Progesterone Versus Progestins: Clinical Dilemmas and Concerns
James H. Liu, MD, NCMCP, Obstetrics and Gynecology and Reproductive Endocrinology, University Hospitals, MacDonald Women’s Hospital, Cleveland, OH

As clinicians, we utilize progesterone and progestins every day for hormone therapy, contraceptive purposes, and control of uterine bleeding, yet we lack in-depth knowledge regarding this steroid and its actions in the female reproductive system. As a result, female development, growth, and reproductive health is at risk. The key question facing us at this time is: How do we best utilize progesterone in women? What do we need to know about the potential effects of the hormone in order to minimize side effects and optimize benefits? The goal of this presentation and Plenary Symposium is to focus on these less obvious effects on biological tissues. We will limit our discussion to mainly compounds used in hormone therapy: progesterone (P4), medroxyprogesterone acetate (MPA), norethindrone (NET), and drospirenone (DSN). Progesterone and progestins are widely distributed throughout the body and have been localized to tissues including endometrium, myometrium, breast, bone, liver, brain, leukocytes, lymphocytes, and vascular endothelium. Dr. Mesiano’s and Dr. Rubinow’s presentations will focus on the role of progesterone and its neurosteroid metabolite allopregnanolone, a powerful modulator of synaptic and extrasynaptic GABA receptors, differ as a function of genetic background. Thus, normal changes in levels of progesterone precipitate depression in women with reproductive-related mood disorders (e.g., PMDD, PPD), and this differential sensitivity to progesterone is also observed in cell lines from women with disorders compared with controls. Further allopregnanolone has demonstrated efficacy in both puerperal and non-puerperal depression as well as in in mouse models of reproductive depression. In contrast, differences in steroid metabolism; receptor activating profile; doses; schedules, routes, and duration of administration; behavioral assay; and context (e.g., genotype, age) do not doubt all contribute to the inconsistency of reported CNS findings for individual progestins. Thus, for all what we have learned about the behavioral effects and underlying mechanisms of action of progesterone, our understanding of the CNS effects of progestins is, by comparison, to the inconsistency of reported CNS findings for individual progestins. We need to stop blaming individual, and see benefit as a shared responsibility of the individual practitioners and the healthcare system. We will look at enhancing joy in our work, so we can maintain an intellectual, behavioral, and emotional commitment to meaningful and satisfying work. We will review the 5 Cs of Resilience to reinforce concrete and practical strategies that individuals can leverage to enhance resilience and maintain the joy in health care.

KEYNOTE ADDRESS

Addressing Practitioner Stress and Burnout: Turning Burnout Into Joy
Manta Gautam, MD, MBA, FRCP, CCPE - Psychiatry, University of Ottawa, Ottawa, ON, Canada; Psychosocial Oncology, The Ottawa Hospital, Ottawa, ON, Canada

At the conclusion of this presentation, participants will be able to: 1) Define and recognize burnout, and appreciate the scope of the issue. 2) Understand the drivers that lead to stress and burnout, and the impact on health care, and can lead to burnout. This presentation is designed to assist practitioners in learning how to recognize the symptoms of burnout, and prevent burnout in themselves and their colleagues. The main causes of stress and burnout will be discussed; as well as the impact of burnout on the person and the system. 4) Implement personalized strategies to prevent burnout. 5) Know the responsibilities of the organization or system in preventing burnout. 6) Understand the drivers that lead to burnout, and the impact on health care.

PLENARY SYMPOSIUM #1

The History of Hormones - Have We Delivered What We Promised?
Wulf H. Utian, MD, PhD, DSc(Med), FRCOG, FACOG, FICS. Case Western Reserve School of Medicine, Cleveland, OH

The history of the female menopause is one riddled with mythology, misogyne, ignorance, broken promises, graft, corruption, hype, unjustified hope, and impose a negative impact on the health and quality of life of women. Ignorance is not bliss! The purpose of this presentation is not to rehash a chronological history of menopause. Instead it is to address through a chronological review of some key historic moments the key question facing us at this time: Is what we do effective in preventing menopause? Numerous examples exist of sensationalistic reports of extravagant claims for new therapies or for unsubstantiated excessive risks of existing treatments, only to require a minimal refutation later, or more often or not, no retraction at all, leaving the misconception alive in public memory. Since time immemorial, humankind has searched for elixirs against aging. This presentation will briefly consider the issues of menopause, aging, and promises of prevention of disease and eternal youth, from the early concepts, to where this has brought us to the present time. To understand the risks and benefits of hormone therapies it is essential that there is a clear understanding of the health issue being addressed. How have we defined menopause and how have concepts changed? What have we defined to be true effects of the menopause, and how far have we come in counteracting them? How have we erroneously blamed menopause on menopause? Have there been medication side effects with hormonal treatment? What have women today believe? The authors’ scientific review of the 5 C’s of Resilience, and identify strategies to enhance resilience and maintain the joy in health care.

PLENARY SYMPOSIUM #2

What the KEEPS and ELITE Studies Have Taught Us
Virginia M. Miller, PhD. Surgery, Physiology and Biomedical Engineering, Mayo Clinic, Rochester, MN

The Kronos Early Estrogen Prevention Study (KEEPs) and the Early versus Late Intervention Trial (ELITE) were designed to determine the effects of menopausal hormone therapy (MHT) on progression of carotid intima-media thickness (CIMT). Using a randomized, double-blind, placebo-controlled design, the KEEPS enrolled women who were within three years of menopause, ie, similar to women seeking MHT in clinical practice; the ELITE enrolled two groups, women ≤ 6 or 10 years past menopause, testing directly the timing hypothesis of drug effects on increases in CIMT. Oral conjugated equine estrogen (oCE), 0.45 mg/day) or transdermal 17β-estradiol (IEI, 50μg/day) with pulsated progesterone (200 mg/day) were used in KEEPS; oral micronized 17β-estradiol (1 mg/day) with pulsated vaginal progesterone was used in ELITE. Rate of increases in CIMT was less in the MHT group compared to placebo in the younger but not in the older group after 5 years of treatment in ELITE. Although increases in CIMT were not affected by the MHT over the 4 years of the trial in KEEPS, both treatments reduced menopausal symptoms and bone mass compared to placebo. In both studies, MHT treatment was not neutral. However, in KEEPS, there were differences in effects of oCEE and IEI on measures of mood and sexual satisfaction. Critical factors contributing to translating results from clinical studies to practice include: timing of initiation, type, dose, and mode of delivery of the product, co-morbidities of study participants/patients, and outcomes, as dose-response efficacy may not be the same for all endpoints.
Hormone Therapy: What Are We Doing in 2019?
JoAnn V. Pinkerton, MD, NCMP. The University of Virginia Health System, Charlottesville, VA.

Despite evidence from the Women’s Health Initiative study (WHI) suggesting hormone therapy (HT) is a relatively safe, viable solution for symptomatic menopausal women under age 60 or within 10 years of menopause, fear limits HT prescriptions and use. HT is associated with an increased risk for heart failure, deep vein thrombosis, strokes, and breast cancer. HT also prevents bone loss and fractures. It is suggested that in women with estrogen-progestin (EPT) will show significant 33% reductions in hip fracture with beneficial effects on bone loss rapidly after discontinuation. If initiated early in the menopause transition, age 50-59 years old 10 years from menopause, HT does not increase coronary heart disease (CHD) risk and may reduce morbidity/mortality risk. HT initiated later increases CHD risk. The 2015 Bochum Cohort Review found HT initiated <10 years after menopause reduced CHD, RR of 0.53 (0.32 to 0.99), increased risk of VTE RR 1.74 (1.11 to 2.73) and reduced death RR 0.70 (0.50 to 0.95). 2017, Manson all-cause pooled (EPT+HT) mortality hazard ratios (HR) at 18 years of cumulative follow up by age at randomization showed less risk if HT was started age 50-59. Absolute risks of stroke, venous thromboembolism (VTE) and pulmonary embolism increase with age or time from menopause. The impact of HT on breast cancer risk is complex affected by type of HT (less risk with ET), dose, duration of use, regimen, route of administration, prior exposure to HT, and individual characteristics. Observation shows use of HT does not alter risk for breast cancer with a history of breast cancer. The risk (race, <1/1000) of breast cancer was increased with EPT compared to ET. At 13 years in the WHI, cumulative follow up of all ages at randomization, EPT showed significant but modest increased risk breast cancer of 1.28 while ET showed significant decreased risk breast cancer of 0.79. The Nurses’ Health Study suggested increased risk after 15 or 20 years of ET use. HT is not increased with age but may change with continuation of HT for up to 10 years. HT initiated after age 65 showed a rare increase in risk for dementia (WHO). ET may have positive cognitive benefits if initiated immediately after early surgical menopause, but neutral effects in the early menopause transition with only tentative observational data support of cognitive benefits. Evidence is insufficient to support HT for the treatment of clinical depression, however improved clinical depression in perimenopausal women. HT significantly reduces new-onset type 2 DM, but is not FDA approved for this purpose. HT helps attenuate abdominal adipose accumulation and weight gain associated with menopause transition. Risk of gallstones, cholecystitis, and cholelithiasis is increased with oral ET and EPT and lower with transdermal or estradiol therapy. Lower VTE and stroke risk are seen with lower doses and transdermal therapy, but lack comparative data. The choice for women with metabolic syndrome, fatty liver, or hypertriglyceridemia. Systemic estrogen requires adequate dose and duration of pregestagen or combination CEE with bazedoxifene for endometrial protection. SERM bazedoxifene with CEE treats VMS, preserves BMD, and protects the endometrium with bone, bleeding, breast and other effects similar to placebo. Compounded bioidentical hormone therapy lacks regulation and monitoring, scientific efficacy and safety data, label outlining risks, and may be over or under dosed. For early menopausal women, observational studies suggest benefits outweigh risks for bone, heart, cognition, VVA/GSM, sexual function, and mood. HT is recommended until at least the age of menopause (52 y). Routinely discontinuing HT after age 65 is NOT supported by data (despite the Beer’s criteria). Continuing HT beyond age 60 should be individualized, with counseling about potential benefits/risks and ongoing surveillance. Benefits likely to outweigh risks for symptomatic women who initiate HT less than age 60 or within 10 years of menopause. If initiating HT more than 10 or 20 years from menopause or 60 years or older, the benefit-risk ratio appears less favorable, with greater absolute risks of CHD, stroke, VTE, and dementia. Reference: The 2017 hormone therapy position statement of The North American Menopause Society. Menopause. 2017;24(7):726-753.

PLENARY SYMPOSIUM #3
Perimenopausal Depression Guidelines
Pauline M. Maki, PhD. Women’s Mental Health Research Program, University of Illinois at Chicago, Chicago, IL.

The North American Menopause Society (NAMS) and the National Network of Depression Centers (NNDCC) recently developed guidelines for the identification and treatment of perimenopausal depression. In clinical practice and research studies, midlife women report a worsening of mood as they transition through the menopause. The risk of major depressive disorder (MDD) also increases as women transition through the menopause, though this risk is primarily observed in women with a history of MDD. Thus, MDD during the transition typically represents a recurrence of a major depressive episode (MDE). It is recommended that antidepressants and psychotherapies remain as front-line treatments for MDD during the menopause transition. However, a key focus of the guidelines is the need to consider treatment of menopausal symptoms in women with MDD, as these symptoms can exacerbate mood problems. Women with vasomotor symptoms (VMS) are at increased risk for elevated depressive symptoms but VMS are less strongly linked to MDE. Estrogen therapy (ET) may have direct benefits to mood when used in appropriate perimenopausal women with depressive symptoms who have concomitant VMS, but is ineffective in postmenopausal women. Such evidence suggests a possible window of opportunity for the effective use of ET in the management of depression during the menopause transition. Unfortunately, there is little data on the combination estrogen plus progestin therapy on clinical depression during the transition. In non-depressed perimenopausal and early postmenopausal women, ET and combination estrogen plus progestin (HT) has been shown to enhance mood. There is emerging evidence that ET can prevent the development of depressive symptoms during the menopause transition. Hormonal contraceptives—particularly when used continuously—have shown some benefits for mood regulation and could be helpful for women experiencing depressive symptoms while approaching menopause. Further research is needed to clarify the role of HT and contraceptives on mood during the menopause transition.

What Happens after Menopause? (The WHAM Study): The Psychological Outcomes
Martha Hickey, MBBCh, FRANZCOG, MD. Obstetrics and Gynecology, University of Melbourne, The Royal Women’s Hospital, Parkville, VIC, Australia.

The WHAM study measured mental health (depression and anxiety), sleep quality, memory and cognition at baseline and up to 12 months after surgical menopause, the modifying effect of systemic Hormone Therapy and comparisons with age-matched controls. These new findings will be presented and the implications for clinical practice will be discussed.

PLENARY SYMPOSIUM #4
Vitamin D and Omega-3 Fatty Acids: Do They Prevent Cancer or Cardiovascular Disease?
JoAnn E. Manson, MD, NCMP. 1Preventive Medicine, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA; 2Epidemiology, Harvard TH Chan School of Public Health, Boston, MA.

