 kg/m² had a nearly 4-fold increased risk of age (male (90%, p < .001), and with significantly lower BMI than subjects with normal BMI (p < .001). Factors associated with aLM loss were age (p = 0.029), BI (p = 0.020), MMSE (p = 0.024), and FAC (p = 0.047). Subjects with BMI < 29 kg/m² had a nearly 4-fold increased risk of losing aLM (RR 3.63, 95% CI 1.20–11.0, p = .007). In the multivariable analysis, corrected for age, MMSE, previous BI, BMI at admission has been shown to be the only protective factor against aLM loss (RR 0.15, 95% CI 0.02–0.94, p = .043).

Conclusions: During rehabilitation after a hip fracture, many factors influence the risk of losing muscle mass, with BMI > 29 kg/m² being the most important protective factor. Overweight in the elderly with hip fracture, protects against loss of muscle mass and is associated with better overall recovery.

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P167

Perception of knowledge of female main cause of mortality, in a population of women from a health care institution in Chile

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Cardiovascular disease (CVD) is the leading cause of death in both men and women in developed countries. In Chile, cardiovascular mortality in women reaches 31% of the overall mortality, establishing itself as the main cause of death. There is misinformation on the subject. In Chile, it is a firmly entrenched belief that the leading cause of death in women is breast cancer, without understanding that the menopause is a CVD risk by itself. The lack of awareness on the issue has led to campaigns to promote the relevance of CVD in women.

The objective of this study is to evaluate the knowledge, by a female population, of the impact of cardiovascular pathology on female mortality.

A survey of women was conducted in a private clinic at Santiago de Chile in the second semester of 2016. A questionnaire of 2 questions was designed, one related to causes of General mortality and another on mortality by specific pathology. The answers were anonymous.

431 women were surveyed. Of them, 60% answered that the main cause of death was oncological pathology, 37% cardiovascular and 3% respiratory. The response to the specific cause of death was 83% breast cancer, 16% acute myocardial infarction and pneumonia in less than 1%.

Conclusion: The level of knowledge in the studied population on the prevalence of mortality due to cardiovascular disease in women is low. Despite the campaigns and education programs implemented during the last decade, the level of awareness has not raised to the expected levels. We need to rethink how to create conscience in the population about the cardiovascular risks in women.

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P168

How well does AMH relate to the timing of menopause? Results of an individual patient data meta-analysis


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Introduction: It is suggested that menopause forecasts can be extrapolated in order to predict the end of natural fertility. Studies available today providing AMH-based menopause predictions all suggest that AMH is capable of predicting age at natural menopause. However, pitfalls in AMH-based menopause prediction continue to limit clinical applicability.

Study design: A systematic literature search was performed to identify prospective cohort studies addressing the relation between baseline AMH levels and time to menopause after which the authors were invited to share the published data in an individual patient data meta-analysis (IPD).

Methods & results: Authors of six out of seven cohorts known were willing to participate in this IPD meta-analysis. AMH was a significant predictor of menopause in a multivariable Cox regression analysis including age (HR 0.59; 95% CI 0.55–0.64). However, the added value of AMH on top of predictions based on age was poor. The individual predictions of age at menopause, composed using a Weibul survival model, did cover the majority of the menopausal age spectrum, but youngest ages at menopause were not included. Also, precision of the forecasts remained poor, as age intervals surrounding individual predictions of age at menopause were wide. Finally, a reduction in the predictive effect of AMH with increasing age was clearly noted in this pooled data.

Conclusion: In this IPD meta-analysis AMH predicted time to menopause. However, major problems surrounding menopause predictions prohibited a solid claim for the use of AMH in day-to-day clinical practice. Future research needs to focus on overcoming the pitfalls of AMH based menopause predictions. These pitfalls are the fact that individualized predictions of age at menopause do not to cover the full age range of menopause, that prediction intervals remain wide, and lastly, that the predictive capacity of AMH tends to drop with increasing age at testing.

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The TyG index: a novel marker of subclinical atherosclerosis and arterial stiffness in lean postmenopausal women

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Background and aim: Insulin resistance (IR) has been shown to promote atherosclerosis, particularly in the female population. The TyG index, the product of fasting serum glucose and serum triglycerides, is a simple marker easily assessed in routine basis that correlates with insulin resistance. The present study aimed to examine the association of the TyG-Index with subclinical arterial disease in relation to BMI in postmenopausal women.

Methods: 473 informed-consenting, non-diabetic postmenopausal women, with no documented cardiovascular disease were included in the study. Carotid artery intima-media thickness (CIMT), flow-mediated dilation of the brachial artery (FMD), pulse wave velocity (PWV) and central pressures (CP) were correlated with the TyG index separately in lean and overweight/obese women.

Results: The TyG index correlated significantly with the majority of the assessed cardiovascular risk factors in both lean and overweight/obese women. However, the TyG index was significantly and independently associated with carotid IMT (r=0.155, p=0.012) and aortic stiffness as measured with PWV (r=0.157, p=0.013) only the group of lean women. In the multivariate analysis, while the metabolic syndrome was a significant determinant of subclinical atherosclerosis only in the overweight/obese group (OR=2.517, 95% CI: 1.078 to 5.878, p-value=0.033), TyG-Index predicted significantly subclinical atherosclerosis only in the lean group (OR=3.119, 95% CI: 1.187 to 8.194, p-value<0.001).

Conclusions: TyG, an easily assessed marker, is associated with carotid atherosclerosis and arterial stiffness mainly in lean women. This may prove a useful marker for identifying high risk women in the normal weight postmenopausal population.

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