Low Libido at Midlife: Will the Answer Ever Be in Our Medicine Cabinets?

Supported in part by grant funding from Shionogi Inc.

Epidemiology of Sexual Problems at Midlife: Who, What & Why?
Raymond C. Rosen, PhD. New England Research Institutes, Watertown, MA

Sexual problems in women cover the gamut from deficient or chronically low desire, arousal difficulties, lack of lubrication, sexual pain problems, and orgasmic difficulties. These problems frequently co-exist in varying combinations, depending on the woman’s age, hormonal status, mental and physical health, prior sexual experience, and other factors. Consistent findings across at least 6 large-scale studies in diverse populations and geographic regions (WISHES, PRESIDE, BACH, NHSLS, NSHAP, Nationwide Survey) include the following main findings: 1) Sexual problems or dysfunction, based on most definitions, are common across most age groups, countries, race-ethnic groups and socio-economic conditions. Reporting and recognition of these problems however varies widely. 2) Sexual desire difficulties outnumber other commonly reported sexual problems in women in most surveys, often in combination with sexual function problems (e.g., lack of arousal or lubrication) or sexual pain. 3) Lubrication and arousal difficulties, sometimes associated with pain and bleeding, are especially common and bothersome in estrogen deficient women, as many women strive to remain sexually active despite loss of estrogenization. 4) The degree of bother or distress associated with an individual women’s experience varies greatly, and is associated with specific risk factors including age (higher age = lower distress), relationship status (committed relationship= greater distress) and overall health (poorer health = greater dysfunction). 5) Overall, studies have shown a low rate of help-seeking or treatment utilization among women with chronic sexual problems, even in women with higher levels of distress, due in part to lack of approved treatments for female sexual dysfunction. 6) Chronic sexual problems in women impact self-esteem, mood, relationships and overall quality of life. There is a strong negative association in most studies with sexual satisfaction and depression (more satisfied = less depressed). 7) Findings from these studies point the way to potential targets for future treatments, both psychosocial and pharmacological, and major areas of unmet need. Epidemiologic studies also contribute to our growing understanding of the etiology and pathophysiology of female sexual dysfunction.
Addressing Sexual Desire Problems of Women Without a Prescription
Sheryl A. Kingsberg, PhD. Case Western Reserve University School of Medicine, Cleveland, OH

Although there are very few outcome studies of psychotherapeutic treatments for hypoactive sexual desire disorder (HSDD), clinically, psychotherapy has been used for decades. This talk will focus on the different models of psychotherapeutic treatments for women with HSDD presenting both to their healthcare provider (HCP) and psychotherapist. Desire is a deceptively intricate concept that is best understood within a biopsychosocial context and differentiating its components: sexual drive, sexual beliefs and sexual motivation. The motivation component reflects, the emotional or interpersonal aspect of desire that is characterized by a woman’s willingness to engage in sexual activity with a given partner (or alone). Although evidence-based research demonstrates that the impact of relationship factors on desire problems is minimal, clinical experience as well as correlational studies show that relationship and sexual satisfaction are closely linked. It is also the case that psychological factors are frequently associated with desire problems. These include childhood trauma and sexual abuse, perceived stress, depression, personality disorders, and body image issues. Cultural, social, and religious values and mores may also negatively impact women’s sexual desire, particularly those from highly restrictive cultures/religions. In addition, there is a paucity of studies regarding the prevalence of low sexual desire in women in same-sex relationships. Sexual responsiveness is thought to decrease with age and the level and amount of sexual activity and reported libido also reportedly decreases after menopause. However, longitudinal studies suggest that relationship factors and other non-biological changes may have a stronger impact. Motivation is impacted by psychological function, relationship quality and concerns about health, occupation or family and, as such, impaired motivation is best served by a psychotherapy intervention.
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The Pharmacologic Treatment of Female Sexual Dysfunction: Future Reality or Wishful Thinking?
Jan L. Shifren, MD, NCMP. Harvard Medical School, Boston, MA

Sexual problems are highly prevalent in midlife women and often associated with distress. Female sexual interest/arousal disorder is the most common sexual problem reported by women. Hormonal changes at menopause as well as other physiological, psychological, sociocultural, interpersonal, and lifestyle factors contribute to midlife sexual concerns. Effective treatment requires an understanding of the cause of the problem. Although many sexual problems can be successfully treated without pharmacologic intervention, at times an option “from the medicine cabinet” may be indicated. Dyspareunia due to vulvovaginal atrophy (VVA) is an important and treatable cause of sexual problems after menopause. Symptomatic VVA is effectively treated by vaginal moisturizers, lubricants, low-dose vaginal estrogen therapy, and ospemifene. Choice of treatment depends on the severity of symptoms and the woman’s medical history and personal preferences. Androgen levels decline with aging and there is some evidence to support the use of testosterone therapy in carefully selected postmenopausal women with low libido associated with distress and no other etiology for their sexual problems. In randomized, double-blind, placebo-controlled studies of postmenopausal women with distressing low libido, testosterone therapy administered by a transdermal patch increased sexual desire, activity, and pleasure. Subsequent studies of a topical testosterone gel in a similar population demonstrated no improvement in any aspect of sexual function compared with placebo, despite achieving similar testosterone blood levels. There are currently no government-approved androgen-containing products for the treatment of female sexual disorders in the United States or Canada. A popular but untested treatment is the use of a small amount of compounded testosterone cream or gel (1-2%) applied topically to the vagina, arms, thighs, or low abdomen. Formulations of topical testosterone approved for the treatment of men increase the risk of excessive dosing when prescribed for women. Women using testosterone should be monitored for adverse effects, including facial hair, acne, voice changes, clitoromegaly, and changes in lipids or liver function tests. Blood testosterone levels should be checked intermittently to ensure that they remain in the normal range for reproductive-aged women. Long-term risks, including possible effects on the risk of cardiovascular disease or breast cancer, are unknown. There is no evidence to support the use of systemic dehydroepiandrosterone (DHEA) for the management of female sexual problems. The use of vaginal DHEA in postmenopausal women with low libido associated with symptomatic VVA is under investigation. Women who elect a trial of androgen therapy should be informed of potential risks and off-label nature of use. A government approved clitoral therapy device (EROS-CTD) may increase clitoral blood flow and improve sexual response in women with sexual dysfunction. Less expensive devices available without a prescription are likely equally effective. Although highly effective for men with erectile dysfunction, phosphodiesterase inhibitors are generally ineffective for women, with benefit limited to those with sexual dysfunction secondary to the use of selective serotonin reuptake inhibitors. Buproprion has been shown to improve sexual arousal and response in several small randomized controlled trials of premenopausal women without depression. Pharmacologic agents under investigation for the treatment of female sexual disorders include fibanserin (serotonin receptor family agonist/antagonist), apomorphine (dopamine agonist), bremelanotide (melanocortin agonist), and combinations of testosterone with sildenafil or buspirone. Given potential risks of pharmacologic agents and a high placebo response in studies of drug treatments for sexual disorders, effective non-pharmacologic options should be first line treatment for midlife women with sexual problems.
Aging America and the Challenges of Changing Demographics

Joseph F. Coughlin, PhD. Massachusetts Institute of Technology, Cambridge, MA

Technology can be forecasted. Economics predicted. But, demographics is said to be destiny. While youthful, the United States is no longer young. In short, the future is gray, small and female. America is aging with one baby boomer turning 68 years old nearly every eight seconds. Fertility rates are barely at replacement level resulting in historically smaller families. And, record numbers of older adults – particularly women – are living alone, further contributing to smaller households. Typically living longer, providing care across the generations, and acting as the primary health decision-maker in most homes, women are set to define the future of an aging America. How might aging, changing roles, and smaller households affect the future well-being of women? Moreover, how will the disruptive demographics of an aging America affect how all of us will live, work and play tomorrow?
Chemoprevention: Who, What, When?
Victor G. Vogel, MD, MHS, FACP. Geisinger Health System, Danville, PA