Whether vitamin D or omega-3 supplementation is beneficial for the prevention of cancer or cardiovascular disease (CVD) is a subject of ongoing debate. The VITamin D and Omeg-3 Triad (VITAL) was designed to fill these knowledge gaps. VITAL is a completed nationwide, randomized, placebo-controlled, 2x2 factorial trial of vitamin D3 (2,000 IU/d) and marine omega-3 fatty acids (EPA; 1 g/d) in the primary prevention of CVD and cancer among 25,871 U.S. men aged ≥50 and women aged ≥55, including 5,106 African Americans. Median treatment duration was 5.3 years. Omega-3 FAs did not significantly reduce the primary cardiovascular endpoint of major CVD events (a composite of myocardial infarction or stroke, and CVD mortality or non-fatal MI), hazard ratio [HR]=0.92 [95% confidence interval 0.80–1.06]) but was associated with significant reductions in total MI (HR=0.72 [0.59–0.90]), percutaneous coronary intervention (HR=0.78 [0.63–0.95]), and fatal MI (HR=0.50 [0.26–0.97]) but not stroke or other CVD endpoints. For major CVD events, a treatment benefit was seen in those with dietary fish intake below the cohort median of 1.5 servings per week (HR=0.81 [0.67–0.98]) but not in those above (p-interaction=0.045). For MI, the greatest risk reductions were in African Americans (HR=0.23 [0.11–0.47]; p interaction=0.001). Supplemental omega-3 FAs were not associated with cancer endpoints during the full trial period, but a signal for a slight increase in total cancer incidence emerged after excluding the first two years of follow-up (HR=1.13 [1.00–1.28]). Vitamin D supplementation did not reduce major CVD events (HR=0.97 [0.85–1.12]), other cardiovascular endpoints, or cancer incidence. However, vitamin D was associated with a 17% reduction in cancer mortality, which reached a statistically significant 25% reduction in analyses excluding early follow-up. Reductions in cancer incidence and mortality were seen in those of normal weight (body mass index [BMI] <25 kg/m²) but not in those with over/obesity (P for interaction by BMI=0.002), and suggestive were seen in African Americans. The pattern of findings suggests a complex balance of benefits and risks for each intervention. Additional research is needed to determine which individuals may be most likely to derive a net benefit from these supplements. (VITALclinicaltrials.gov identifier: NCT01169259)

Vitamin D and Omega-3 Fatty Acids: Do They Have Benefits for Mood, Depression, or Cognition?
Olivia I. Okereke, MD, MS. 1Psychiatry, Massachusetts General Hospital and Harvard Medical School, Boston, MA; 2Medicine, Brigham and Women’s Hospital and Harvard Medical School, Boston, MA.

Depression in late-life is common and highly disabling. Frequently, depression is under-recognized and under-treated in older adults, particularly among minorities. Furthermore, residual symptoms and dysfunction from depression are significant problems, even when appropriate treatment is provided. Therefore, prevention of late-life depression is imperative. Similarly, late-life cognitive decline has emerged as one of today’s greatest health challenges. Given the projected aging of the population, maintaining cognitive function into older ages is of major public health importance, and prevention and early intervention may be most effective to achieve this goal. In response to the need for effective prevention of late-life depression and cognitive decline, two ancillary studies to the VITamin D and Omega-3 A3 Trial – VITAL-DEP (VITAL-Depression Endpoint Prevention, NCT011696435) and VITAL-COG (VITAL-Cognitive decline, NCT01669915) – were initiated in concert with the launch of VITAL. These studies will test the effects of two highly plausible agents – vitamin D and marine omega-3 fatty acids – for the prevention of depression, promotion of long-term positive mood and reduction of cognitive decline among older adults, over a treatment period of 5+ years. Implemented among the full cohort of VITAL participants, VITAL-DEP represents a
first-of-its-kind, large-scale study to address simultaneously the strategies of universal, selective and indicative prevention in depression. Special attention is given in VITAL-DEP to whether effects of the agents may vary by key factors, such as race, geographic region, and baseline co-morbidity and biochemical nutrient levels. Conducted among nearly 4,000 older adults, with over-sampling of black participants, VITAL-COG addresses vulnerability among minorities, as higher risk of cognitive decline with aging as well as potential racial susceptibility to low vitamin D levels has been observed among black adults. Furthermore, evaluation of outcomes is enhanced by deep-phenotyping assessments that were completed in a subset of over 1,000 participants, who received in-person psychiatric diagnostic interviews, underwent cognitive testing, and provided self-reports on dimensional measures of depression, anxiety, daily functioning, subjective memory, social support, caregiving activity, and alcohol use behaviors. Taken together, the results of the VITAL-DEP and VITAL-COG studies provide high-quality evidence regarding the causal effects of vitamin D and fish oil on mood and brain health.

**PLENARY SYMPOSIUM #5**

**Bad to the Bone: The Expanding List of Medications Associated with Osteoporosis**

Nelson B. Watts, MD, FACP, MACE, CCD. Mercy Health Osteoporosis and Bone Health Services, Cincinnati, OH

**Individualizing Osteoporosis Treatment**

Michael R. McCloskey, MD. 1 Oregon Health and Science University, Portland, OR; 2 Mary MacKillop Center for Health Research, Australian Catholic University, Melbourne, VIC, Australia

Osteoporosis is a chronic condition characterized by low bone mass and disorders of bone architecture, impairing bone strength and leading to fragility fractures. With the combination of bone mineral density (BMD) testing and other clinical risk factors for fracture including age and prior fracture history, patients with osteoporosis can be stratified into those at moderate, high, or very high risk of fracture. Several classes of drugs improve bone mass and strength and reduce fracture risk, but none correct the underlying structural deficits or “cure” osteoporosis. Thus, long-term management is required. Bisphosphonates and denosumab, both anti-remodeling agents, are the drugs considered for long-term use. Information about their efficacy and safety over 10 years is available. Switching to an alternate therapy should be considered for patients remaining at high risk of fracture after 5 years of bisphosphonate therapy. Bone-forming agents, including PTH receptor agonists teriparatide and abaloparatide and, very recently, romosozumab, have been shown to reduce fracture risk more quickly than anti-remodeling drugs in patients at very high risk of fracture. Based upon these findings, updates in treatment guidelines suggest that patients at very low risk of fracture should receive only non-pharmacological management. For those at moderate fracture risk, beginning therapy with raloxifene or an oral bisphosphonate would be appropriate. For patients at high risk of fracture, treatment with either IV zoledronic acid or denosumab is recommended while for patients at very high or imminent risk of fracture – including patients with a recent fragility fracture – therapy with either a PTH receptor agonist or romosozumab, followed by a potent anti-remodeling agent to maintain or amplify the gains in bone strength would be considered. Re-evaluating patients’ adherence to and toleration of therapy as well as their fracture risk at regular intervals are important parts of the long-term management of patients with osteoporosis. Emerging evidence suggests that measuring BMD by DXA at the total hip site is the most effective way to monitor the effectiveness of treatment. This raises the possibility of using total hip BMD as a treatment “target” and choosing therapies most likely to allow an individual patients to reach that treatment goal. There is no single “best treatment” for osteoporosis. Individualizing initial therapy, followed by regular monitoring and shifting treatment strategies when appropriate, will provide the optimum benefits (clinical and cost) for the patients that we treat.

**NAMS/PFIZER WULF H UTIAN ENDOWED LECTURE**

The New Frontier: Averting Menopause at 22 for Pediatric Cancer Survivors

Teresa K. Woodruff. Obstetrics and Gynecology, Northwestern University, Chicago, IL

Facing a cancer diagnosis at any age is devastating. However, young cancer patients have the added burden that life-preserving cancer treatment, including surgery, chemotherapy, and radiotherapy, may compromise their future fertility and can result in early menopause. The possibility of reproductive dysfunction as a consequence of cancer treatment has a negative impact on the quality of life of cancer survivors. The field of oncofertility, which merges the clinical specialties of oncology and reproductive endocrinology, was developed to explore and exploit fertility preservation options and endocrine support to better manage the reproductive status of cancer patients. Fertility preservation includes a particular challenge because many female gametes are rare and difficult to acquire. Moreover, managing pediatric gonadal function has specific complexities that will be addressed in this presentation. Indeed, this presentation will provide a comprehensive overview of how cancer treatments affect fertility and what the diverse fertility preservation modalities and treatments available are currently available or being developed for young women, and describe current measures of ovarian reserve that can be used pre- and post-cancer treatment.

**PLENARY SYMPOSIUM #6**

The Human Microbiome in Precision Medicine

Jack A. Gilbert, PhD. Pediatrics and Scripps Institution of Oceanography, University of California School of Medicine, San Diego, San Diego, CA

The human microbiome is quickly being recognized as a dynamic part of the human ecosystem, and research is starting to demonstrate that using ecology to understand this ecosystem has profound benefits for patient wellbeing. The immune system connects the microbe with the world, and yet the microbial communities in our bodies are central to modulating the immune response. Changes in the human microbiome have substantial influence on atopy, neurological disorders, metabolic disorders, and a range of complex conditions and interaction diseases. We will discuss evidence of these mechanisms of interaction and how we have started to disturb the delicate balance of the immune-microbe equilibrium; development and function of our immune systems. Applying new strategies to identify how the microbial ecosystem correlates with diseases states and treatment efficacy through Microbiome-Wide Association Studies (MWAS) is altering the trajectory of precision medicine, and providing a new framework for facilitating patient care and clinical decision making. Using a combination of observational studies, clinical trials, and discordance of microbiome-related therapies, pointing to concerns about over-promising of microbiome as a real treatment strategy. There is considerable concern about the need to move beyond studies that identify correlations between the microbiome and disease, toward intervention trials that will actually explore specific mechanistic relationships. It truly is time to start delivering on the promise of the microbiome.

The Vagina Dialogues: Vaginal Microbiota and Menopause

Caroline Mitchell, MD, MPH1,2. Obstetrics, Gynecology, and Reproductive Biology, Harvard Medical School, Boston, MA; 3Vincent Center for Reproductive Biology, Massachusetts General Hospital, Boston, MA

The community of microbes colonizing the vagina have a profound impact on reproductive and sexual health. Communities dominated by Lactobacillus species are associated with lower risk for HIV acquisition, bacterial sexually transmitted infections and persistent HPV infection in premenopausal women. These associations have not been well studied in postmenopausal women. After menopause, many women lose vaginal colonization with lactobacilli and testing often identifies gram negative rods such as E. coli colonizing the vagina. It is not well known whether the vaginal microbiota drive postmenopausal vaginal discomfort, or are a symptom of the same underlying process that leads to the discomfort. Regardless of whether vaginal microbiota are associated with postmenopausal vaginal discomfort, modulation of the vaginal microbiome may mitigate risk for genital infections, urinary tract infections and cervical dysplasia. Currently, the most reliable strategy for promoting vaginal Lactobacillus colonization after menopause is treatment with estrogen, however, additional therapies are in development.

**PLENARY SYMPOSIUM #7**

Prevention and Screening in Colorectal Cancer

Cynthia M. Yoshida, MD. Gastroenterology and Hepatology, Department of Medicine, University of Virginia, Charlottesville, VA

At the conclusion of this presentation, participants will be able to: 1) Understand the current CRC screening guidelines (including the most recent guidelines by the American Cancer Society to begin screening at age 45); 2) Define the appropriate use and pros/cons of CRC screening tests. The American Cancer Society (ACS) estimates there will be 145,600 new cases and 51,020 deaths from colorectal cancer (CRC) in 2019. Numerous societal/task force endorsed guidelines have traditionally recommended screening adults over age 50 with either stool-based or structural/visual tests. CRC incidence rates in adults over age 55 have been declining 3.7% annually from 2006-2015, largely due to the uptake of CRC screening and modifications in risk factors. But an alarming statistic is that CRC incidence has increased by 1.8% annually in younger adults over this same time period. Adults born around 1990 have twice the risk of colon cancer and four times the risk of rectal cancer compared with adults born around 1950. In May 2018, the ACS released an updated guideline with a qualified recommendation that CRC screening begin at age 45 in average risk patients. This presentation will review current CRC screening guidelines and will define the appropriate use as the pros/cons of recommended screening tests. References: Wolfe A, et al. Colorectal cancer screening for average-risk adults: 2018 guideline update from the American Cancer Society. Cancer 2018;124(4):250-281. Rex DR, et al. Colorectal cancer screening: Recommendations for physicians and patients from the U.S. Multi-Society Task Force on Colorectal Cancer. Gastrointest Endosc. 2017;86(1):18-33. US Preventive Services Task Force; Bibbins-Domingo K, Grossman DC, Curry SJ, et al. Screening for colorectal cancer: US Preventive Services Task Force recommendation statement. JAMA 2016;315:2564-75.
Breast Cancer Prevention: The Importance of Lifestyle

Dawn M. Sussmali, DO. Hematology Oncology, Mayo Clinic Florida, Jacksonville, FL. Breast cancer is the most common cancer in women worldwide and among women in the US. Expert reports estimate that one in three breast cancer cases could be prevented by lifestyle. The World Cancer Research Fund (WCRF) and the American Institute for Cancer Research (AICR) are the world’s largest source of scientific evidence on how certain lifestyle and dietary risk factors can influence cancer risk. In 2018, the WCRF/AICR Cancer Update Project Third Expert Report updated breast cancer prevention recommendations categorized by menopausal status, where possible, and includes modifiable elements of breast cancer risk with respect to weight management, physical activity, nutrition, alcohol consumption and smoking. The National Center for Health Statistics CDC estimates that 41.1% of US women age 20 and older were obese as of 2015-2016. For postmenopausal women, there is a 1.5 to 2.0 times increased risk of breast cancer if a woman is obese. Body fatness is suggested to increase the susceptibility to cancer as a result of hyperinsulinemia, increased estradiol and inflammation. According to the U.S. Centers for Disease Control and Prevention, physical activity could prevent one in eight breast cancer cases. There is strong evidence demonstrating a dose-response relationship between greater amounts of physical activity and a lower risk of breast cancer, independent of BMI. In 2018, the Physical Activity Guidelines Advisory Committee recommended a minimum of 150 minutes of moderate-intensity aerobic exercise weekly for healthy living. Alcohol is a carcinogen attributable to 6.4% of breast cancer cases. Women should avoid alcohol for cancer prevention. Any amount of alcohol increases the risk of breast cancer and the more a woman drinks the higher the breast cancer risk. The systemic effects of alcohol contributing to tumorogenesis include elevated acetaldehyde, inflammation, interference with folate metabolism, and increased estradiol. Though methodological challenges in dietary research exist there are hundreds of observational studies suggesting poor dietary quality increases the risk of breast cancer and dying as a result of breast cancer. The EPIC study, a large prospective European study, showed a 16% reduced breast cancer risk in women with the highest adherence to the 2007 WCRF/AICR recommendations. The Cancer Update Project 2017 pooled analysis observed a significant lower breast cancer risk with non-standardized consumption of alcohol versus any consumption. The Women’s Health Initiative showed a beneficial effect of alcohol on heart disease, diabetes, stroke, pancreatitis, and liver disease. Breast cancer, and cancers of the GI tract. Although one alcoholic drink daily was previously thought to have a beneficial effect on CVD, global data reported in 2018 showed that even one alcoholic drink may be harmful. The rising rates of high risk drinking and AUD in women of middle age are of serious concern, especially because of the vulnerability of women to the toxic effects of alcohol, and the low rate of women seeking treatment programs. These observations highlight the importance of screening for high risk alcohol use and AUD in women, and identification and removal of barriers to treatment. More research is needed to gain a better understanding of the risk factors for excess alcohol consumption in women so that effective prevention and treatment programs may be developed. Table 1. Changes in 12 month Alcohol Use, High Risk Drinking and AUD 2001-2002 to 2012-2013 National Epidemiological Survey of Alcohol and Related Conditions References: 1. Slade T, Chapman C, Swift W et al. BMJ Open 2016; 6 (10) e011827. 2. Grant BF, Chou P, Saha TD, et al. JAMA Psych. 2017; 74(9): 911-23. 3. White AM, Slater ME, Ng G, et al. Alcoholism Clin Exp Res 2018; 42(2): 352-9.