Risk for breast cancer can be easily and rapidly assessed using validated, quantitative models. Multiple randomized studies show that the selective estrogen response modifiers (SERMs) tamoxifen and raloxifene can safely reduce the risk of invasive breast cancer in postmenopausal women. Overall, there is a 38% reduction in breast cancer incidence, and 42 women would need to be treated to prevent one breast cancer event in the first 10 years of follow-up. Reduction is larger in the first 5 years of follow-up than in years 5–10, but no studies treated for longer than 5 years. Thromboembolic events are significantly increased with all SERMs while vertebral fractures are reduced. Tamoxifen provides net benefit to all premenopausal women who are at increased risk while raloxifene reduces risk nearly as much in postmenopausal women and offers increased safety. Both tamoxifen and raloxifene reduce the incidence of in situ cancers. The MAP3 trial showed a 65% reduction in the annual incidence of invasive breast cancer in postmenopausal women who were at moderately increased risk for breast cancer who took the aromatase inhibitor exemestane. The IBIS-II trial showed a 53% reduction in the risk of invasive breast cancer in postmenopausal women aged 40-70 years old who took the aromatase inhibitor anastrozole. Of the 50 million white women in the U.S. aged 35 to 79 years, 2.4 million would have a positive benefit/risk index for chemoprevention. Tamoxifen increases the risk of uterine malignancy while raloxifene does not; both drugs reduce the risk of non-vertebral fractures. Raloxifene causes fewer thromboembolic events than does tamoxifen. Two aromatase inhibitors anastrozole and exemestane have been shown to reduce the risk of breast cancer in postmenopausal women with an apparently greater safety profile than tamoxifen, although no randomized comparisons for risk reduction have been done. Despite the compelling results of chemoprevention trials using SERMs for breast cancer risk reduction, there has been minimal use of either tamoxifen or raloxifene by women at increased risk for breast cancer. Studies monitoring SERM sales have shown that only 5% to 20% of women who matched the eligibility criteria of the breast cancer prevention trials opted for SERM therapy for breast cancer risk reduction. Additional studies reported that use actually decreased with only 6% of women offered a SERM agreeing to take this medication. A benefit/risk index can quantify both beneficial and adverse outcomes from chemoprevention with tamoxifen or raloxifene. This index helps decide whether to initiate chemoprevention by comparing the benefits and risks of raloxifene versus tamoxifen. Risks and benefits of treatment with raloxifene or tamoxifen depend on age, race, breast cancer risk, and history of hysterectomy. Over a 5-year period, postmenopausal women with an intact uterus have a better benefit/risk index for raloxifene than for tamoxifen. For postmenopausal women without a uterus, the benefit/risk ratio is similar. The benefits and risks of raloxifene and tamoxifen are described in published tables that can help identify groups of women for whom the benefits of chemoprevention outweigh the risks. Chemoprevention with a SERM may be particularly beneficial to women with atypical hyperplasia, a 5-year Gail model risk of more than 5%, lobular carcinoma in situ, or two or more first-degree relatives with breast cancer based on published data. There are no primary prevention studies to evaluate the optimum duration of tamoxifen therapy for reducing the risk of breast cancer, but completed clinical trials in the adjuvant therapy setting show that using tamoxifen for 10 years is more beneficial than only 5 years of use. No trials are being conducted or are planned to examine the ideal duration of therapy in the risk-reduction setting. Published practice guidelines say that agents to reduce the risk of breast cancer should be offered to women who are at increased risk after a discussion of the risks and benefits.
What’s New in Breast Imaging?
Jennifer A. Harvey, MD. University of Virginia School of Medicine, Charlottesville, VA

Breast cancer screening is moving beyond annual mammography. Tomosynthesis, contrast-enhanced mammography, screening ultrasound (US), and fast screening MRI are all advanced breast imaging techniques that are available and may be used for breast cancer screening though the indications for these tests are emerging. • Tomosynthesis (“3D mammography) improves breast cancer detection by 30%, while also increasing specificity by about 30%. Women with scattered and heterogeneously dense breasts are most likely to benefit from tomosynthesis. Tomosynthesis is associated with an increased radiation dose, though a synthesized 2D image reduces dose. • Contrast-enhanced mammography (CEM) uses vascular enhancement to detect breast cancer, similar to breast MRI. Studies on CEM are evolving, with only small studies to date. One study of 52 women with both MRI and CEM showed that both detected lesions with high sensitivity (96%). Disadvantages of CEM are starting an IV, contrast-reaction, and small increase in radiation dose (about 30% higher). The cost is relatively inexpensive. • Screening breast US results in detection of about 30% more cancers that are typically small and invasive, in women with heterogeneous or dense breasts. The cost is a high false positive rate; 4-5% will undergo biopsy and only 7% will be malignant. • Screening breast MRI is expensive and currently reserved only for those at very high lifetime risk of breast cancer (>20%). Newer techniques are evolving however that may considerably shorten the acquisition time to 10-15 minutes, which implies that costs would be lower and the test more available for adjunct screening. Newer techniques will still require IV administration of a gadolinium based contrast agent. As these advanced imaging techniques evolve, decisions must be made about who gets which examination. Stratification of resources should ideally be based on optimization of detection method for that patient and her baseline risk.
Rethinking Breast Cancer Screening
Russell P. Harris, MD, MPH. University of North Carolina, Chapel Hill, NC

It is understandable that breast cancer screening technology (as with screening technologies for other conditions) doesn’t stand still, but continues to evolve. At the same time, some evidence-based screening panels have started scaling back the intensity of their recommendations. We need a more thoughtful approach to deciding what screening strategy (i.e., starting age, stopping age, frequency of screening, sensitivity of the screening test) provides optimal value. Using the lens of value to consider screening strategies requires that we ask competing strategies to quantify their health benefit to weigh against harms and costs. Optimal value occurs when a strategy shows that the magnitude of health benefits clearly justifies the harms and costs incurred. Although many newer technologies have endeavored to justify themselves by demonstrating increased cancer detection, finding more cancers is not necessarily a health benefit. In fact, finding cancers that are unlikely to progress, or cancers that could be treated as effectively later, could well increase harms and costs without any incremental health benefit. In screening, what is important is not how much you find, but rather what kind of abnormality you find. Benefit only occurs when abnormalities are detected that would have progressed to a health problem in the person’s lifetime and could be more easily treated if found earlier rather than later. Because of the need to consider the value of screening strategies, we should require strong evidence of benefits, harms, and costs before implementing any screening program. In the meantime, we should only use screening strategies that have been shown to have high value.
Diagnostic Challenges: Whom to Treat
Ethel S. Siris, MD. Columbia University Medical Center, New York, NY

Osteoporosis is a disorder of reduced bone strength associated with a high risk for fractures that increases with age among postmenopausal women. Until recently, the diagnosis was officially made on the basis of a bone density test that found a T-score value of ≤-2.5 at the spine or hip. In May, 2014, a working group of the National Bone Health Alliance (Siris et al, Osteoporosis International 2014; 25:1439-1443) published a position paper recommending a formal expansion of the diagnostic criteria for using the term osteoporosis in postmenopausal women and in men over 50. A T-score of ≤-2.5 or lower continues to be one way to make the diagnosis of osteoporosis. A hip fracture, with or without a bone density test, or, in the setting of low bone mass by DXA, a vertebral, proximal humerus, pelvis, or – in some cases – a wrist fracture also permit a diagnosis of osteoporosis. Finally, in patients with osteopenia, a FRAX output reflecting a ≥3% 10 year probability of hip fracture or a ≥20% probability of a major osteoporotic fracture would also permit a diagnosis of osteoporosis. Thus, in some cases a BMD diagnosis of osteopenia, in the setting of certain fractures or high risk by FRAX, would result in the clinical diagnosis of osteoporosis. These criteria for diagnosis are consistent with the indications for treatment to lower fracture risk in this population as recommended in the National Osteoporosis Foundation’s (NOF) Clinician’s Guide. Treatment is recommended for patients with T scores at spine or hip ≤-2.5, for those with a hip or vertebral fracture, and for those with cut points for 10 year absolute hip fracture risk ≥3% or for major osteoporotic fracture ≥20%. In all cases calcium and vitamin D sufficiency, fall risk reduction and pharmacologic therapy with FDA-approved osteoporosis treatments are indicated, since these individuals carry a diagnosis of osteoporosis and are clearly at elevated fracture risk. One caveat is that not all osteoporosis therapies have been studied to determine anti-fracture efficacy based on FRAX risk or on low bone mass and a fracture type listed above, in the absence of a hip T-score of ≤-2.5 or lower. Prescribing clinicians will need to familiarize themselves with entry criteria for such trials. There has been a great deal of controversy in recent years, given the costs of some treatments and potential side effects that may be associated with all therapies, as to whether or not to treat patients to prevent bone loss in cases where short term risk for fracture is not severely elevated, based on age, but who have low bone mass and evidence of rapid bone loss. Short term use (3-5 years) of a bisphosphonate or longer term use of a SERM may be appropriate in younger postmenopausal women with low BMD and additional risk factors for rapid bone loss, including recent discontinuation of estrogen, surgical or chemo-therapy induced menopause or use of aromatase inhibitors, or in the setting of documented aggressive bone loss that over time might lead to very low T-scores. In such patients the benefit/risk equation must be thoughtfully considered with the patient, but intervention with prescription therapy to “prevent osteoporosis” may be indicated. It is clear, however, that in the setting of either low BMD or osteoporosis by DXA testing a person who has sustained a recent fracture, especially a hip, vertebral, proximal humerus, pelvis, or certain wrist fractures, is at high short term risk of additional fractures and needs treatment for the secondary prevention of osteoporotic fracture.
Controversies in Long-Term Care of the Patient With Osteoporosis
Elizabeth Shane, MD. Columbia University Medical Center, New York, NY

Antiresorptive therapy with bisphosphonates (BPs) and denosumab has been proven to reduce bone loss and prevent fractures in postmenopausal women. In the last decade, however, osteonecrosis of the jaw (ONJ) and atypical femoral fractures (AFFs) have emerged as possible complications of long-term antiresorptive therapy for postmenopausal osteoporosis. Although BPs and denosumab have not been proven to be causal, these potential complications are associated with substantial morbidity and have prompted questions on the optimal duration of antiresorptive therapy for postmenopausal osteoporosis. In this talk, I will review ONJ and AFFs and their relationship to antiresorptive therapy, and discuss the relative risks of antiresorptive therapy in light of their established benefits for prevention of osteoporotic fractures. ONJ associated with BP therapy was first reported in cancer patients in 2003 and in patients with osteoporosis in 2006. Since that time, cases have also been reported in association with other antiresorptive therapies, specifically denosumab (Prolia) and with antiangiogenic agents. The American Association of Oral and Maxillofacial Surgeons (AAOMS) recently (June 2014) published an updated Position Paper, in which they recommend that ONJ be termed Medication-Related ONJ (MRONJ). MRONJ can be diagnosed in patients with current or previous treatment with antiresorptive or antiangiogenic agents, exposed bone or bone in the maxillofacial region that can be probed through an intraoral or extraoral fistula(e) that has persisted for more than eight weeks, and who have no history of radiation therapy to the jaws or obvious metastatic disease to the jaws. Based the AAOMS review of data, although the risk of developing ONJ in patients exposed to oral BPs, IV BPs, or denosumab in the doses used to treat osteoporosis may increase with increasing duration of therapy (>4 years), it is very low and, in fact, comparable to patients in placebo arms of studies of IV bisphosphonates or SC denosumab. There is also evidence for a relationship between AFFs and use of BPs (and to a much lesser extent, denosumab). AFFs are low trauma, subtrochanteric and femoral shaft fractures that begin in the lateral femoral cortex, and are characterized by transverse or short oblique orientation and periosteal callus formation at the site of fracture initiation. They have other unique clinical features, including prodromal pain and bilaterality. These fractures can occur in patients who have not been treated with BPs and their true incidence is unknown. However, they appear to be more common in patients who have been exposed to long-term BPs, usually for more than 5 years (median treatment 7 years). AFFs are far less common than typical and common femoral neck and intertrochanteric fractures and other major osteoporotic fractures that BPs prevent. However, recognition of these associations has prompted consideration of the consequences of long-term use and the optimal duration of therapy for patients with osteoporosis. The concept of a drug holiday has arisen with the goal of providing a hiatus during which reduced bone turnover caused by the BP may partially recover (or increase), perhaps reducing risk of these adverse events. Patients whose fracture risk has been reduced by BP therapy (bone density has improved and no fractures have occurred), might be candidates for a drug holiday after 3-5 years of continuous treatment. On the other hand, for individuals who are still at high risk for fracture after 5 years of BP therapy (femoral neck T score <=2.5 or <=2.0 with a prevalent vertebral fracture, and/or an intervening fragility fracture), a drug holiday may not be wise as the risk of new vertebral fractures is higher in such patients. In this situation, the risks of stopping therapy may exceed the risks of continuing therapy. The optimal length of the BP drug holiday is also not known, nor is it clear how long to treat with denosumab, as the antiresorptive effects wane after 6-8 months and bone gains revert to baseline by 2 years. Thus, each case must be individually considered.
Nuts and Bolts of Hormone Therapy
Lubna Pal, MBBS, MRCOG. Yale School of Medicine, New Haven, CT

Menopausal management has transformed over the past decade, with an obvious shift to a relatively cautious stance regarding place of hormone therapy (HT) in the management of menopause related symptoms. While today’s practitioner is increasingly appreciative that the choice of therapy must be individualized to address the unique needs of an individual woman, questions regarding optimal dosage, hormone formulation (natural vs synthetic), hormone regimen (continuous, combined, cyclic, intermittent), and the preferred route of HT (oral vs non oral) for managing menopausal symptoms are sources of conundrum for many. In this era of virtual connectivity, “proverbial” and “anecdotal” information that is accessible at the click of a button adds to the complexity of clinician-patient discussions, frequently influencing patient choices and management decisions. This session will offer a succinct yet critical review of the evidence, and will walk the audience through a succession of considerations to help identify the optimal management approach for addressing the needs of an individual symptomatic menopausal woman.
Hormone therapy (HT) treats symptomatic menopausal women at risk for bone loss but the progestogen component needed to protect against uterine cancer has been associated with safety and tolerability concerns including irregular bleeding, breast tenderness, and increased breast density. The FDA approved tissue selective estrogen complex (TSEC) is a novel therapy, partnering conjugated estrogens (CE) with the estrogen agonist/antagonist (SERM) Bazedoxifene (BZA) to reduce the risk of endometrial hyperplasia without the need for a progestogen. In the Selective estrogens, Menopause, And Response to Therapy (SMART) phase 3 trials of healthy, primarily Caucasian postmenopausal women with a uterus, CE 0.45 mg and 0.625mg/BZA 20mg reduced hot flush frequency by 74% and 80%, respectively, versus 51% for placebo (SMART-2, highly symptomatic) and hot flush severity up to 54%, improved measures of vulvar/vaginal atrophy with improvement in VMI, vaginal pH and MBS (SMART-3 dose related), and prevented bone loss at years 1 and 2 (SMART 1). LS BMD at 12 months increased by 1.51% and 1.21% more than placebo, comparable but less than CE/MPA at 2.57% (SMART-58). CE 0.45 mg and 0.625mg/BZA 20 mg showed a favorable safety and tolerability profile, with low rates of spotting/bleeding and high rates of cumulative amenorrhea up to 84%, similar to placebo and more favorable than CE 0.45mg/MPA 1.5 (SMART-5) and breast tenderness comparable to placebo and less than CE/MPA group (SMART-5). Incidence of endometrial hyperplasia at year 1 was < 1% (SMART-1,5) with minimal increases in endometrial thickness. No increase in breast density, ovarian cyst formation or cancer of breast, ovary or endometrium over placebo was seen with cardiovascular, cerebrovascular and VTE events similar to placebo. Secondary endpoints showed improvements in sleep, menopause-related QOL, and treatment satisfaction. Compared to traditional HT, CE 0.45 and 0.625/BZA 20 mg offers an effective therapy with an improved safety and side effect profile over conventional therapy. Additional studies are needed—duration longer than 2 years, minority ethnic populations, BMI >34 and at high risk for endometrial or breast cancer.
Long-Term Issues in Hormone Therapy Management
Andrew M. Kaunitz, MD, FACOG, NCMP. University of Florida College of Medicine, Jacksonville, FL