Aspirin for the Primary Prevention of Cardiovascular Disease: What Do the 2019 ACC/AHA Guidelines Recommend?

Erin D. Michos, MD, MHS, FAHA, FACC. Johns Hopkins University School of Medicine, Baltimore, MD

Aspirin is a well-established therapy for the secondary prevention of atherothrombotic cardiovascular disease (ASCVD) among individuals with established ASCVD. In primary prevention, the absolute risks of vascular events are lower than in secondary prevention; however the complication rates (ie, bleeding) are comparable. Recent evidence from randomized clinical trials have shown less benefit for prophylactic aspirin when used in combination with other contemporary ASCVD preventive therapies. In 2018, the ASCEND, ARRIVE, and ASPREE trials were published. ASCEND evaluated over 15,000 adults who had diabetes but no ASCVD and found that the absolute benefit of reduction in serious vascular events by low dose aspirin was largely counterbalanced by the increased risk of death. In the ARRIVE trial of 12,546 adults who were estimated to be at intermediate ASCVD risk, there was no benefit of aspirin for reducing major adverse cardiovascular events but increased risk of GI bleeding. Finally, in the ASPREE trial of 19,114 adults aged >65, suggesting more harm than benefit. These findings guided the updated aspirin recommendations in the 2019 American College of Cardiology (ACC) and American Heart Association (AHA) guidelines for the primary prevention of cardiovascular disease (Table). These recommendations differ from prior AHA guidelines recommending aspirin could be considered for patients with 10-year ASCVD risk ≥10%. The 2019 guidelines state most healthy people do not need to take aspirin. There may still be select patients age 40 to 70 who have a very high risk of ASCVD who may benefit from aspirin if low risk for bleeding. One might still consider low dose aspirin (75 to 100 mg/day) among current smokers, those with a strong family history of premature ASCVD, those with very elevated cholesterol optimally treated with statins, those with subclinical atherosclerosis such as a coronary artery calcium scores >100, and select patients with diabetes at high ASCVD risk. However, these decisions are needed in the context of a clinician-patient risk discussion. Clinicians should qualitatively evaluate for bleeding risk and withhold aspirin in primary prevention patients with increased risk such as prior GI bleeding or ulceration, known bleeding disorder, severe liver disease, thrombocytopenia, concurrent anticoagulation or NSAID use, or uncontrolled hypertension.

**PLENARY SYMPOSIUM #8**

Alcohol Use in Midlife Women

Connie B. Newman, MD, FACP, FAHA, FAMWA. Endocrinology and Metabolism, New York University School of Medicine, New York, NY

Problematic alcohol use in women increased globally throughout the 20th century, narrowing the male to female gender gap from 3.0 in the early 1900’s to 1.2 in the 1990’s. In the past 10-15 years, in the US, high risk drinking and alcohol use disorder (AUD) increased, especially in women, in the middle aged and elderly, minorities, and the socioeconomically disadvantaged. Analysis of face to face surveys in about 40,000 US adults found that the prevalence of any 12 month alcohol use was 73% in 2012-2013, which represented an increase of 11.2% from 2001-2002 (Table 1). The prevalence of high risk drinking (4 or more drinks/day in women, 5 or more drinks/day in men) was 12.6% in 2012-2013 which represented a 30% increase during the decade. The greatest change in high risk drinking occurred in women (58%) and in age groups 45-64 and 65 and over, AUD as defined by DSM-IV and reflecting alcohol dependence and/or abuse, increased by 49% with a higher proportional increase in women (82%) and the middle and elderly age groups. In addition, alcohol-related emergency department visits in the US were significantly higher in 2014 compared to 2006, 5.0 million vs 3.1 million, respectively, largely due to chronic alcohol consumption in women aged 45 to 65 years. The rising rates of high risk drinking and AUD in midlife women are not completely understood, but could be related to stress from work, or perhaps to retirement, financial pressures, empty nest, or challenges associated with the menopause transition. Depression is more common in women with AUD compared to men. Further, women are less likely than men to work treatment for alcohol use disorder. Sex differences in the metabolism of alcohol and chronic complications of excessive alcohol use indicate that females are especially vulnerable to its toxic effects. Women are more sensitive to the short term effects of alcohol because of lower gastric alcohol dehydrogenase (ADH), and body water. As a result of reduced gastric ADH, alcohol first pass metabolism is decreased, causing higher blood levels and another small amount of ethanol. This may explain why women become addicted to alcohol with less exposure (fewer drinks) over shorter periods of time. Women are also more at risk for long-term adverse effects of alcohol. Alcohol use in women, compared to men, is associated with a higher relative risk of alcoholic liver disease, cirrhosis, and liver failure. Alcohol use also increases the risk of hypertension, heart disease, diabetes, stroke, pancreatitis, and mental health problems, breast cancer, and cancers of the GI tract. Although one alcoholic drink daily was previously thought to have a beneficial effect on CVD, global data reported in 2018 show that even one alcoholic drink may be harmful. The rising rates of high risk drinking and AUD in women of middle age are of serious concern, especially because of the vulnerability of women to the toxic effects of alcohol, and the low rate of women seeking treatment programs. These observations highlight the importance of screening for high risk alcohol use and AUD in women, and identification and removal of barriers to treatment. More research is needed to gain a better understanding of the risk factors for excess alcohol consumption in women so that effective prevention and treatment programs may be developed. Table 1. Changes in 12 month Alcohol Use, High Risk Drinking and AUD 2001-2002 to 2012-2013 National Epidemiological Survey of Alcohol and Related Conditions References: 1. Slade T, Chapman C, Swift W et al. BMJ Open 2016; 6 (10) e011827. 2. Grant BF, Chou P, Saha TD, et al. JAMA Psych. 2017; 74(9): 911-23. 3. White AM, Slater ME, Ng G, et al. Alcoholism Clin Exp Res 2018; 42(2): 352-9.

### Table 1. Changes in 12 month Alcohol Use, High Risk Drinking and AUD 2001-2002 to 2012-2013 National Epidemiological Survey of Alcohol and Related Conditions

<table>
<thead>
<tr>
<th>Period</th>
<th>Prevalence %</th>
<th>Change</th>
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<tr>
<td>2001-2002</td>
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<td></td>
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<tr>
<td>2012-2013</td>
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<td>4.3</td>
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<td>Men</td>
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Women, Ethics, and Cannabinoids
Oyedjie Ayoimndie, FRCPsych, MBA. Psychiatry and Psychology, Queen’s University, Kingston, ON, Canada

Cannabis products have been consumed across cultures for centuries. In the 20th century, the illegal status of marijuana (cannabis) in many countries was associated with the policing and regulation of access despite the wide availability and high levels on consumption. In recent years, attitudes change and emerging scientific evidence have caused a stir across jurisdictions worldwide. The growing use of cannabis for medical purposes has been supported by policy and legislative changes with direct impacts on healthcare systems. Legalization or decriminalization of cannabis for either medical or recreational purposes in an increasing number of U.S. states and federally in Canada continues to drive changes across gender, ages, generations, and geographical boundaries. Exposed to increasing information on cannabis, the lay public and scientific community alike are challenged with filtering latest evidence from anecdote and misinformation. This culture shift is consolidating the position of cannabis in contemporary social discourse. While there are over 100 different cannabinoids, core knowledge is limited to mainly delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD). There has also been a considerable knowledge growth regarding terpenes, the unique aromatic characteristics of the cannabis bud. The psychoactive and potentially intoxicating effect of THC derived from the female plant and plays a pivotal role in recreational use of cannabis and some medical application. CBD on the other hand with a non-intoxicating effect has been widely positioned in health and wellbeing spheres. The percentages of THC and CBD as well as their ratios contribute to the characteristics of each cannabis preparation interacting with the endocannabinoid system of the consumer. Both cannabinoids with their modes and routes of consumptions have contributed to a multi-billion dollar medical and recreational cannabis industry. While research consistently demonstrates male predominance in cannabis consumption, an area of growth that has not attracted the same scholarly attention is the role of cannabinoids across the lifecycle of women. There is emerging evidence of gender differences in the pharmacodynamics and pharmacokinetics of cannabinoids. With THC for instance, metabolic, hormonal and body fat distribution differences can contribute to different effects. With higher prevalence of anxiety and depression in females, the complex interaction of cannabis for symptom relief (anxiolytic) and the potential to worsen symptoms (anxiogenic) effects needs more detailed understanding. Where research has focused on specific ethical issues regarding women, the highlight has been on pregnancy and breastfeeding, with evidence suggesting the risk of neurodevelopmental harm to the unborn child and early childhood difficulties in some children. Emphasis being more on child than maternal health. The use of cannabinoids for menstrual disorders has also attracted interest and controversy. Given the heterogeneity of cannabinoids, their commercialization across cosmetics, cuisine and couture for medical lifestyle and recreational purposes, challenges medical and scientific knowledge with individual consumer response. While cannabis products have been predominantly smoked, and edible consumption continues to grow in preference, increased awareness of the perineum to palpation, severe tenderness of the posterior vestibule (without tenderness in the anterior vestibule), and tight and tender puboccygeus and transverse perinei muscles normal. A thorough examination has revealed that the patient initially had some vaginal dryness and mild dyspareunia beginning at the age of 50 but that these symptoms resolved after the initiation of vaginal CEE cream. Her current sexual pain symptoms began three months after she began an aggressive exercise regimen in preparation for her upcoming wedding. Further questioning reveals that she is having severe anxiety in anticipation of her marriage because her fiancé has been emotionally abusive and focused on her weight. The combination of these data suggests that her pain is "provoked vestibulodynia associated with overactive pelvic floor muscle dysfunction." In this situation, however, the patient would likely be better served by a treatment regimen consisting of cognitive behavior therapy, relationship counseling, and pelvic floor physical therapy, rather than a medical or surgical treatment.
S-1. Vasomotor Symptoms and Risk of Cardiovascular Disease Events in the Study of Women’s Health Across the Nation

Rebecca C. Thurston, PhD2, Helen Vlahos1, Carol A. Derby, PhD2, Karen Matthews1, 2, Maria Brooks1, Elizabeth Jackson, MD, MPH, PhD, Siobhan Harlow, PhD, Hadine Joffe, MD, MSc2, Samar R. El Khoudary, PhD, MPH1, Psychiatry, University of Pittsburgh, Pittsburgh, PA; 2Epidemiology, University of Pittsburgh, Pittsburgh, PA; 3Neurology, Harvard Medical School, Boston, MA

Objective: Emerging work links menopausal vasomotor symptoms (VMS) to an adverse cardiovascular disease (CVD) risk factor profile and subclinical CVD. However, data linking VMS to clinical CVD is rare. Most studies rely upon retrospective VMS reports, subject to biases. The Study of Women’s Health Across the Nation (SWAN) is a longitudinal 20-year study of the menopause transition. With VMS and CVD events assessed prospectively, SWAN is uniquely positioned to test VMS-CVD relations. We explored associations of VMS with clinical CVD events in SWAN.

Methods: SWAN enrolled 3302 pre-/early perimenopausal women, ages 42-52, with a uterus and a nonovary, and not on hormone therapy (HT) and followed them for up to 20 years. Approximately annually, VMS (hot flashes, night sweats; none, 1-5 days, 6 days, prior two weeks) were assessed via questionnaire and CVD events (myocardial infarction, stroke, heart failure, percutaneous coronary intervention, bypass surgery) via interview (medical record verified for a subset). Cause of death was coded via death certificate. Relations between VMS [baseline, proportion of visits with frequent (≥6 days) VMS] and combined CVD events [first adjudicated/self-reported event or CVD mortality] were tested in Cox models (covariates: site, age, race, number of visits attended, education, financial strain, menopause status, smoking, physical activity, blood pressure, body mass index, lipids, insulin resistance, medication use). Results: Of the 3272 women studied (47% White, 28% African American, 9% Japanese, 5% Chinese, 9% Hispanic), 231 had a CVD event over follow up. Frequent baseline VMS were associated with a higher risk for later CVD events [1-5 days: HR=1.05 (95%CI=.75-1.47), p=.76; ≥6 days: HR=1.62 (95%CI=1.10-2.38), p=.01, relative to no VMS, multivariable]. More frequent VMS over time were also associated with higher risk for later CVD events [HR=2.01 (95%CI=1.30-3.11), p=.002, relative to no VMS, multivariable]. Conclusion: Women with frequent VMS or persistent VMS over the transition had higher CVD event risk independent of risk factors. Frequent VMS, particularly when persistent, may indicate later CVD risk.