Although providing guidance to patients regarding duration of hormone therapy (HT) represents a topic commonly encountered by clinicians caring for menopausal women, this issue is surrounded by controversy. The median duration of bothersome hot flashes is more than 10 years, underscoring that many women who initiate HT soon after the onset of menopause to treat symptoms will face decisions regarding long-term use of HT. Unfortunately, clinical trial data do not address the benefits and risk of long-term use of HT. As pointed out in the NAMS 2012 Hormone Therapy Position Statement, determining the optimal duration of HT is challenging both for clinicians and for patients. This presentation addresses clinical situations for which long-term HT might be appropriate and provides practical guidance regarding prudent therapeutic choices for women using HT for an extended duration. Because extended use of estrogen progestin therapy (EPT) increases the risk of breast cancer, the benefit-risk ratio for extended use is less favorable than for ET. In women who seek use of EPT for an extended duration, periodic discussions between the clinician and woman regarding the elevated risk of breast cancer associated with long-term use of EPT are appropriate. In older women using HT for an extended duration, transdermal estrogen (0.05 mg or lower dose estradiol patch) may be safer with respect to risk of VTE and stroke. When use of HT is being considered solely for the prevention of osteoporosis, lower than standard doses are appropriate.
Cosmetic Concerns in Menopause
Dina N. Anderson, MD, FAAD. Mt. Sinai Medical Center, New York, NY

In addition to night sweats and hot flashes, the precipitous decline in estrogen during menopause has significant effects on skin hydration and elasticity. The presence of estrogen helps stimulate collagen and oil production. As these levels start to decline in perimenopause, production of oil and collagen decline as well as a decreased capacity to retain moisture. This leads to a drying effect of virtually every cutaneous and mucosal surface on the body, sometimes accompanied by an itching sensation. These effects tend to intensify as menopause progresses. In addition to dryness and an impaired skin barrier, women will start to notice more fine and coarse wrinkling. This is primarily caused by decreased fibroblastic activity leading to a lack of procollagen I formation as well as subcutaneous fat atrophy. Skin may start to feel looser and skin may start to sag, especially around the jaw, neck, and cheeks. Fine lines tend to become more prominent around the eyes and upper lip, especially in women who smoke. Physicians and patients play a role together to help combat these effects and minimize accelerated skin aging due to hormonal fluctuations. Avoiding excessive UV exposure is paramount, as sun will accelerate patchy dry skin, brown spots, and wrinkles. Dietary improvement with a focus on smarter fats can help cutaneous hydration and oral and topical antioxidants can help quench free radical production. Isoflavone rich soy products are biosimilar to estrogen and should be included in the dietary plan. Topical emollients after short, warm baths will help restore some barrier function, leaving skin softer and smoother. Topical preparations with HQ or other skin bleaching agents, retinoids, or alpha and beta acid creams combined with physical based-micronized sunblock can improve brown spots. Peels and lasers are useful adjuncts to even out skin tone that tends to become blotchy as we get older. Finally, a myriad of cosmetic therapies can help fine lines and wrinkles and sagging skin. Laser and tightening devices, toxin injections, line filling agents, volumizing injectables and collagen stimulators utilizing poly-L-lactic acid can all be part of a regimen to reverse some of the changes from estrogen depletion. A multifaceted approach targeting diet, skincare and aesthetic enhancements between patient and physician can help make a woman look and feel better in her 50’s than she did in her 30’s and 40’s.
Assessing Skin Lesions: When is the Skin Problem Benign and When Should You Worry About it Being Potentially More Aggressive?
Helen Shim-Chang, MD. Icahn School of Medicine at Mount Sinai, New York, NY

Differentiating a benign skin disorder or lesion from a potentially more aggressive or malignant one is usually done easily. The benign skin disorder or skin eruption (“rash”) tends to be more chronic, symptomatic, and easily treated. Examples are contact dermatitis commonly to feminine hygiene products, seborrheic dermatitis, psoriasis, and intertrigo. The benign lesions tend to be more symmetric, even-colored, non- or slow growing (months to years) and non-ulcerated and non-symptomatic. Examples include seborrheic keratosis, congenital and acquired melanocytic nevi, labial lentigo, and benign familial pemphigus. The aggressive, potentially more difficult disorder can be acute or chronic. They are progressive, can cause significant morbidity, and if not accurately diagnosed and treated, may result in a permanent skin dyspigmentation or scarring. Examples include lichen planus, lichen sclerosus et atrophicus, Pemphigus vulgaris, and Cicatricial Pemphigoid. The malignant skin lesions tend to show irregular, infiltrative borders, fairly rapid growth (weeks to months), friable, ulcerated, partially or fully nodular and may manifest as pain or itch. Examples include Bowen’s Disease, Basal Cell Carcinoma, Extramammary Paget’s Disease, and Malignant Melanoma. Exceptions to this general approach can cause diagnostic dilemmas and may require extensive and detailed history taking or specialized tests to arrive at an accurate diagnosis.
Hair: Too Much, Too Little
Bethanee J. Schlosser, MD, PhD. Northwestern University Feinberg School of Medicine, Chicago, IL

Significant changes in hair follicle dynamics occur with menopause and may result in either undesirable hair loss and/or hair growth. Hirsutism affects 10% of women worldwide, and female pattern alopecia affects 50% of women during their lifetimes. Alterations in hair growth patterns in the form of female pattern alopecia and hirsutism adversely impact quality of life of many women. Women presenting with hirsutism and/or female pattern alopecia should undergo diagnostic evaluation for hyperandrogenemia in order to differentiate those changes in hair growth attributed to the hormonal alterations that accompany the natural aging process versus underlying pathologies. Historical inquiry should include the timing of onset and rate of progression of signs of hyperandrogenism, as well as additional signs of virilization. Laboratory and additional diagnostic evaluation of hyperandrogenemia should be performed utilizing a systematic and algorithmic approach. Currently available medical therapies for the treatment of female pattern alopecia and hirsutism aim to reduce the levels and bioavailability of circulating androgens and to reduce their physiologic action at target tissues. Such medical therapy can provide significant benefit when utilized in appropriately selected women.
Adult Stem Cells: The Body’s Innate Regenerative Potential
Arnold I. Caplan, PhD. Case Western Reserve University, Cleveland, OH