S-2. Comparison of cardiovascular risk factors between two atherosclerosis measures in postmenopausal women

Roksana Karim, PhD, Wemui Xu, BS, Intira Sriprasert, Howard Hodis, Wendy Mack. Preventive Medicine, University of Southern California, Los Angeles, CA

Objective: Subclinical atherosclerosis is commonly assessed by carotid artery intima-media thickness (CIMT), a quantitative analysis of B-mode images of the arterial wall obtained by ultrasonography. Ultrasonographic images can also be analyzed for echomorphology (measured as grey scale median, GSM) to determine qualitative aspects of the arterial wall. Greater echogenicity indicates fibrous and calcium deposition whereas, echolucency indicates lipid deposition. A handful of reports from the Prospective Investigation of the Vasculature in the Uppsala Seniors (PIVUS) study report that echogenicity of the carotid artery intima-media complex is associated with common cardiovascular (CV) risk factors and can be a novel independent predictor of mortality. Our objective for the current study is to compare the risk factors of CIMT and GSM of the carotid artery intima-media complex in postmenopausal women participating in a completed clinical trial, the Early vs Late Intervention Trial with Estradiol (ELITE) were used for this cross-sectional study. CIMT and GSM were measured by B-mode ultrasonography in the far wall of right common carotid artery. Basic CV risk factors including age, race, BMI, smoking, weekly hours of physical activity, systolic and diastolic blood pressure, lipids (LDL-cholesterol, HDL-cholesterol, triglycerides), glucose, and markers of inflammation (IL-6, leptin, adiponectin, ghrelin, resistin, TNFα) were measured at the baseline visit. Linear regression models were used to assess associations of CV risk factors with atherosclerosis outcomes. Multivariate models included the groups of risk factors one at a time along with the basic risk factors (age, race, BMI, physical activity). The R-squared value for each model minus the R-squared for the basic model were compared between CIMT and GSM. Results: In univariate analysis, age, race, BMI, SBP, DBP, LDL, HDL and IL-6 were significantly associated with both CIMT and GSM; R-squared for all common risk factors but age were greater for GSM associations. Serum glucose, triglycerides, leptin, adiponectin, ghrelin and physical activity were significantly associated with GSM only. Adjusted for age, race, BMI and physical activity, R2 values for the lipids, DBP, glucose, and markers of inflammation models were greater for GSM associations, whereas R2 values for SBP was greater for the CIMT association. Conclusion: While GSM and CIMT share some common CV risk factors, GSM is associated with a greater number of CV risk factors. GSM also showed a greater correlation with lipids, glucose, and markers of inflammation whereas CIMT.
S-3. Associations of endogenous sex hormones with carotid plaque burden and characteristics in midlife women

Yannia Cortés, PhD, MPH, FNP, Emma Barinas-Mitchell, PhD, Natalie Suder Egnont, DrPH, Shalender Bhasin, MD, Ravi Jasuja, PhD, Nanette Santoro, MD, Rebecca C. Thurston, PhD. 1University of Pittsburgh, Pittsburgh, PA; Nursing, University of North Carolina at Chapel Hill, Chapel Hill, NC; Cardio ChemRisk, Pittsburgh, PA; 2Brigham and Women’s Hospital, Boston, MA; 3University of Colorado, Aurora, CO

Objective: Cardiovascular disease (CVD) is the leading cause of death in women. Endogenous sex hormones have long been postulated to be involved in the pathogenesis of CVD in women. The menopause transition is accompanied by variability of sex hormone secretion, which may adversely affect CVD risk factors (i.e., body fat distribution, insulin secretion, lipoproteins). Carotid plaque assessment by ultrasound is an easy and cost-effective measure of carotid atherosclerosis that is associated with future CVD events. Carotid plaque characteristics, such as plaque echogenicity, an ultrasound measure that reflects plaque composition, may identify unstable plaques that are more likely to rupture, precipitating a major cardiovascular event. It has been suggested that measures of carotid plaque burden (number of plaques, total plaque area [TPA]) and characteristics (calcification, echogenicity) more accurately predict CVD events than carotid intima-media thickness or plaque presence alone. Although a growing body of evidence indicates strong links between endogenous sex hormones and CVD among midlife women, few studies have considered sex steroids in relation to carotid plaque and its characteristics. Our aim was to evaluate estrone (E1), estradiol (E2), testosterone (T), sex hormone binding globulin (SHBG), and free T (FT) in relation to measures of carotid plaque burden and characteristics in midlife women. Design: The MsHeart Study was a cross-sectional study of 304 nonsmoking perimenopausal and postmenopausal women aged 40-60 years who were free of clinical CVD. The MsHeart Study had the following aims: to examine associations between hot flashes and CVD risk factors. Participants underwent physical measurements, psychosocial and medical history assessments, ambulatory hot flash monitoring, phlebotomy (inflammatory markers, sex hormones), and a carotid artery ultrasound. E1, E2, and T were assayed using liquid chromatography–tandem mass spectrometry, the gold standard for steroid sex hormones. FT was calculated from total sex hormone levels, sex hormone binding globulin (SHBG), and free T (FT) in relation to measures of carotid plaque burden and characteristics in midlife women. Results: The current analysis included MsHeart participants with evidence of carotid plaque burden and characteristics. Participants were on average 54 years old, overweight, 72% were non-Hispanic White, and 82% were postmenopausal. In adjusted models, higher E1 were related to greater grey-scale median $\beta$-value = 0.015, P-value = 0.009, 0.54, indicating greater carotid plaque burden. Further, higher E1 was related to greater grey-scale median [OR (95% CI) = 2.31 (1.26, 4.22), multivariable], characteristic of more stable (low-risk) carotid plaque. E2 and T were not associated with carotid plaque burden or characteristics. Conclusion: Higher SHBG and lower FT were related to greater carotid plaque area, indicating greater burden. Higher E1 was related to plaque echogenicity, indicating more stable plaque. Our findings highlight the potential importance of endogenous sex hormones in the development of carotid atherosclerosis as women age.

Sources of Funding: This work was supported by the National Institutes of Health, National Heart Lung and Blood Institute, National Institute on Aging, and the National Heart, Lung, and Blood Institute (Grants RO1HL10564, K24123565 to R-C-T, R43AG045011, R44 AG045011 to R-J). UL1TR000005; S10RR023461). Additional support to S.B. was provided by the Boston Claude D. Pepper Older Americans Independence Center grant P50AG16379 and by a grant from the CDC Foundation.

S-4. Novel Atherosclerotic Changes Unveiled by Ion Mobility Lipoprotein Particle Fractionation and Measurement of Subclinical Atherosclerosis Composition in Postmenopausal Women

Roksana Karim, PhD3, Stephanie Kim1, Howard Hodis2, Intira Sriprasert1, Ronald Krauss3, Wendy Mack1. 1Preventive Medicine, University of Southern California, Los Angeles, CA; 2Medicine, University of Southern California, Los Angeles, CA; 3Children’s Hospital Oakland Research Institute, San Francisco, CA

Objective: Lipoprotein (LP) particles are circulating protein-lipid complexes playing key roles in distribution and utilization of cholesterol and triglycerides (TG). LPs are dynamic and comprise a spectrum of particles that contribute to atherosclerosis based on their chemical/physical properties, including size. LDL-cholesterol, the sum of cholesterol in all LDL particles, is a biomarker of atherosclerosis risk, whereas HDL-cholesterol, the sum of cholesterol in all HDL particles, is a biomarker of atherosclerosis protection. It is not clear if all LP fractions of LDL and HDL are associated with CVD risk factors. Methods: This study was a cross-sectional analysis of LP fractions with CIMT and GMS. Results: Total LDL-cholesterol was adversely associated with both CIMT and GMS; TG levels were associated with GMS only. Levels of very small-, small- and medium-sized LDL particles, but not large LDL or HDL, were associated with thicker arterial wall (greater CIMT) and greater arterial wall lipid deposition (lower GMS). Levels of medium- and large-sized VLDL particles were associated with lower GMS but not with CIMT. Small-sized HDL particles were associated with greater arterial wall lipid deposition (lower GMS) whereas large-sized HDL particles were associated with less lipid deposition (higher GMS). The majority of these associations were evident in early (46 years), but not in late (10 years) postmenopausal women. Conclusion: Although the standard lipids measures of LDL- and HDL-cholesterol and TGs are known correlates of atherosclerosis, not all LP fractions are associated with atherosclerosis. LP particle measurements can yield specific information regarding atherosclerosis risk beyond that provided by standard lipids. In addition, lipids and LP fractions have differential impact with atherosclerosis components (wall thickness vs lipid deposition). These data indicate that not all LP fractions are atherogenic and that LP particle atherogenicity is specific to particular atherosclerosis components. These novel findings merit further exploration and determination of clinical importance and mechanism. Sources of Funding: NIH NIA(R01-AG024154 and R01-AG059690) Association of LP particles with subclinical atherosclerosis

<table>
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<th>Standard lipids panel (mmol/L)</th>
<th>CIMT (mm)</th>
<th>p-value</th>
<th>BG (mg/dL)</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Total LDL-cholesterol</td>
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<td>Total HDL-cholesterol</td>
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<td>&lt;0.001</td>
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<td>Lipoprotein particle fractions (nmol/L)</td>
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<tr>
<td>LDL large (a)</td>
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<td>LDL large (b)</td>
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<td>HDL small</td>
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<td>0.74</td>
<td>-28.7 (17.6)</td>
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<tr>
<td>HDL small (a)</td>
<td>4.69 (14.2)</td>
<td>0.74</td>
<td>-28.7 (17.6)</td>
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<td>HDL small (b)</td>
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<td>-28.7 (17.6)</td>
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* indicates LP fractions in the order of largest to the smallest
S-5. The Cardiovascular Cost of Silence: Relationships Between Self-Silencing and Carotid Plaque in Midlife Women

Karen Jakszewska MSc1, Yuefang Chang PhD1, Emma Barinas-Mitchell PhD2, Karen Matthews1,2, Pauline M. Maki1, Rebecca C. Thurston PhD2,3, Psychiatry, University of Pittsburgh, Pittsburgh, PA; 2Epidemiology, University of Pittsburgh, Pittsburgh, PA; 3Psychiatry, University of Illinois at Chicago, Chicago, IL; 4Neurosurgery, University of Pittsburgh, Pittsburgh, PA

Objective: Individuals engage in a range of behaviors to maintain close relationships, some of which may be costly to one’s own health. One such behavior is self-silencing, or inhibiting one’s self-expression to avoid conflict and relationship loss. Self-silencing has been linked to worse mental and self-reported physical health in women, but it has not been examined in relation to women’s cardiovascular health, particularly using direct measures of the vasculature. Vascular imaging, including of carotid atherosclerosis, allows for indexing future cardiovascular disease (CVD) risk in midlife women among whom clinical CVD is rare. In a community sample of midlife women, we tested whether self-silencing was associated with carotid atherosclerosis, controlling for a range of potentially confounding factors.

Design: 304 late perimenopausal and postmenopausal nonsmoking women aged 40 to 60 participated in a study of cardiovascular health at midlife. Women completed the Silencing the Self Scale which measures self-expression in intimate relationships (e.g., “Caring means putting the other person’s needs in front of my own” and “I rarely express my anger at those close to me”). Women also provided self-reports (demographics, medical history, depression), physical measures (blood pressure, height, weight), and underwent phlebotomy (lipids) and ultrasound imaging of the carotid artery to quantify carotid plaque. Cross-sectional associations between self-silencing and carotid plaque (0, 1, a2) were assessed in multinomial logistic regression models adjusted for age, race, education, blood pressure, body mass index, low density lipoprotein cholesterol, medications (for blood pressure, lipid, diabetes), and depression.

Results: Women were on average aged 54 years; 72.5% identified as Non-Hispanic white, 22% African American, 5.4% other ethnicities. Forty-six percent showed evidence of plaque and 24% had a score of a2. Greater self-silencing was related to increased odds of plaque a2 [OR (95% CI) = 1.14 (1.02, 1.28), p=0.02], adjusting for covariates (Figure 1). Conclusion: Self-silencing was associated with greater carotid plaque independent of socio-demographics, CVD risk factors, and depression. Given increased public health interest in women’s experiences in intimate relationships, our results suggest that women’s socio-emotional expression may be relevant to their cardiovascular health.

Sources of Funding: NIH (R01HL105647, K242132365, UL1TR000005 to RCT; RF1AG053504 to RCT and PM)

Figure 1. Self-Silencing and Carotid Plaque

THURSDAY CONCURRENT SESSION #2

S-6. Relationship of hot flashes with sleep quality and daytime functioning in perimenopausal and menopausal women

Russel M. Walters, PhD1, Jordana Composto2, Erin Leichman, PhD2, Jodi Mindell, PhD3, Jennifer D. Johnson & Johnson, Philadelphia, PA; 1Saint Joseph's University, Philadelphia, PA; 2Somn, Philadelphia, PA

Objective: To examine the relationship of hot flashes with sleep and daytime functioning in perimenopausal and menopausal-aged women. Design: 1,109 perimenopausal and menopausal aged women (45-60 years), recruited through social media, completed a comprehensive online sleep assessment modified for mobile experience, including the Insomnia Severity Index (ISI), Epworth Sleepiness Scale (ESS), anxiety GAD-7, and questions about attempted sleep solutions. Results: 27% of perimenopausal- and menopausal-aged women reported that hot flashes disrupt their sleep. Women in the perimenopausal and menopausal age range who experienced hot flashes had significantly higher ISI (7.8 vs 15.6, p=0.001) and anxiety scores (11.1 vs 9.0, p=0.001) than those who did not experience hot flashes. There was a trend for higher ESS scores for those with hot flashes (13.4 vs 12.8, p=.10). Women who have hot flashes also reported higher rates of other forms of physical discomfort, including muscle pain (65% vs 24%), cramps (65% vs 24%), leg pain (52% vs 18%), heart burn (39% vs 8%), and indigestion (39% vs 8%). Women of perimenopause and menopause age who experienced hot flashes also reported higher rates of current use of OTC sleeping medication (not including melatonin), 27% vs 20%. Melatonin (43% vs 34%) and prescription sleeping medication use (25% vs 17%) had a similar pattern. Women reported similar rates of other elements of the bedtime routine, for example phone usage, reading, exercise, and watching TV, across age groups. Conclusion: Hot flashes are a common disrupter of sleep for perimenopausal and menopausal women. Experiencing hot flashes is associated with higher rates of symptoms of insomnia, anxiety, and other forms of physical discomfort in these women. Furthermore, experiencing hot flashes is also associated with higher use of over-the-counter and prescription sleeping medication use. Future studies should focus on recommendations to target hot flashes to help improve sleep in this unique population.

Sources of Funding: Johnson & Johnson Consumer Inc., Skillman, NJ, USA.


Nicole G. Jaffe, PhD1, Leaha H. Rubin, PhD2, MPH3, Nigel J. Crowther, PhD2, Shane A. Norris, PhD2, Pauline M. Maki4. 1Chemical Pathology, National Health Laboratory Service and University of the Witwatersrand Faculty of Health Sciences, Johannesburg, South Africa; 2Psychiatry, University of Illinois at Chicago, Chicago, IL; 3Neurology, Psychiatry, and Epidemiology, Johns Hopkins University School of Medicine, Baltimore, MD; 4SAMRC/Developmental Pathways for Health Research Unit, University of the Witwatersrand, Chris Hani Baragwanath Hospital, Johannesburg, South Africa; 3Psychology, University of Illinois at Chicago, Chicago, IL

Objective: Studies, conducted largely in North America and Europe, demonstrate that menopausal symptoms and menopausal stage influence cognitive function. The associations of menopausal symptoms and stage in a large cohort of sub-Saharan African women, where these associations are understudied, were evaluated. Design: A uniform experience of menopause amongst women of different cultures is challenging, and therefore tools accounting for cultural and ethnic specifics of menopausal symptoms should be used. We hypothesized that premenopausal women would show better cognitive performance than women later in the transition, and that menopausal symptoms would be inversely related to cognition. Design: This cross-sectional study included 702 black urban South African women aged between the ages of 40 and 60 from the Study of Women Entering and in Endocrine Transition (SWEET). During a 3-year recruitment window, 902 women were randomly selected for recruitment for the SWEET. Of these, 200 women were excluded due to: age > 60 years (n=35), refusal (n=79), death (n=37), terminal illness (n=3), or inability to contact (n=46). Participants completed the Symbol Digit Modalities Test (SDMT), a measure of processing speed and incidental recall. Menopausal stage was ascertained using the STRAW 10 criteria and symptoms using the Menopause Rating Scale. Body anthropometry and hormonal assays were obtained, and a negative HIV antibody test was obtained. Cognitive symptoms of the menopause, terminal illness, educational level and smoking and snuff use. Multivariable linear regression analyses were used to examine adjusted associations between menopausal stage and menopausal symptoms on cognition. Results: 27% of perimenopausal- and postmenopausal symptoms on cognitive performance. Results: 27% of perimenopausal- and postmenopausal symptoms on cognitive performance. Results: Late reproductive women performed significantly faster on the SDMT processing speed outcome than early and late post-menopausal women (p<0.001), and women transitioning performed significantly better than early (p=0.006) and late post-menopausal women (p=0.001). However, in adjusted analyses, menopausal stage was not associated with processing speed (p=0.35) largely because of a strong relationship between performance and age (r=0.31, p=0.001), nor was it associated with incidental recall on the SDMT (p=0.64). However, more severe symptoms of hot flashes and fearfulness were associated with slower processing speed (p<0.05), and more severe mood symptoms were associated with worse incidental recall (p=0.008). In unadjusted analyses, higher estradiol levels were associated with improved processing speed (r=0.16, p=0.001) and higher FSH levels were associated with decreased processing speed (r=-0.19, p=0.001), but these associations were no longer significant in adjusted analyses (p>0.72). Conclusion: These findings examined the extent to which cognitive symptoms of the menopause, objectively measured by the SDMT, were related to menopausal stage and menopausal symptoms. Menopausal symptoms, but not stage, were associated with cognitive function in this large cross-sectional study of sub-Saharan African women. These associations in women who generally have limited recognition of the menopause suggest that cognitive symptoms of menopause are not related to cultural expectations and assumptions of the menopause and may reflect a common underlying neurobiological substrate.

Sources of Funding: Medical Research Council of South Africa (MRC), the National Health Laboratory Service (NIHLS) Research Trust, the University of the Witwatersrand Iris Ellen Hodges Cardiovascular Research Trust and the National Research Foundation (NRF) of South Africa.

S-8. Lorcaserin for management of weight and hot flashes in midlife women

Robert S. Conwell, PhD1, Stephanie Fainion, Ryan Hurt, MD2, Shawn Fokken, Ivana Croghan, Ph.D3, Mayo Clinic, Rochester, MN

Objective: Weight gain accompanied by an increased tendency for central fat distribution is common among women in midlife. Vasomotor symptoms (VMS) due to menopause are also very common in women of this age group. A weight loss treatment for midlife women that might also relieve menopausal symptoms is therefore appealing. Lorcaserin is a selective serotonin 2C receptor agonist that is FDA approved for weight loss in appropriate patients. Unreported observational evidence suggests that it may potentially improve VMS. The goal of this pilot study was to evaluate the efficacy of lorcaserin for weight loss and management of over-the-counter and prescription menopausal symptoms in overweight midlife women. Design: This was an open label pilot study of 20 overweight midlife women, ages 45-60 years, who were experiencing severe VMS. Participants received lorcaserin 10 mg twice daily for 12 weeks followed by 12 additional
S-9. Child maltreatment and vasomotor symptoms among midlife women
Mary Carson, B.S.1, Rebecca C. Thurston, PhD2,1. 1Psychology, University of Pittsburgh, Pittsburgh, PA; 2Psychiatry, University of Pittsburgh, Pittsburgh, PA. Objective: Childhood abuse is related to adverse health outcomes. However, the relation of childhood maltreatment to characteristics of the menopause transition, particularly to vasomotor symptoms, is not well understood. Early data suggested a relation between childhood abuse and self-reported vasomotor symptoms, but associations have not been examined using physiologic measures of vasomotor symptoms. This study tested whether a history of childhood abuse and neglect are associated with more frequent menopausal vasomotor symptoms at midlife, utilizing both physiologic and self-report measures of vasomotor symptoms. Design: This analysis was conducted in the MsHeart cohort, which was comprised of nonsmoking perimenopausal and postmenopausal women aged 40 to 60 years with and without vasomotor symptoms. Participants completed psychosocial measures including the Child Trauma Questionnaire, underwent ambulatory physiologic (sternal skin conductance) and self-report measurement of vasomotor symptoms during wake and sleep, and completed actigraphy measurement of sleep. Relationships between childhood abuse/neglect and vasomotor symptoms during wake and sleep were tested in linear regression models controlling for demographic factors, body mass index, and menopausal status.
Results: The sample was comprised of 295 women, 44% (N=129) of whom had a history of childhood abuse or neglect. Among the women who reported vasomotor symptoms at baseline, an average of 5 vasomotor symptoms per 24 hours were detected on physiologic monitoring (wake: 11; sleep: 3). Among women reporting vasomotor symptoms, childhood sexual or physical abuse was associated with more frequent physiologically-recorded vasomotor symptoms during sleep [sexual abuse: b(SE)=1.45(52), p<.006; physical abuse: b(SE)=.97(47), p=.03; multivariable]. Associations were not accounted for by sleep quality or characteristics. Among women with vasomotor symptoms, a physical or sexual abuse history was associated with approximately 1.52-fold increased number of sleep vasomotor symptoms. Conclusion: This is the first study to consider relations between childhood abuse and physiologically- assessed vasomotor symptoms. Findings indicated that childhood abuse was prevalent and associated with more frequent physiologic vasomotor symptoms during sleep.

Sources of Funding: This research was supported by the National Institutes of Health, National Heart, Lung, and Blood Institute (R01HL056047, K24HL123565 to Thurston) and the University of Pittsburgh Department of Psychology.

Figure 1. Adjusted sleep VMS by abuse or neglect history in women reporting VMS at baseline

S-10. Child abuse and vasomotor symptoms over midlife
Mary Carson, B.S.1, Rebecca C. Thurston, PhD2,1. 1Psychology, University of Pittsburgh, Pittsburgh, PA; 2Psychiatry, University of Illinois at Chicago, Chicago, IL. Objective: To examine the relation of childhood abuse to characteristics of the menopause transition, such as vasomotor symptoms (VMS), is relatively understudied. Newer data indicates that VMS may last longer than previously thought. In previous cross-sectional analyses, we showed that childhood abuse was associated with more frequent physiologically-detected VMS at a single time point. Leveraging unique longitudinal physiologic measurements of VMS at two time points over five years, we tested whether childhood abuse was associated with VMS over time.

Design: 75 nonsmoking women aged 40-60 (65% non-Hispanic White women, 35% non-White women) reporting VMS were recruited. At baseline and follow-up five years later, women completed 24 hours of ambulatory physiologic (sternal skin conductance) measurement of VMS during wake and sleep, physical measurements, demographic assessments, and psychosocial assessments, including the Child Trauma Questionnaire, a validated measure of childhood abuse and neglect (scored yes/no according to clinical cut points). Relationships between childhood abuse and change in VMS over time were tested in linear regression models controlling for age, race/ethnicity, education, body mass index (BMI), and in additional models, baseline VMS, or depressive and anxious symptoms. Results: 46% of the sample reported abuse or neglect during childhood. Among women reporting VMS, a history of childhood emotional abuse was associated with greater increase in wake physiologically-recorded VMS over time (b(SE)=5.73(1.89), p<.003), adjusted for age, race/ethnicity, education, and BMI. Emotional abuse was associated with greater increase in baseline VMS (b(SE)=2.92(1.41), p<.04, multivariable) or for depressive or anxious symptoms. Whereas women without a history of emotional abuse showed a decrease in VMS between visits (decrease of on average 4 VMS/day), women with a history of emotional abuse showed an increase in VMS between visits (increase of on average 1.3 VMS/day). Emotional abuse is associated with an increase in physiologically-detected VMS over midlife.

Sources of Funding: This work was supported by the National Institutes of Health, National Heart Lung and Blood Institute (ROIHL056047, K24HL123565 to Thurston), National Institute on Aging (RF1AG053504 to Thurston and Maki) and the University of Pittsburgh Clinical and Translational Science Institute (NIH Grant UL1TR000005).

THURSDAY CONCURRENT SESSION #4

Updates from the MsFLASH Clinical Trials Network – A Panel Discussion
Katherine A. Guthrie1, Caroline Mitchell2, Sujatha Srivinasan3, Susan D. Reed4. 1Public Health Sciences Division, Fred Hutchinson Cancer Research Center, Seattle, WA; 2Obstetrics, Gynecology, and Reproductive Biology, Harvard Medical School, Boston, MA; 3Vaccine and Infectious Disease, Fred Hutchinson Cancer Research Center, Seattle, WA; 4Women’s Reproductive Health Research Program, University of Washington School of Medicine, Seattle, WA.

BACKGROUND/OBJECTIVE: Both estrogen replacement therapy and medical management are utilized to control bothersome menopausal symptoms. However, the relationship between hormone therapy and vaginal symptoms is not well understood.

STUDY DESIGN: Double blind, randomized, placebo-controlled trial with outcomes measured at baseline, 4 and 12 weeks. SITES: Seattle, WA; Minneapolis, MN.

PARTICIPANTS: Women aged 50-70 with ≥ 1 moderate to severe symptom of vulvovaginal itching, pain, irritation, dryness or pain with penetration; ≥ 2 years postmenopausal; no acute vaginitis or history of chronic vaginitis; no use of hormone therapy in the past 2 months; and no use of vaginal moisturizer or antibiotics in the past month. METHODS: Analyses included women enrolled in the trial who provided vaginal swabs and cervicovaginal lavage at all 3 time points. The vaginal microbiota was characterized by sequencing of the V3V4 region of the 16S rRNA gene. Mass-spectrometry-based targeted metabolomics was used to detect 171 small molecule metabolites in vaginal fluid. Gram stained slides were scored according to Nugent criteria. VAG1 (1) and VAG2 (2) represent the two main vaginal microbiota populations. RESULTS: VAG1 and VAG2 were present in the vaginal fluid in 35% of women at baseline and 25% at week 12. The relationship between these two populations with a variety of clinical characteristics is shown in the table below. The data were summarized using mean ± SD for continuous variables and frequency percentages for nominal variables. RESULTS: At the end of 12 weeks, mean change in weight was -2.4 kg [90% CI (−3.2)–(−1.7), p<.001]. However, the participants gained the weight back after remaining off the drug for 12 weeks, and the final mean weight at the end of the study was not significantly different from the mean baseline weight. The waist circumference and BMI followed similar trends, although the 12-week difference in the waist circumference was not statistically significant. The participants also reported significant clinical improvement in VMS, with a meanSD change in self-reported hot flush frequency from baseline to week 12 of -5.4±3.9, corresponding to a decline of approximately 1-3 standard deviations. There was a rapid increase in VMS within 2 weeks of discontinuation of lorcanerin with insignificant difference from baseline of -2.2±2.4 (p=0.05). Conclusion: In addition to its weight loss-inducing effect, lorcanerin may have an additional beneficial effect on VMS in midlife women. However, a randomized placebo-controlled trial is needed to confirm this finding, to evaluate for potential placebo-effect, and to distinguish the potential effect of lorcanerin versus weight loss itself on VMS.