Marrow derived adult Mesenchymal Stem Cells (MSCs) can be isolated and culture expanded. Although these cells are capable of differentiating into lineages that result in the fabrication of bone, cartilage, muscle, marrow stroma, tendon/ligament, fat and other connective tissues, MSCs have recently been shown to be intrinsically therapeutic. Such culture expanded adult/MSCs are immuno-modulatory especially in muting T-cells and, thus, allogeneic MSCs have been used to mute or cure graft-versus-host-disease and Crohn’s disease and are now being tested in certain autoimmune diseases. Furthermore, these allo-MSCs set-up a regenerative micro-environment which is anti-apoptotic, anti-scarring, mitotic for tissue intrinsic progenitors and angiogenic. These immuno and trophic activities result from the secretion of a spectrum of powerful bioactive molecules that, in combination, support localized regenerative events. The MSCs reside in every tissue of the body and function as perivascular cells (pericytes) until a focal injury occurs. At sites of injury, the pericyte is released and functions as an MSC that provides molecular assistance in activities leading to tissue regeneration. Such broad spectrum recuperative activities by MSCs form the basis for the “New Medicine” that will be discussed.
Plenary Symposium 6
Cardiovascular Disease in Women: Heart Failure, Atrial Fibrillation, and Making Sense of the New CVD Guidelines

Understanding the New ACC/AHA and JNC-8 Guidelines: Risk Assessment, Cholesterol, Lifestyle, and Hypertension
C. Noel Bairey Merz, MD, FACCD. Cedars-Sinai Medical Center, Los Angeles, CA

Description: The American College of Cardiology /American Heart Association (ACC/AHA) released a clinical practice guideline in November 2013 on the treatment of blood cholesterol to reduce cardiovascular risk in adults. This synopsis summarizes the guidelines. Methods: In 2008 the National Heart, Lung and Blood Institute (NHLBI) convened the Adult Treatment Panel (ATP-IV) panel to update the 2001 ATP-III cholesterol guidelines based on rigorous systematic review and meta-analysis of randomized controlled trials that examined ASCVD outcomes. The panel commissioned independent systematic evidence reviews for low-density-lipoprotein-cholesterol (LDL-C) and non-HDL-cholesterol (non-HDL-C) as targets in secondary and primary prevention, the impact of specific lipid drugs on ASCVD events and adverse effects. The panel’s draft recommendations were transitioned to the ACC/AHA. Recommendations: This abstract summarizes key features of the guidelines in eight areas: All adults should adhere to a healthy lifestyle. 1. Statin therapy is recommended for adults in groups demonstrated to benefit: a. Secondary prevention in patients with clinical ASCVD (acute coronary syndromes, myocardial infarction, stable angina, coronary or other arterial revascularization, stroke, TIA, peripheral arterial disease of atherosclerotic origin), and for primary prevention in: b. LDL-C levels ≥190 mg/dl, c. Diabetes, age 40-75 years, and LDL-C levels 70-189 mg; d. No diabetes, age 40-75 years, >7.5% 10-year ASCVD risk. 2. Statins have an acceptable margin of safety when used in properly in selected individuals and appropriately monitored. 3. Engage in a clinician-patient discussion prior to initiating statin therapy, especially for in lower risk primary prevention in patients. 4. Use the newly developed Pooled Cohort Equations for estimating 10-year ASCVD risk. 5. Initiate the appropriate intensity of statin therapy. 6. Evidence is inadequate to support treatment to specific LDL-C and/or non-HDL-C goals. 7. Regularly monitor patients for adherence to lifestyle and statin therapy. Summary: Millions of U.S. adults are at increased ASCVD risk – some having experienced an ASCVD event; others because of ASCVD risk factors. Adherence with healthy lifestyle behaviors, control of blood pressure and diabetes, and avoidance of smoking is recommended for all adults. Statin therapy should be used to reduce ASCVD risk in individuals likely to experience a clear net benefit – those with clinical ASCVD, or primary prevention for adults with LDL-C >190 mg/dl, diabetes aged 40-75 years, or >7.5% 10-year ASCVD risk without diabetes. A clinician-patient discussion that considers potential ASCVD risk reduction, adverse effects and patient preferences is needed to decide whether to initiate statin therapy, especially in lower risk primary prevention. Appropriate intensity of statin therapy based on ASCVD risk and potential for adverse effects is recommended, rather than focusing on specific LDL-C or non-HDL-C goals. Five of 7 statins, including a high intensity statin, are available in the U.S. as low cost generics. Until heart healthy lifestyles are adopted throughout the lifespan, the need for preventive measures utilizing evidence-based drug therapy will remain high. As with all clinical guidelines, the 2013 ACC/AHA Cholesterol Guidelines must be implemented in conjunction with sound clinical judgment.
Heart Failure in Women: Issues Unique to Women
Veronique L. Roger, MD, FAHA. Mayo Clinic, Rochester, MN

Heart failure is a complex clinical syndrome that can result from any abnormality that impairs the ability of the ventricle to fill or eject blood. Heart failure had been touted as a new epidemic in 1997 and indeed hospital discharges for heart failure have increase exponentially over time. They typically have been higher in women compared to men. The investigation of the heart failure epidemic indicated that the incidence of heart failure was stable and perhaps even declining in women in several studies including from Framingham and Olmsted County. The survival after heart failure diagnosis has improved over time. The combination of stable or decreasing incidence and improving survival indicate that the epidemic of heart failures is an epidemic of survivors with individuals being repeatedly admitted to the hospital as a result of their longer life expectancy with prevalent disease. Heart failure can present with preserved or reduced ejection fraction and the proportion of individuals who present with preserved ejection fraction is 57% women compared to that of reduced ejection fraction, which is 42% women. There is a slight female predominance among patients with heart failure and preserved ejection fraction, however as the incidence of heart failure overall is lower in women, there is a disproportionate burden of heart failure with preserved ejection fraction in women. In addition, among women who experience heart failure, in 63% of the cases the ejection fraction is preserved. Imaging methods have demonstrated that heart failure with preserved ejection fraction itself is a heterogeneous entity. In particular, female sex is associated with a higher prevalence of abnormal ventricular geometry and worse diastolic function indices. Elderly women with heart failure are particular vulnerable to hospitalizations and treatment advances have been essentially absent in heart failure with preserved ejection fraction. A major concern in the 2013 heart failure guidelines is that most trials failed to randomize a sufficient number of women. Indeed the enrollment of women in cardiovascular clinical trials from 1997 to 2009 however has remained approximately 30%. This limits the inference that can be drawn from these trials and applied to women as well as the clinical relevance of these findings for women. Taken collectively common constitute a call for action to improve our understanding in heart failure in women.
Atrial Fibrillation in Postmenopausal Women: Risk Factors, Diagnosis, and Management
Anita M. Kelsey. Saint Francis Hospital and Medical Center, Hartford, CT