Sources of Funding: Department of Medicine, Mayo Clinic, Rochester, MN
vaginal discomfort. 3) Among the 144 women with vaginal microbiota data at baseline, we compared the diversity of the vaginal microbiota between women whose Nugent scores were less than 6 (low), intermediate (6-10), or BV positive (11-15) and assess associations of individual taxa and individual Amsel criteria. CONCLUSIONS: Our results show that the vaginal environment changes with treatments for postmenopausal vaginal discomfort, and whether changes in the vaginal ecosystem are a marker or cause of bothersome vaginal symptoms. Findings provide new insight into the pathophysiology of postmenopausal vaginal symptoms. Criteria for diagnosing postmenopausal BV is problematic as one of the 4 Amsel criteria, pH, is almost always elevated; new standards for an optimal vaginal ecosystem in postmenopausal women are needed.

TOP-SCORING ABSTRACT PRESENTATIONS

S-11. Effect of the Neurokinin 3 Receptor Antagonist Fezolinetant on Menopausal VasoMotor Symptoms and Patient-Reported Outcomes: Results of a Randomized, Placebo-Controlled, Double-Blind, Dose-Ranging Study

Carolyn Gibson, PhD, MPH1, Shira Maguen2, Feng Xia2, Deborah Barnes1,2,3. 1VA Greater Los Angeles Healthcare System, Los Angeles, CA; 2Department of Medicine, University of Pittsburgh, Pittsburgh, PA; 3VA Pittsburgh Healthcare System, Pittsburgh, PA

Objective: To assess the effects of fezolinetant on menopausal vasomotor symptoms (VMS), which result from loss of thermoregulatory control. Fezolinetant is a neurokinin 3 receptor antagonist that modulates the function of kisspeptin/neurokinin B/dynorphin neurons in the hypothalamus, which is responsible for thermoregulation. This study evaluated the efficacy of fezolinetant on VMS and patient-reported outcomes (PROs). Design: In this phase 2b, double-blind study (NCT03192176), women age >40 to 65 y with moderate/severe VMS (≥50/week) were randomized to receive fezolinetant 15, 30, 60, or 120 mg QD or placebo (PBO). Criteroprim efficacy outcomes were changes in frequency and severity of VMS at wk 4 and 12. Secondary endpoints included response (≥50% reduction in VMS) and changes in Hot Flash-Related Daily Interference Scale (HFDRIS), Greene Climacteric Scale (GCS), and Menopause-Specific Quality of Life (MENQol) questionnaire scores at wk 4 and 12. Pairwise comparisons were made using least squares (LS) means for continuous variables and odds ratios for categorical variables. Changes from baseline for PROs were compared with published minimum important difference (MID) values, where available. Results: Of 356 women randomized, 352 received at least one dose of study drug (safety population; mean [SD]: age 54.6 [14.7; 73% white]; 287 [81%] completed the study. Fezolinetant reduced daily moderate/severe VMS frequency vs PBO, with LS mean differences of −1.9 to −3.5 at wk 4 and −1.8 to −2.6 at wk 12 (all P<0.05). LS mean differences from PBO in severity scores were −0.4 to −1 at wk 4 (all P<0.05) and −0.2 to −0.6 at wk 12 (P<0.05, 60 and 90 mg BID and 60 mg QD). Percentages of patients with ≥50% reduction in VMS at last on-treatment assessment were higher with fezolinetant 15, 30, 60, and 90 mg BID (83.7%, 81.4%, 88.1%, and 94.7%) and 30, 60, and 120 mg QD (82.1%, 88.1%, and 84.1%) than PBO (58.5%; all P<0.05 for odds ratios for response vs PBO). LS mean differences from placebo on HFDRIS, GCS, and MENQol are shown in the Table below for all fezolinetant doses. In all dose groups, LS mean changes from baseline in HFDRIS at wk 4 (PBO: −2.2; fezolinetant: −2.3 to −3.8) and wk 12 (PBO: −2.9; fezolinetant: −3.3 to −4.3) exceeded the MID (1.2; [Bushmakin et al. Menopause 2014;21:815]) at wk 4 (PBO: −1.8; fezolinetant: −1.9 to −3.6) and wk 12 (PBO: −2.3; fezolinetant: −2.9 to −4.4). Conclusion: Fezolinetant reduced frequency and severity of VMS, which was accompanied by clinically meaningful improvements in PROs.

Sources of Funding: Abbvie, Inc.

Table. PROs: LS mean differences (95% CI) between fezolinetant and PBO

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>15 mg BID</th>
<th>30 mg BID</th>
<th>60 mg BID</th>
<th>90 mg BID</th>
<th>60 mg QD</th>
<th>90 mg QD</th>
<th>120 mg QD</th>
</tr>
</thead>
<tbody>
<tr>
<td>HFDRIS</td>
<td>−2.1 (−3.0, −1.3)</td>
<td>−2.0 (−2.9, −1.1)</td>
<td>−1.9 (−2.8, −1.0)</td>
<td>−1.8 (−2.7, −0.9)</td>
<td>−1.7 (−2.6, −0.8)</td>
<td>−1.6 (−2.5, −0.7)</td>
<td>−1.5 (−2.4, −0.6)</td>
</tr>
<tr>
<td>GCS-VMS</td>
<td>−0.7 (−1.5, −0.0)</td>
<td>−1.4 (−2.2, −0.6)</td>
<td>−1.3 (−2.1, −0.5)</td>
<td>−1.3 (−2.1, −0.5)</td>
<td>−1.3 (−2.1, −0.5)</td>
<td>−1.3 (−2.1, −0.5)</td>
<td>−1.3 (−2.1, −0.5)</td>
</tr>
<tr>
<td>MENQol-VMS</td>
<td>−0.5 (−1.3, 0.3)</td>
<td>−1.0 (−1.8, −0.2)</td>
<td>−1.0 (−1.8, −0.2)</td>
<td>−1.0 (−1.8, −0.2)</td>
<td>−1.0 (−1.8, −0.2)</td>
<td>−1.0 (−1.8, −0.2)</td>
<td>−1.0 (−1.8, −0.2)</td>
</tr>
</tbody>
</table>

S-12. “How much desire should I have?”: A qualitative study of low libido in postmenopausal women

Laurence Skillern, MD1, Steven Ramael, MD1, Chris Young, MD2, 1Altus Research, Lake Worth, FL; 2OGEDA SA, subsidiary of doss. In all dose groups, LS mean changes from baseline in HFRDIS at wk 4 (PBO: −2.9; fezolinetant: −2.9 to −3.6) and wk 12 (PBO: −1.8; fezolinetant: −1.9 to −3.6) and wk 12 (PBO: −2.3; fezolinetant: −2.9 to −4.4). Conclusion: Fezolinetant reduced frequency and severity of VMS, which was accompanied by clinically meaningful improvements in PROs. 1Department of Medicine, University of Pittsburgh, Pittsburgh, PA; 2Medical University of Utah, Salt Lake City, UT; 3Psychiatry, University of Pittsburgh, Pittsburgh, PA

Objective: Epidemiologic data suggests that while a majority of postmenopausal women (≥50% reduction in VMS at last on-treatment assessment were higher with fezolinetant 15, 30, 60, and 90 mg BID (83.7%, 81.4%, 88.1%, and 94.7%) and 30, 60, and 120 mg QD (82.1%, 88.1%, and 84.1%) than PBO (58.5%; all P<0.05 for odds ratios for response vs PBO). LS mean differences from placebo on HFDRIS, GCS, and MENQol are shown in the Table below for all fezolinetant doses. In all dose groups, LS mean changes from baseline in HFDRIS at wk 4 (PBO: −2.2; fezolinetant: −2.3 to −3.8) and wk 12 (PBO: −2.9; fezolinetant: −3.3 to −4.3) exceeded the MID (1.2; [Bushmakin et al. Menopause 2014;21:815]) at wk 4 (PBO: −1.8; fezolinetant: −1.9 to −3.6) and wk 12 (PBO: −2.3; fezolinetant: −2.9 to −4.4). Conclusion: Fezolinetant reduced frequency and severity of VMS, which was accompanied by clinically meaningful improvements in PROs.
and pain (chronic pain OR 1.58, 95% CI 1.50-1.67; back pain OR 1.40, 95% CI 1.34-1.47). Conclusion: A history of MST is common among postmenopausal women Veterans and associated with a range of medical and mental health diagnoses. Although prior trauma is not often considered in the clinical care in this population, both VA and community providers caring for older women Veterans should recognize the prevalence and importance of MST in aging-related health and health care. These findings call attention to the need for additional research in this understudied population, and the importance of trauma-informed care approaches for women across the lifespan.

Sources of Funding: This research was supported by Department of Defense Grant W81XWH-16-0507 (PI: Yaffe) and in part by the VA Advanced Fellowship Program in Women's Health, San Francisco VA Health Care System and VA HSR&D Career Development Award (CDA IK2 HX002402; CJG). The content is solely the responsibility of the authors and does not necessarily represent the official views of the Department of Veterans Affairs.

S-14. Postmenopausal Pellet vs. FDA approved Hormonal Therapy: An Assessment of Serum Estradiol and Testosterone Levels

Xuezhi Jiang, MD, PhD1,2; Sneh Kamarajugadda1; Cassandra Mitchell1, Anna Bossert1, Kirthik N. Parthasarathy, MD 1, Rhea Mathew 1, Shama Khan 1, Kristine Leaman, MD 1, Shahab S Minassian, MD1, Peter F. Schatz, DO3, Mark B. Woodland, MD,3 1OB/GYN, Reading Hospital, Tower Health, West Reading, PA; 2OB/GYN, Sidney Kimmel Medical College of Thomas Jefferson University, Philadelphia, PA

Objective: The objective of this study was to assess the serum estradiol (E2) and total testosterone (T) levels in postmenopausal women treated with non-FDA approved Pellet Hormonal Therapy (PHT) and FDA approved Hormonal Therapy (FHT). Design: A retrospective cohort study was designed to compare two cohorts (PHT vs. FHT). A total of 539 postmenopausal women with menstrual symptoms were identified from the Reading Hospital Electronic Medical Record System through pharmacy coding, including 384 on PHT (estradiol [E2, 6-37.5mg] and/or testosterone [T, 12-137.5mg] pellets) and 155 on FHT. Data on patient histories, demographics, side effects (e.g. abnormal uterine bleeding [AUB], mood swing, anxiety, breast tenderness, change in hair pattern, acne, weight gain), and endocrine pathology findings have been previously presented by our group. Serum E2 and T levels, treatment duration, and the number of lab follow-up were extracted from medical records. Results: Women on PHT had significantly longer treatment duration in years than those on FHT (mean SD: 3.92 [2.34] vs. 3.33 [4.64], p<0.0001). Of 384 women on PHT, 373 (97.1%) had serum E2 and T monitored at least once, with mean (SD) total number of E2 and T follow-up of 6.81 (4.57) and 4.98 (3.52), respectively. Of 155 women on FHT, 33 (21.2%) had serum E2 and T monitored at least once, with mean (SD) number of E2 and T follow-up of 0.39 (0.86) and 0.14 (0.49), respectively. Both mean (SD, Min-Max) highest E2 (pg/mL) and highest T (pg/mL) are significantly higher in PHT group than those in FHT (E2: 237.70 (168.55, 10-11111) vs. 93.45 (130.77, 5.5-465.8), T: 192.84 (82.31, 4.3-475) vs. 15.19 (19.52, 0.2-70), P<0.0001). Of those on PHT, 4 women had E2 level > 1000 pg/mL and 9 women with T level > 400 pg/mL. Conclusion: When compared with women on FDA-HT, women on PHT had a significantly higher level of peak E2 and T during the treatment. Although most women had E2 and T tested when they were on PHT, the frequency of laboratory monitoring was still lower than expected.

Sources of Funding: None

Table 1. Comparison of serum E2 and T level between Pellet and FDA-HT cohorts

<table>
<thead>
<tr>
<th></th>
<th>PHT (n=384)</th>
<th>FHT (n=155)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>HT duration (years)</td>
<td>3.92±2.34</td>
<td>3.33±4.64</td>
<td>0.0001</td>
</tr>
<tr>
<td># of lab follow-up</td>
<td>6.81±4.57</td>
<td>4.98±3.52</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Lowest E2 (pg/mL)</td>
<td>59.07±120.4</td>
<td>49.40±120.39</td>
<td>0.2374</td>
</tr>
<tr>
<td>Highest E2 (pg/mL)</td>
<td>237.70±168.55</td>
<td>93.45±130.77</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Lowest T (pg/mL)</td>
<td>46.61±90.84</td>
<td>56.0±63-415</td>
<td>0.0977</td>
</tr>
<tr>
<td>Highest T (pg/mL)</td>
<td>192.84±82.31</td>
<td>182.4±475</td>
<td>0.3827</td>
</tr>
</tbody>
</table>

* P values were calculated by Mann Whitney U test based on mean (SD) comparison

PHT: Pellet HT; FHT: FDA approved HT

FRIDAY CONCURRENT SESSION #1


Sheryl A. Kingsberg, PhD,1,2 Sneha Dahir, DNP1, Brooke M. Faught, DNP, 1 Shelli Graham, PhD, 1 Brian Bernick, MD, 1 Sebastian Mirkin, MD, 1 St. Louis University, St. Louis, MO; 2Omaha OB/GYN Associates, PC, Omaha, NE; 3Women’s Institute for Sexual Health, Nashville, TN; 4TherapeuticsMD, Boca Raton, FL

Objective: To assess the growth of the vulvar vaginal atrophy (VVA) therapy market. In the 12-week, phase 3 REJOICE trial (NCT02253173), the 17-betaestradiol (E2), softgel, vaginal insert (TX-004HR) significantly improved percentages of superficial and parabasal cells, vaginal pH, and pain in women with vaginal atrophy (VVA) and moderate to severe dyspareunia (Constance G et al., Menopause 2017;24:409-416). A new 4 mg E2-based vaginal insert was approved by the FDA in May 2018 as Imvexxy® (TherapeuticsMD, Boca Raton, FL). The objective of this analysis was to determine the acceptability of TX-004HR in women who had been treated with other hormone therapies (HT) for VVA at screening. Design: Postmenopausal women with VVA and moderate to severe dyspareunia received 4 µg, 10 µg, or 25 µg E2 vaginal inserts or placebo daily for 2 weeks and then twice weekly for 10 weeks. Prior to enrollment, women using HT at screening required a 4- to 8-week washout period depending on HT type. At the end of the study, each subject was given a 5-question acceptability survey. Results of this survey in women who required a washout period were summarized descriptively. Results: A total of 764 women were randomized to the REJOICE trial; 53 were using HT at screening and required a washout period. Five women discontinued the study early and did not complete the survey and 9 responded they had not used previous VVA symptom treatment, leaving 39 surveys for this analysis. HT use at screening in these women included vaginal creams (n=16), tablets (n=6), or rings (n=5); systemic therapy (oral/patch; n=11); or soy/black cohosh (n=1) and women were randomized to 4 mg (n=10), 10 mg (n=9), and 25 mg (n=11) E2 vaginal inserts, respectively. Most women (92%) believed the product was easy to use, and the majority of women rated the ease of insertion as excellent or good (77%); 30/39. More than two-thirds of women (69%); 27/39 were very satisfied or satisfied with the softgel vaginal insert (at screening), they were using vaginal creams (n=13), vaginal

Percent change per year in prescriptions for VVA symptoms

S-16. Postmenopausal Women Using a Softgel Estradiol Vaginal Insert to Treat Moderate to Severe Dyspareunia Were Satisfied with It and Preferred It Over a Previous Treatment

Becky Beck, MD,1 Melissa Dahir, DNP1, Brooke M. Faught, DNP1; Shelli Graham, PhD;2 Brian Bernick, MD; Sebastian Mirkin, MD;3 St. Louis University, St. Louis, MO; 1Omaha OB/GYN Associates, PC, Omaha, NE; 2Women’s Institute for Sexual Health, Nashville, TN; 3TherapeuticsMD, Boca Raton, FL

Objective: To assess the growth of the vulvar vaginal atrophy (VVA) therapy market. In the 12-week, phase 3 REJOICE trial (NCT02253173), the 17-betaestradiol (E2), softgel, vaginal insert (TX-004HR) significantly improved percentages of superficial and parabasal cells, vaginal pH, and pain in women with vaginal atrophy (VVA) and moderate to severe dyspareunia (Constance G et al., Menopause 2017;24:409-416). A new 4 mg E2-based vaginal insert was approved by the FDA in May 2018 as Imvexxy® (TherapeuticsMD, Boca Raton, FL). The objective of this analysis was to determine the acceptability of TX-004HR in women who had been treated with other hormone therapies (HT) for VVA at screening. Design: Postmenopausal women with VVA and moderate to severe dyspareunia received 4 µg, 10 µg, or 25 µg E2 vaginal inserts or placebo daily for 2 weeks and then twice weekly for 10 weeks. Prior to enrollment, women using HT at screening required a 4- to 8-week washout period depending on HT type. At the end of the study, each subject was given a 5-question acceptability survey. Results of this survey in women who required a washout period were summarized descriptively. Results: A total of 764 women were randomized to the REJOICE trial; 53 were using HT at screening and required a washout period. Five women discontinued the study early and did not complete the survey and 9 responded they had not used previous VVA symptom treatment, leaving 39 surveys for this analysis. HT use at screening in these women included vaginal creams (n=16), tablets (n=6), or rings (n=5); systemic therapy (oral/patch; n=11); or soy/black cohosh (n=1) and women were randomized to 4 mg (n=10), 10 mg (n=9), and 25 mg (n=11) E2 vaginal inserts, respectively. Most women (92%) believed the product was easy to use, and the majority of women rated the ease of insertion as excellent or good (77%); 30/39. More than two-thirds of women (69%); 27/39 were very satisfied or satisfied with the softgel vaginal insert (at screening), they were using vaginal creams (n=13), vaginal
tables [n=5], systemic therapies [n=5], vaginal rings [n=3], and other [n=1]. More than two-thirds of women (69%, 27/39) very much or somewhat preferred the vaginal insert compared with their previous VVA symptom therapies: 11 women were using vaginal creams, 5 vaginal tablets, 6 systemic therapies, 4 vaginal rings, and 1 other therapy at screening. When asked whether they would consider using the vaginal insert again, the majority said that they would definitely or probably (74%; 29/39) consider it. These women at screening were using vaginal creams (n=13), vaginal tablets (n=5), systemic therapies (n=6), vaginal rings (n=4), and other therapies (n=1). Conclusion: Most women who completed the Day-to-Day Impact of Vaginal Aging (DIVA) questionnaire to rate the impact of vulvovaginal symptoms on day-to-day activities, sexual function, emotional functioning, and body image, each on a 0 to 10 (4 to 7) scale. Participants were assigned to treatment arms of estradiol vaginal insert with placebo gel (n=98), vaginal moisturizer with placebo gel (n=97), or dual placebo (n=94). These results support the hypothesis of E2 therapy and cardiovascular benefit.

S-18. Effect of Estradiol Dose and Serum Estradiol Level on Metabolic Measures in Early and Late Postmenopausal Women in the REPLISHN trial

Intrauterine systemic and the leading cause of the death in the US. Hormone therapy (HT) appears to exert a cardioprotective effect in women less than 60 years of age or less than 10 years since menopause. This study aimed to identify the association of estradiol (E2) dose and serum E2 levels from HT on metabolic measures in early (≤6 years) and late (>6 years) postmenopausal women using data from the REPLISHN trial. Design: REPLISHN was a randomized, double-blinded, placebo-controlled, multi-center trial testing endometrial safety and efficacy on vasomotor symptoms with TX-001HR, an oral combined E2 and progesterone (P4) (1/100 mg, 0.5/100 mg, 0.5/50 mg, 0.25/50 mg) agent or placebo in postmenopausal women (n=100) per month. The E2 level was estimated by 2 mg E2 dose and 1 pg/mL serum E2 level. The change in each metabolic parameter was estimated by 0.25 mg E2 dose and 1 pg/mL serum E2 level. Results: A total of 1,216 early and 297 late postmenopausal women were included. Mean age (SD) was 53.2 (7.1) years. More than two-thirds of women preferred the softgel estradiol vaginal insert was easy to use and were satisfied with it. More than two-thirds of these women preferred the softgel estradiol vaginal insert over their previous VVA treatment and would consider using it again.

Sources of Funding: TherapeuticsMD

S-17. Treatment-related sensitivity to change and minimal clinically important change in the day-to-day impact of postmenopausal vaginal symptoms: Results from a Multicenter Randomized Trial

Carolyn Gibson, PhD, MPH1, Alison Huang2, Joseph Larson1, Caroline Mitchell1, Susan Dien1, Andrea LaCroix1, Katherine Newton1, Susan D. Reed1, Katherine A. Guthrie1. 1San Francisco VA Health Care System, San Francisco, CA; 2University of California, San Francisco, San Francisco, CA; 3Fred Hutchinson Cancer Research Center, Seattle, WA; 4Vincent Center for Reproductive Biology, Massachusetts General Hospital, Harvard School of Public Health, Boston, MA; 5University of Minnesota, Minneapolis, MN; 6University of San Diego, San Diego, CA; 7Kaiser Permanente, California Washington Health Research Institute, Seattle, WA; 8University of Washington, Seattle, WA.

Objective: Vulvovaginal symptoms, including dryness, irritation, and pain with intercourse, are common among postmenopausal women and associated with impaired sexual functioning and quality of life. Prior assessment of symptom treatment strategies has been limited by the lack of sensitive patient-centered outcome measures that assess change in symptom impact on functional and quality-of-life domains. This study aimed to: 1) examine change in the impact of postmenopausal vulvovaginal symptoms on multiple aspects of well-being and functioning in relationship to treatment; and 2) guide meaningful interpretation of scores on a structured-item questionnaire measure of condition-specific impact.

Design: Data were drawn from 289 postmenopausal women in the MsFLASH Vaginal Health Trial, a 12-week, double-blind, placebo-controlled randomized trial of treatment for vulvovaginal symptoms. Women were randomized to receive estrogen vaginal 10 mcg estradiol tablet + placebo gel (n=98), vaginal moisturizer + placebo tablet (n=97), or dual placebo (n=94). At baseline and 12-week follow-up, participants completed the Day-to-Day Impact of Vaginal Aging (DIVA) questionnaire to rate the impact of vulvovaginal symptoms on four domains (activities of daily living, emotional well-being, sexual functioning, and body image), each on a 0 to 10 (4 to 7) scale. Participants were assigned to treatment arms of estradiol vaginal insert with placebo gel (n=98), vaginal moisturizer with placebo tablet (n=97), or dual placebo (n=94). At baseline and 12-week follow-up, participants completed the Day-to-Day Impact of Vaginal Aging (DIVA) questionnaire to rate the impact of vulvovaginal symptoms on four domains (activities of daily living, emotional well-being, sexual functioning, and body image), each on a 0 to 10 (4 to 7) scale. Participants were assigned to treatment arms of estradiol vaginal insert with placebo gel (n=98), vaginal moisturizer with placebo tablet (n=97), or dual placebo (n=94). These results support the hypothesis of E2 therapy and cardiovascular benefit.

Sources of Funding: TherapeuticsMD unrestricted research grant

Estimated change from baseline of metabolic measures per 0.25 mg increase of estradiol dose and 1 pg/mL serum increase of estradiol level by postmenopausal strata

<table>
<thead>
<tr>
<th>Variables</th>
<th>Early postmenopause Estimate (95%CI)</th>
<th>p-value</th>
<th>Late postmenopause Estimate (95%CI)</th>
<th>p-value</th>
<th>Interaction p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol (mg/dL)</td>
<td>E2 dose: -1.45 (-2.45, -0.45)</td>
<td>0.02</td>
<td>E2 dose: -0.26 (-0.36, -0.16)</td>
<td>0.82</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>E2 level (mg/dL): (0.08, 0.02)</td>
<td>0.004</td>
<td>E2 level (mg/dL): (0.16, 0.06)</td>
<td>0.29</td>
<td>0.13</td>
</tr>
<tr>
<td>High-density lipoprotein cholesterol (mg/dL)</td>
<td>E2 dose: 0.38 (0.06, 0.70)</td>
<td>0.04</td>
<td>E2 dose: -0.72 (0.48, -1.06)</td>
<td>0.92</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>E2 level (mg/dL): (0.00, 0.01)</td>
<td>0.84</td>
<td>E2 level (mg/dL): 0.02 (0.05, 0.00)</td>
<td>0.54</td>
<td>0.74</td>
</tr>
<tr>
<td>Low-density lipoprotein cholesterol (mg/dL)</td>
<td>E2 dose: -1.49 (-2.45, -0.56)</td>
<td>0.002</td>
<td>E2 dose: -0.37 (-2.14, 0.49)</td>
<td>0.70</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>E2 level (mg/dL): (0.06, 0.01)</td>
<td>0.004</td>
<td>E2 level (mg/dL): (0.18, 0.08)</td>
<td>0.66</td>
<td>0.06</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>E2 dose: -0.07 (-1.11, 0.27)</td>
<td>0.42</td>
<td>E2 dose: -0.16 (1.74, 0.06)</td>
<td>0.06</td>
<td>0.003</td>
</tr>
<tr>
<td></td>
<td>E2 level (mg/dL): (0.06, 0.16)</td>
<td>0.002</td>
<td>E2 level (mg/dL): 0.08 (0.42, 0.27)</td>
<td>0.42</td>
<td>0.11</td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>E2 dose: -0.48 (-0.57, 0.00)</td>
<td>0.05</td>
<td>E2 dose: -0.13 (0.05, 0.00)</td>
<td>0.10</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>E2 level (mg/dL): (0.05, 0.01)</td>
<td>0.003</td>
<td>E2 level (mg/dL): (0.07, 0.00)</td>
<td>0.34</td>
<td>0.18</td>
</tr>
</tbody>
</table>

Estimates are from mixed effect model adjusted for baseline measure and progestrone level; Interaction p value tests interaction between estradiol dose or estradiol level with time-since-menopause (years); E2=estradiol

S-19. Do genetic variations in estrogen transportation and metabolism affect the severity of menopausal symptoms?

Ekta Kapoor, Stephanie Faubion, Virginia M. Miller, PhD, Shawn Fokken, Juliana M. Kipling Doi, MPH, Kristin Mara, Ann Meyer, Mayo Clinic, Rochester, MN.

Objective: Menopausal symptoms can have a significant impact on the quality of life of midlife women. Moreover, vasomotor symptoms (VMS) of menopause are increasingly being recognized as a predictor for future disease, including cardiovascular disease in postmenopausal women. However, the severity of symptoms is highly variable among individuals. The role of genetic variation in estrogen metabolism in the pathophysiology
of menopausal symptoms has not been well studied. The current study was designed with the goal of understanding the relationship between menopausal symptoms and genetic variation in estrogen metabolism.

**Objective:** To retrospectively review indications for bilateral salpingo-oophorectomy (BSO) at the time of hysterectomy performed by general gynecologists. To determine the proportion of cases where there was potential for ovarian preservation, possibly avoiding surgical menopause.