Atrial fibrillation (AF) is the most common cardiac dysrhythmia currently affecting 2.3 million US adults with a prevalence that increases with age, disproportionately affecting postmenopausal women. Women have an increased risk of death, cardiovascular events, and stroke secondary to AF when compared to a male cohort with similar risk profile. Identification of gender based differences in AF can alert clinicians to issues unique to women with improved diagnosis, management and outcomes. Postmenopausal women have changes in atrial refactoriness that predispose them to AF. Risk factors for AF are more common in women and include hypertension, valvular heart disease, diabetes mellitus, obesity, hyperthyroidism and possibly early menopause. It is possible that women with AF have a higher stroke risk because of gender biased treatment of other concomitant stroke risk factors such as hypertension. Coronary artery disease is another important risk factor for AF with a prevalence that is higher in men, but is frequently underdiagnosed with treatment delays in women. Age is an important risk factor for AF especially in elderly women. The 2014 guidelines for stroke prevention in women specifically recommend active screening, particularly in women >75 years of age, in the primary care settings, using pulse followed by ECG to identify AF. Women are more symptomatic with AF and experience a lower quality of life after diagnosis. Management of AF is defined by two primary objectives: 1. stroke prevention and 2. rate or rhythm control. Anticoagulation is critical to stroke prevention and should be initiated at the time of diagnosis of AF. While previously used stroke risk scores failed to identify the increased risk of stroke in women, the CHA2DS2-VASc score has been recommended as the only score to apply when assessing stroke risk in nonvalvular AF in the 2014 guidelines for AF management. The CHA2DS2-VASc score gives one point for each moderate stroke risk factors: congestive heart failure, hypertension, age > 65 years, diabetes mellitus, vascular disease history (prior MI, peripheral artery disease or aortic plaque), and female gender, and two points for stroke, TIA or thromboembolism. Anti-thrombotic therapy with oral anticoagulation (OAC) is recommended for all patients who have AF and more than one moderate stroke risk factor according to the CHA2DS2-VASc score. Aspirin (81-325 mg) can be used as an alternative to OAC in low risk patients who have no associated comorbidities (i.e. lone AF) or in those with contraindications to OAC. Non-pharmacologic closure of left atrial appendage is appropriate in patients not eligible for anticoagulation at risk for stroke. OAC was traditionally achieved with the vitamin K antagonist, warfarin, but several newer anticoagulation agents may be considered in nonvalvular AF. These include Factor Xa inhibitors, ribaroxaban and apixaban, the direct thrombin inhibitor, dabigatran, and others awaiting approval by the US FDA. These guidelines uniquely recommend choice of OAC be made on an individualized basis with shared decision-making between the physician and the patient after discussion of the absolute and relative risks of stroke and bleeding, and the patient’s values and preferences. The second objective in management of AF is rate and rhythm control. Neither conversion to sinus rhythm or rate control has survival advantage, and either is appropriate for women. An initial strategy of rate control is recommended when AF is identified. Strategies for medical or electrical cardioversion can be made after consideration of duration of AF and need for transesophageal echocardiography to exclude left atrial thrombus. Long term management can include catheter ablation and surgical (MAZE) procedures for certain AF patients.
The Triad of Sleep Disturbances, Stress/Anxiety, and Pain: Epidemiology, Assessment, and Treatment

Abstract Not Received from Speaker

The Epidemiology of Sleep Disturbances, Stress/Anxiety, and Pain
Maurice M. Ohayon, MD, PhD
Stress/Anxiety and Chronic Pain: Interactions, Assessment, and Treatment Approaches
Christina McCrae, PhD. University of Florida and Shands Sleep Disorders Center, Gainesville, FL

Stress and anxiety and related conditions, such as depression and insomnia, are commonly found in patients with chronic pain, and may contribute to its development. The hyperarousal associated with stress and anxiety may contribute to central sensitization, a form of maladaptive neural plasticity involving increased responsiveness of the central nervous system to stimuli. Central sensitization leads to the development of alldynia (ie, painful response to a normally innocuous stimulus) and (likely) hyperalgesia (ie, increased response to a painful stimulus) in chronic pain sufferers and contributes to the development and maintenance of chronic pain. Researchers have found positive associations between chronic pain and psychological symptoms, and women may be particularly at risk. Breivik and colleagues noted that 21% of the respondents in their large-scale study reported that they had been diagnosed with depression because of their pain. Additionally, Duquesnoy and colleagues noted psychological disorders in 75% of their sample of chronic low back pain patients. Among this sample, 80% of patients reported experiencing negative effects of pain on their everyday life, 58% reported experiencing negative effects of pain on their emotional life, and 46% reported experiencing negative effects of pain on their sexual activity. Stress, anxiety, and depression have been associated with volumetric changes in cortical and subcortical brain regions, and have been shown to improve following intervention for pain and other stress-related disturbances. It is important to recognize that an individual does not need to have a diagnosable anxiety or other stress-related disorder for psychiatric factors to have a negative impact on pain. Subclinical symptoms of anxiety, stress, insomnia, and depression often accompany chronic pain. In terms of treatment, pain medications are the most common approach to managing chronic pain. However, two meta-analytic reviews support the efficacy of cognitive behavioral treatment of chronic pain. Typically, CBT-P is a multi-component treatment package that includes behavioral interventions such as relaxation training techniques, activity pacing, and operant reinforcement of physical activity, combined with cognitive therapy aimed at reduction of maladaptive thinking patterns and substitution of more adaptive thinking patterns. CBT-P has been found to be superior to waitlist control, physical therapy, and uni-dimensional medical treatments. Compared to waitlist control, CBT-P produces small to moderate effects on pain, disability, mood, and catastrophizing at post-treatment. However, compared to active controls, improvements are only seen in degree of disability and catastrophizing, not pain or mood. The American Psychological Association (1995 Task force), the American Pain Society (APS Practice Guideline for the Management of Fibromyalgia Syndrome), and the International Association for the Study of Pain (IASP Core Curriculum) have all endorsed the treatment as empirically supported and standard of care for a variety of chronic pain conditions. Exciting new research suggests that treatment that targets not only pain, but also its stress related correlates may produce positive changes in structural or functional changes in brain regions associated with central sensitization, thereby attenuating it. While these findings are exciting, they are preliminary in nature. More research is needed to determine and establish the potential of such treatment to produce long term reversal of central sensitization.
Sleep Disturbance and Chronic Pain: Interactions and Interventions
Michael V. Vitiello, PhD. University of Washington, Seattle, WA

Osteoarthritis (OA), which affects 50% of older adults, is one of the most common comorbidities associated with poor sleep. More than half of OA sufferers report pain during the night and arthritis pain is one of the most common factors associated with sleep disturbance. Both insomnia and pain adversely affect function, mood, and cognition, and their healthcare costs are substantial. There is a growing body of literature indicating that poor sleep is associated with increased pain threshold and next-day pain. A recent systematic review concluded that sleep disturbance is a stronger predictor for the development and maintenance of chronic pain than the reverse suggesting that improved sleep in chronic pain populations may improve pain outcomes. Cognitive behavioral therapy for insomnia (CBT-I) is a well-established, evidence-based treatment with positive long-term effects. CBT-I is efficacious in populations with a variety of comorbid medical conditions, including chronic pain. Several trials evaluating CBT-I in pain populations have reported positive sleep outcomes, but they have shown mixed benefits on pain. Unfortunately, these studies have suffered from methodological limitations that make it difficult to draw firm conclusions from their results. We recently completed a large RCT (Lifestyles) of older adults with comorbid OA pain and insomnia. Lifestyles had notable strengths compared to earlier trials; a large population-based sample (n = 367), broad eligibility criteria, treatment delivery in a primary care setting, very low subject attrition, and a highly credible and accepted attention control. Primary analyses found that across 2 and 9 months a combination CBT for pain and insomnia (CBT-PI) was associated with more favorable outcomes for insomnia severity than either CBT for pain alone (CBT-P) or control. However, at 18 months benefits were non-significant for all treatment arms. Post-hoc analyses of participants with greater baseline insomnia and pain severity showed significant reductions in pain for CBT-PI compared to CBT-P, and moderate, albeit non-significant treatment effects for insomnia severity and sleep efficiency in the CBT-PI group. Further, although effect sizes for sleep and pain were attenuated over time, at 18 months they were greater for both outcomes for CBT-PI compared to the other two treatment arms. This pattern was consistent with the a priori hypothesis that improving sleep could improve pain. The failure to find statistically significant and sustained improvements may have resulted from trial limitations. First there was considerable screening to baseline regression to the mean in both insomnia and pain severity scores. Second there was greater than planned for intraclass correlations of pain and sleep because of group-based interventions, which reduced the effective sample size of the trial. Given these unanticipated limitations, it is possible that Lifestyles was unable to detect clinically meaningful benefits of CBT-PI for sleep and pain outcomes, particularly among the patients with less severe insomnia at baseline. Consequently, a secondary “Improver” analysis was conducted testing the hypotheses that short-term (2-month) improvements in insomnia symptoms (regardless of treatment) predict long-term benefits in sleep, pain, and fatigue outcomes at 9 and 18 months. Lifestyles participants with clinically significant improvement in insomnia symptom severity from baseline to 2 months (regardless of treatment) showed sustained beneficial sleep outcomes on multiple measures of self-reported sleep quality at both 9 and 18 months, while Non-Improvers did not. These initial and sustained improvements in sleep quality were associated with clinically significant long-term improvements in pain severity, arthritis symptoms and fatigue. A parallel analysis found that short-term improvements in pain severity predicted long-term reductions in pain severity, arthritis symptoms, and depression, but only modest and inconsistent improvements in sleep outcomes. Overall, the results of the Lifestyles trial support the hypothesis that successful treatment of sleep disturbance in pain populations with co-morbid insomnia may yield benefits for reduced pain over the long-term, contingent on achieving robust and sustained improvements in sleep. Supported by PHS grant AG031126.
Thyroid Hormone Disorders at Midlife and Beyond: Detection and Management. Too little?
Cynthia A. Stuenkel, MD, NCMP. University of California, San Diego, School of Medicine, La Jolla, CA