**Design:** We performed a retrospective review of hysterectomies performed by gynecologists at six Ontario, Canada hospitals from July 2016 to June 2018. Data was extracted from health records coding (ICD-10) and electronic medical records. Of patients who had concurrent BSO, age, preoperative diagnoses, surgical factors (presence of endometriosis and adhesions) and surgery training (minimally invasive surgery (MIS) fellowship versus no fellowship) were recorded. Cases of BSO were classified as ‘indicated’ or ‘avoidable’. Criteria for avoidable BSO were: age less than 51 years old, benign preoperative diagnosis other than endometriosis, absence of intraoperative endometriosis and adhesions. The remainer of cases were classified as ‘indicated’. Chi square test was used to compare proportions, and odds ratios were calculated.

**Results:** Of the 2656 hysterectomies reviewed, 749 (28%) patients had concurrent BSO. Of these, 509 (68%) were indicated and 240 (32%) were avoidable based on preoperative diagnosis. The most common preoperative diagnoses for indicated BSO were: malignancy (231/509 patients, 45%), endometrial hyperplasia (105 patients, 21%) and endometriosis (52/509 patients, 10%). There was a significant inter-hospital variation in the proportion of indicated BSO ranging from 45.3% to 76.9%, and the presence of endometriosis (74/154, 48%) and laparoscopic hysterectomy (432/575, 75%). Of the patients with avoidable BSO, 105/239 (43.9%) were less than 51 years of age. Of this group, 59/105 (56%) had endometriosis and 30 had adhesions. This means that ovarian preservation may have been reasonable in at least 55% of cases of women who had hysterectomy and BSO. **Conclusion:** A large proportion of BSOs performed at the time of hysterectomy were avoidable, i.e. lacked a preoperative diagnosis indicating BSO. There was significant institution and provider-level variation in the rates of indicated BSO. Quality improvement initiatives could focus on standardizing practice with respect to BSO among gynecologic surgeons, potentially avoiding surgical menopause for some women.

**Sources of Funding:** none

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**S-21. Metabolic Predictors of Performance on Modified Mini Mental State (3MS) in a Randomized Controlled Trial:**

**Objective:** To determine the proportion of cases where there was potential for ovarian preservation, possibly avoiding surgical menopause. Decreased CYP3A4 activity was associated with higher hot flash severity (p=0.019) after adjustment for hormone therapy use. In addition, there was a trend toward fewer somato-vegetative symptoms among individuals with decreased CYP2C9 activity (p=0.063) and decreased CYP3A4 activity (p=0.036; p=0.025 after adjustment for hormone use). **Conclusion:** Our preliminary results demonstrate that variation in estrogen metabolism pathways is associated with VMS severity, and potentially other menopausal symptoms. Further studies including multivariate analyses to better understand the interplay between these genetic variants are underway. This work represents a step toward better understanding of the influence of genetics on menopausal symptoms, and may lead to individualized use of hormone therapy for management of menopausal symptoms.

**Sources of Funding:** none

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**FRIDAY COMMON SESSION #2**

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**S-20. Predictors of bilateral salpingo-oophorectomy at the time of hysterectomy and the potential for ovarian preservation:**

**Objective:** To retrospectively review indications for bilateral salpingo-oophorectomy (BSO) at the time of hysterectomy performed by general gynecologists. To determine the proportion of cases where there was potential for ovarian preservation, possibly avoiding surgical menopause.

**Design:** We performed a retrospective review of hysterectomies performed by gynecologists at six Ontario, Canada hospitals from July 2016 to June 2018. Data was extracted from health records coding (ICD-10) and electronic medical records. Of patients who had concurrent BSO, age, preoperative diagnoses, surgical factors (presence of endometriosis and adhesions) and surgery training (minimally invasive surgery (MIS) fellowship versus no fellowship) were recorded. Cases of BSO were classified as ‘indicated’ or ‘avoidable’. Criteria for avoidable BSO were: age less than 51 years old, benign preoperative diagnosis other than endometriosis, absence of intraoperative endometriosis and adhesions. The remainer of cases were classified as ‘indicated’. Chi square test was used to compare proportions, and odds ratios were calculated.

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**Sources of Funding:** none

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**S-22. Exploring workability and conditions to improve work participation among female healthcare workers aged 45-60 years:**

**Objective:** To determine the proportion of cases where there was potential for ovarian preservation, possibly avoiding surgical menopause. Decreased CYP3A4 activity was associated with higher hot flash severity (p=0.019) after adjustment for hormone therapy use. In addition, there was a trend toward fewer somato-vegetative symptoms among individuals with decreased CYP2C9 activity (p=0.063) and decreased CYP3A4 activity (p=0.036; p=0.025 after adjustment for hormone use). **Conclusion:** Our preliminary results demonstrate that variation in estrogen metabolism pathways is associated with VMS severity, and potentially other menopausal symptoms. Further studies including multivariate analyses to better understand the interplay between these genetic variants are underway. This work represents a step toward better understanding of the influence of genetics on menopausal symptoms, and may lead to individualized use of hormone therapy for management of menopausal symptoms.

**Sources of Funding:** none

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**FRIDAY COMMON SESSION #2**

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**S-20. Predictors of bilateral salpingo-oophorectomy at the time of hysterectomy and the potential for ovarian preservation:**

**Objective:** To retrospectively review indications for bilateral salpingo-oophorectomy (BSO) at the time of hysterectomy performed by general gynecologists. To determine the proportion of cases where there was potential for ovarian preservation, possibly avoiding surgical menopause.

**Design:** We performed a retrospective review of hysterectomies performed by gynecologists at six Ontario, Canada hospitals from July 2016 to June 2018. Data was extracted from health records coding (ICD-10) and electronic medical records. Of patients who had concurrent BSO, age, preoperative diagnoses, surgical factors (presence of endometriosis and adhesions) and surgery training (minimally invasive surgery (MIS) fellowship versus no fellowship) were recorded. Cases of BSO were classified as ‘indicated’ or ‘avoidable’. Criteria for avoidable BSO were: age less than 51 years old, benign preoperative diagnosis other than endometriosis, absence of intraoperative endometriosis and adhesions. The remainer of cases were classified as ‘indicated’. Chi square test was used to compare proportions, and odds ratios were calculated.

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**Sources of Funding:** none

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**S-22. Exploring workability and conditions to improve work participation among female healthcare workers aged 45-60 years:**

**Objective:** To determine the proportion of cases where there was potential for ovarian preservation, possibly avoiding surgical menopause. Decreased CYP3A4 activity was associated with higher hot flash severity (p=0.019) after adjustment for hormone therapy use. In addition, there was a trend toward fewer somato-vegetative symptoms among individuals with decreased CYP2C9 activity (p=0.063) and decreased CYP3A4 activity (p=0.036; p=0.025 after adjustment for hormone use). **Conclusion:** Our preliminary results demonstrate that variation in estrogen metabolism pathways is associated with VMS severity, and potentially other menopausal symptoms. Further studies including multivariate analyses to better understand the interplay between these genetic variants are underway. This work represents a step toward better understanding of the influence of genetics on menopausal symptoms, and may lead to individualized use of hormone therapy for management of menopausal symptoms.

**Sources of Funding:** none
Sources of Funding: our findings will result in improving workability, less risk of absence and continued exercise, smoking cessation, and information about effective treatments of menopause.

This study confirmed the negative association between bothersome menopause symptoms and risk of absence from work as shown by others. A 27% risk of menopause associated absence in healthcare workers aged 45-60 was found. Suggestions to improve workability at organizational level relate to work load and environment, communication and autonomy. Specific needs symptomatic women bring to the attention of employers are more awareness of their complaints, positive support and menopause-specific education about coping at the workplace. Benefits of responsible health behavior e.g. exercise, smoking cessation, and information about effective treatments of menopause complaints also deserve more emphasis. Whether targeted interventions based upon our findings will result in improving workability, less risk of absence and continued participation of menopausal women in the workforce needs further study.

Sources of Funding: None

S-23. Age at menopause and mortality in Taiwan: a cohort analysis

Te Yi Shen, PhD student, Carol Strong, Tsung Yu. Public Health, College of Medicine, National Cheng Kung University, Tainan, Taiwan

Objective: Previous research suggests that age at menopause may be associated with increased risk of all-cause, cardiovascular disease (CVD) and cancer mortality; however, findings were inconsistent across populations and not many studies have been conducted in Asia. The aim of our study was to investigate the association of age at menopause with risk of all-cause, CVD and cancer mortality in later life, in a cohort of postmenopausal women in Taiwan. Design: We used data from the MJ Health Database (http://www.mjhf.org/main/index/en) in Taiwan and included a cohort of 36,931 postmenopausal Taiwanese women who entered health check-up programs during (1999 to 2016). Information on age at menopause and confounding factors (i.e., educational attainment, smoking status and comorbidities) were collected from health survey or medical examination at the baseline visit. Mortality data were obtained from the national death registry and we followed participants until July, 2018. We assessed the association between age at menopause and all-cause, CVD and cancer mortality using Cox proportional hazards regression model. Age at menopause was categorized into <40-44, 45-49, 50-54 (reference group) and 55-60 years in the analysis. Results: The average follow-up time were 14.6 years and 5,316 deaths were identified. After adjustment for birth cohort, educational attainment, smoking status and comorbidities (history of hypertension, diabetes and hyperlipidemia), results showed a slightly higher risk of all-cause death in women who had menopause at 45-49 years (Hazard Ratio [HR] = 1.07, 95% CI: 1.01, 1.14) than the reference group. Women who had menopause earlier were also associated with increased risk of CVD mortality, in particular for women who had menopause at 45-49 years (HR = 1.22, 95% CI: 1.07, 1.40), while the risk seemed to decline in women who had later (55-60 years) menopause (HR = 0.84, 95% CI: 0.70, 1.02). We found no statistically significant associations between age at menopause and cancer mortality, although higher risks were all noted in women who had menopause at <40-44, 45-49 and 55-60 years, as compared to the reference group. Conclusion: Earlier age at menopause is associated with increased all-cause mortality and CVD mortality in Taiwanese women. Besides, women who had earlier or later age at menopause may be related to higher cancer mortality. Age at menopause could be deemed an important disease marker that indicates risk of death in later life for midlife women.

Sources of Funding: This study is supported by the Ministry of Science and Technology in Taiwan


Lisa Larkin, MD1, Alexandra Magnante. 1McMedicine, Cincinnati, OH; 2Genetics, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH

Objective: Increasing awareness of breast cancer risk can lead to reduced morbidity if those at risk take steps to reduce risk or undergo screening to detect cancer earlier. We provided breast cancer education, individualized risk assessments, and management recommendations to women during breast cancer education sessions. We assessed changes in accuracy of breast cancer risk perception, risk factor awareness, and behaviors pre- and post-education. Design: Women were recruited via social media and word-of-mouth. 102 attended one of three education sessions between August and November 2018. Education sessions addressed breast cancer risk factors, screening modalities, published screening recommendations, and risk assessment models. Attendees completed a baseline risk assessment survey (RAS) prior to the education session. Information gathered in the baseline RAS was used to generate Tyrer-Cuzick (v8) model-calculated lifetime breast cancer risk and provided to each participant at the education session. Fifteen four participants responded to a follow-up risk assessment survey (RAS2) one month after the education session. McNemar test was performed to test marginal differences in risk perception and behavioral modifications for participants who completed the baseline RAS and RAS2.

Results: Risk perception was more accurate, compared to the Tyrer-Cuzick (v8) risk assessment, in the RAS2 compared to the baseline RAS (p<0.001). There was a significant difference in the percentage of participants who correctly identified breast density (p<0.001), alcohol (p<0.001), nulliparity (p<0.001), early menarche (p<0.001), and late menopause (p<0.002) as breast cancer risk factors between the baseline RAS and the RAS2. There were no significant differences in reported physical activity, alcohol consumption, or fruit and vegetable intake between the baseline RAS and RAS2. Nearly 40% (n=21) reported scheduling mammograms and 50% (n=6) reported scheduling a genetics consultation of those receiving such recommendations.

Conclusion: Individual breast cancer risk perception and awareness of breast cancer risk factors improved significantly after a model-calculated risk assessment and breast cancer education session. Significant modifications in risk-reducing behaviors were not identified. An individualized breast cancer risk assessment and an educational intervention may improve the accuracy of breast cancer risk perception and may aid in identifying individuals who would benefit from genetic counseling or testing.

Sources of Funding: This research was supported by an unrestricted research grant from Clever Crazes for Kids.

Outcomes of the International Consensus Position Statement on Androgens in Women

Susan R. Davis1, Nicholas Panay2, James H. Liu, MD, NCMIP, Sharon J. Parish, MD1
1Women’s Health Research Program, School of Public Health and Preventive Medicine, Monash University, Melbourne, VIC, Australia; 2Queen Charlotte’s & Chelsea and Westminster Hospitals and Imperial College, London, United Kingdom; 3Obstetrics and Gynecology, University Hospitals Cleveland and Case Western Reserve University School of Medicine, Cleveland, OH; 4Weill Cornell Medical College, New York, NY

Despite widespread use of testosterone therapy for women, a consensus on guidelines for indications for use, potential benefits and risks and treatment goals was lacking. In recognition of this unmet need, the International Menopause Society invited key leading societies, whose members might prescribe androgenic sex steroids for women, to participate in the development of an International Consensus Position Statement on the use of testosterone therapy for women. This Position Statement has been endorsed by multiple international organisations, including The North American Menopause Society and was published on line in September 2019 in Climacteric, Maturitas, the Journal of Sexual Medicine and the Journal of Clinical Endocrinology and Metabolism. The presentations in this symposium, to be delivered by co-authors of the Position Statement, will summarize the key recommendations included in the Position Statement, with supportive data for these recommendations.

FRIDAY CONCURRENT SESSION #4