Thyroid disorders are one of the most common endocrinopathies in women. Thyroid stimulating hormone (TSH) level was found to be outside the normal range in almost 10 percent of SWAN participants (the Study of Women Across the Nation followed over 3,000 multiethnic women through the menopause transition). Expert guidelines do not agree on screening recommendations for all women, but most do agree that aggressive case-finding in midlife women makes sense. Hypothyroidism, most often due to Hashimoto's thyroiditis, is the most common thyroid disorder in women. Symptoms—including fatigue, dry skin, leg cramps, voice change, constipation, and heavier, longer menstrual cycles—could be confused with those of the menopause transition. Laboratory abnormalities such as increased LDL cholesterol or triglyceride levels may provide another clue. The diagnosis of hypothyroidism depends upon an elevated TSH level (usually > 10 mIU/L) and confirmation of low free T4 level. Antithyperoxidase antibodies (TPOAb) should be measured and are often positive. Patients with overt hypothyroidism merit replacement therapy with synthetic thyroxine (levothyroxine), usually starting with doses of 50 to 100 micrograms per day, less if the patient has a history of coronary heart disease (CHD). Thyroxine replacement therapy is titrated by 12.5 to 25 micrograms every six to eight weeks, depending upon the TSH response, with TSH normalization the goal of therapy. Taking thyroid hormone with food or calcium, vitamins, or iron supplements may interfere with thyroxine absorption. Some patients take their daily dose with water 30 to 60 minutes before breakfast; others prefer taking it 3 to 4 hours after the day’s last meal. Mild elevation of TSH with normal FT4 might be consistent with a diagnosis of ‘subclinical’ hypothyroidism. This diagnosis can be challenging as normal TSH levels increase with age and minimal TSH elevations at any age can be transient. The TSH should be rechecked in 3 to 6 months to see if TSH elevation persists above the normal range before considering treatment. Some observational studies link subclinical hypothyroidism with increased risk of CHD, heart failure, and mortality, although clinical trials demonstrating benefit of treating subclinical hypothyroidism are lacking. If the patient has a persistent TSH between 4.5 and 10 mIU/L, and symptoms of hypothyroidism or evidence of cardiovascular disease, heart failure, or cardiovascular risk factors, expert guidelines recommend treatment consideration. Subclinical hypothyroidism does not require full replacement doses—often 25 to 75 micrograms will suffice. Once the TSH falls into the normal range, monitor every 6 to 12 months taking care not to overtreat and cause iatrogenic subclinical hyperthyroidism. In summary, thyroid disorders are common in women, increase with age, and can be associated with significant symptoms and morbidity. Maintaining a high index of suspicion will facilitate identification and treatment of appropriate women.
Thyroid Hormone Disorders at Midlife and Beyond: Detection and Management. Too much?
Susan J. Mandel, MD, MPH. University of Pennsylvania, Philadelphia, PA

Thyrotoxicosis, a disorder of excess thyroid hormone, disturbs almost every physiologic system by either genomic or nongenomic effects. The diagnosis is made by a suppressed serum TSH and either normal (subclinical) or elevated (overt) thyroid hormone levels. It is more common in women than men, and the incidence increases with age. Between 0.5-1% of adults have overt hyperthyroidism and subclinical hyperthyroidism is identified more frequently in ~2%. In addition, a low but detectable serum TSH level with normal thyroid hormone concentrations may resolve spontaneously on repeat testing so the diagnosis of subclinical hyperthyroidism should only be made when TSH suppression persists. Overall the most common cause of hyperthyroidism is Graves’ disease. However in the elderly subclinical hyperthyroidism is most often associated with toxic nodular goiter. Symptomatology associated with hyperthyroidism correlates with the degree of the thyroid hormone elevation. Common systemic manifestations include a rapid pulse rate with an elevated systolic BP, warm moist skin, a stare or lid lag, dyspnea on exertion, proximal muscle weakness and decreased exercise tolerance, insomnia, increased anxiety or moodiness, tremor, weight loss and hyperdefecation. However, in the elderly, the adrenergic symptoms caused by thyroid hormone excess can be masked and weight loss may be the only presenting symptom (apathetic hyperthyroidism). Generally, cardiovascular signs predominate and new onset atrial fibrillation may occur in up to 8% of patients within one month of the diagnosis of overt hyperthyroidism, with a higher risk in older patients and those with pre-existing cardiovascular disease. Large epidemiologic studies also report an association between subclinical hyperthyroidism and atrial fibrillation, albeit weaker than that with overt hyperthyroidism. Bone loss occurs in hyperthyroid postmenopausal women, more at cortical than trabecular sites. In one study, women over age 65 with serum TSH levels <0.1mIU/L followed for only 4 years had an increased risk for both hip and vertebral fractures. However, studies evaluating sequential changes in bone density with treatment of hyperthyroidism report variable results. Subclinical hyperthyroidism, whether endogenous or due to overtreatment with levothyroxine (LT4) for hypothyroidism, is associated with increased bone resorption and reduced bone density, but no increase in fracture rate has been reported. The treatment options for Graves’ disease include antithyroid drugs (ATD), radioiodine therapy (RAI), or surgery and treatment choice varies geographically. Historically, the preference was for radioiodine in the United States, but recent data document a rise in antithyroid drug prescriptions indicating a shift in therapy recommendation. The objective of ATD therapy is to induce remission, which is more likely after a 12-18 month course of therapy, whereas the aim of RAI is to ablate the thyroid, resulting in hypothyroidism and LT4 therapy. Treatment choice should be targeted to the individual patient and should consider the likelihood of remission, presence of other medical comorbidities, and patient preference. The main therapies for toxic multinodular goiter are RAI or surgery (ATD does not cause remission), and the choice must take into account goiter size, age, comorbidities and patient preference. Although overt hyperthyroidism merits treatment, treatment of subclinical hyperthyroidism is controversial because no controlled trials to show benefit have been performed. The 2011 American Thyroid Association Guidelines panel strongly recommends treatment of subclinical hyperthyroidism when the TSH is <0.1mIU/L in patients >65 years of age, and in those with cardiac risk factors, heart disease, osteoporosis, or hyperthyroid symptoms. When the TSH is >0.1mIU/L but below the reference lower limit, treatment should be considered for those 65 and older and those with cardiac disease.
Over-diagnosed: Making People Sick in the Pursuit of Health

H. Gilbert Welch, MD, MPH. Geisel School of Medicine at Dartmouth, Hanover, NH

Over the past several decades, there has been a growing enthusiasm for early diagnosis—engaging many physicians in a systematic search for abnormalities in people who are well. While most consider only the potential benefits, in this talk, Dr Welch exposes the often-ignored harm: overdiagnosis. Diagnoses of a great many conditions, including high blood pressure, osteoporosis, diabetes, and even cancer, have skyrocketed over the last few decades, yet many of the individuals given these diagnoses are not destined to ever develop symptoms (or die) from their condition. They are overdiagnosed. And overdiagnosed patients, Dr Welch points out, cannot benefit from treatment—since there is nothing to fix. But they can be harmed. Understanding the trade-offs involved is critical so that health care systems don’t further narrow the definition of normal and—ironically—turn more and more people into patients.
Clinical Implications of Pelvic Floor Dysfunction  
Andrew I. Sokol, MD. Georgetown University School of Medicine, Washington, DC

Pelvic floor dysfunction (PFD) encompasses an array of symptoms, including pelvic organ prolapse (POP), urinary and fecal incontinence, pain, and dyspareunia. The reported prevalence is up to 50%, and recent data suggest a 20% lifetime risk of surgery for either POP or urinary incontinence. POP occurs with descent of one or more pelvic structures: the uterus and/or cervix, bowel, bladder, or rectum. This condition affects more than 3 million in the United States and it is estimated that this number will approach 5 million by 2050. Vaginal childbirth remains the most important risk factor for the development of POP, while age, weight, chronic constipation, and genetics also play roles. While, these disorders are rarely life threatening, they cause significant distress, financial burden and suffering. Women with POP present with a variety of complaints including vaginal bulging or protrusion, bladder, bowel, and sexual dysfunction. However, the one symptom that is almost consistently acknowledged by patients with advanced POP is the presence of a vaginal bulge, while other symptoms attributed to POP have weak to moderate correlations with worsening pelvic organ support. POP not only affects women’s physical well being, but also has important psychological ramifications and often significantly degrades women’s quality of life. Women with advanced POP have decreased generic and condition-specific health-related quality of life (HRQOL) compared to women with normal vaginal support. The prevalence of urinary incontinence in adult women has been estimated to be between 10-40%, and is considered severe in approximately 3-17%. Broadly, UI can be divided into stress urinary incontinence, urgency incontinence, and mixed incontinence. The etiology of UI is multifactorial; risk factors include age, pregnancy, vaginal delivery, menopause, hysterectomy, obesity, urinary tract infections, functional and/or cognitive impairment, chronic cough, and constipation. These are potentially debilitating social problems with significant cost implications to the individuals and the healthcare service estimated in billions of dollars in the United States. Six percent of admissions to nursing homes are attributable to UI. In women being evaluated for POP, up to 73% report urinary incontinence, 86% report urinary urgency and/or frequency, 34-62% report voiding dysfunction and 31% complain of fecal incontinence. UI symptoms can range from mild to debilitating, sometimes imposing significant lifestyle restrictions. Pelvic floor disorders are a multidimensional phenomenon and “success” of treatment is often difficult to define. Many studies evaluating the treatment of POP have focused on anatomic success without considering other important areas such as symptoms, quality of life, or socioeconomic outcomes. For an individual patient, the most important outcome of a surgical procedure is the relief of her symptoms and improvement in her quality of life. For these reasons, it is recommended that investigators describe the impact of treatment on HRQOL as well as sexual function.
Plenary Symposium 9

Pelvic Floor: Function and Dysfunction
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Abstract Not Received from Speaker

Management of Incontinence and Pelvic Floor Dysfunction
Marsha K. Guess, MSc, MD
Potential Factors Contributing to Weight Gain in Midlife
Wendy M. Kohrt, PhD. University of Colorado, Aurora, CO

The question of whether the menopause transition disrupts energy balance in a manner that promotes weight gain remains controversial. Because the transition is a process that can occur over several years, it is challenging to isolate the independent effects of the menopause on body weight regulation from those of aging. The influence of ovarian hormones on body weight and adiposity has been evaluated using a variety of research approaches (cross-sectional comparisons of pre- and postmenopausal women, prospective observations across the menopause, suppression of ovarian hormones in premenopausal women, hormone therapy in postmenopausal women), but the findings are not consistent. However, compelling evidence from basic and preclinical studies indicates that the loss of ovarian hormones, and specifically estradiol, has a marked effect on bioenergetics. Most notably, removal of the effects of estrogens through either receptor deletion or ovariectomy results in a profound decline in spontaneous physical activity. In ovariectomized animals, this can be prevented or reversed with estradiol treatment. Whether the loss of ovarian hormones exerts a similar effect on physical activity in women has received little attention. Evidence will be presented that the pharmacologic suppression of ovarian hormones in women causes a decrease in total energy expenditure that is attributable to both a decrease in physical activity and a decrease in metabolic rate. If similar changes occur as a result of the menopausal loss of ovarian hormones, the prevention of weight gain in midlife will require appropriate compensatory behaviors.
In an “obesogenic” environment characterized by large portions of palatable, inexpensive, energy-dense foods, finding ways to encourage women to eat appropriate amounts and avoid weight gain is challenging. Much of the emphasis in the dietary management of obesity has been on how changing the proportion of macronutrients affects energy intake and body weight. Popular diets urge consumers to eat less fat or carbohydrates or to increase their protein intake. The results of randomized controlled trials aimed at determining whether such advice is effective have been mixed. Even when a particular macronutrient was associated with the amount of weight lost during the active treatment phase, significant differences across diets were not sustained during the maintenance phase. With similar results coming from several recent large trials, health policy recommendations for weight management have shifted away from macronutrient-based advice to a food-based approach emphasizing portion control, energy density, and energy intake. Effective dietary therapy for weight management should include strategies that match energy intake to energy needs while providing optimal nutrition and controlling hunger. Studies of the influence of foods on hunger and satiety have suggested that a diet reduced in energy density and with adequate amounts of fiber and protein provides an effective and nutritionally adequate approach. Foods with a low energy density (ED) provide less energy relative to their weight (kcal/gram) than foods with a high ED. Therefore, for the same number of calories, a larger more satiating portion can be consumed when the ED is reduced. An evidence-based review by the 2010 US Dietary Guidelines Advisory Committee concluded “that strong and consistent evidence in adults indicates that dietary patterns relatively low in energy density improve weight loss and weight maintenance.” Although an understanding of the role that ED plays in energy balance is quite recent, there have been a number of relevant laboratory-based studies, longitudinal population-based studies, and randomized controlled trials to inform this relationship. These studies indicate that people eat a fairly consistent amount (weight or volume) of food on a day-to-day basis so that reductions in ED are associated with a spontaneous reduction in energy intake. A low-ED diet is not restrictive and can be tailored to accommodate individual preferences. Decreases in energy intake can be achieved by swapping higher-ED foods for lower-ED foods, incorporating lower-ED ingredients into mixed dishes to reduce ED, and “filling up first” with a low-ED first course. Since a range of eating patterns can be reduced in ED, this type of diet has wide applicability and thus can be a key component of a lifestyle that encourages a healthy well-balanced diet for weight management. The presentation will summarize evidence related to the influence of ED on satiety, energy intake, and body weight and will provide practical, achievable approaches for using ED to prevent weight gain and promote health.
Behavioral and Medical Approaches to Prevent Weight Gain and Promote Healthy Nutrition Habits in Midlife Women
Scott Kahan, MD, MPH. 1George Washington University School fo Medicine, Washington, DC; 2Johns Hopkins Bloomberg School of Public Health, Washington, DC

This session will discuss behavioral and medical approaches to the prevention and treatment of midlife weight gain in women. Topics to be discussed include patient assessment and stratification, supportive treatments, behavioral therapy strategies, and pharmacotherapy options. Evidence-based behavioral strategies focused on multimodal interventions will be reviewed. Monotherapy and combination pharmacotherapy will be discussed.