an adverse experience. This pilot trial sought to quantify the effect of RLX on hot flashes compared to placebo. Paroxetine (PAX), a selective serotonin reuptake inhibitor (SSRI) approved for treatment of depression and anxiety, can reduce hot flashes via a non-hormonal mechanism and was included as a positive control. This pilot trial could be used to determine the sample size for future studies comparing the hot flash effects of RLX with other agents. **Design:** 42 healthy postmenopausal women were randomized in a 3:3:1 ratio to receive either 60 mg RLX, placebo (PBO) or 20 mg PAX (double dummy design) for 12 weeks. Eligible subjects were recently postmenopausal women ≥40 years, who had their last menstrual period between 3 months and 5 years prior to screening, and who had between 5 and 50 hot flashes per week as recorded in the study diary during the screening period. The incidence of hot flashes and their severity (using a 4-point severity) were recorded using a paper diary for 5 one week periods during the study as follows: immediately after the screening visit to determine eligibility, the week prior to randomization, and on treatment weeks 4, 8 and 12. Sleep was assessed at the end of each weekly hot flash diary using the Sleep Problems Scale Questionnaire. To evaluate the primary hypothesis of the effect of RLX versus PBO on the change from baseline to week 12 for weekly hot flash frequency, an ANOVA was performed with factors for strata (≤22 and >22 baseline hot flashes per week) and treatment group. Treatment differences in the all-patients treated population were estimated and least squares means and 95% confidence intervals (CIs) calculated. This study was conducted in the United States and approved by independent review boards. **Results:** 41 patients completed the study and were included in the analysis. Baseline values for frequency and severity were generally similar between groups (29-30 hot flashes/week, 52-57 weekly severity score). The change in frequency and severity from baseline to week 12 is shown in the table. The difference between placebo and raloxifene was not statistically significant for either measure. There was no significant between group differences for the Sleep Problems Scale. All treatments were well tolerated. **Conclusion:** In this study, RLX treatment resulted in a small decrease in hot flash frequency and severity score, instead of an expected increase. However, this decrease was numerically less than the decrease in patients treated with PBO, and may be attributed to a general tendency for decreased hot flashes in clinical studies, illustrated by the large PBO effect. The absence of a statistical significant difference between RLX and PBO should be interpreted with caution due to the small size of the study. The large effect of PBO observed (~37% reduction in weekly frequency) is consistent with other hot flash studies. PAX was included as a positive control and significantly reduced hot flash frequency and severity score compared to baseline. Although the effect of PAX should be interpreted with caution due to the small sample size, the effect is consistent with other studies of this therapy. Based on this study, an estimated sample size of 64 patients per group would be needed to have 80% power in a study to demonstrate a difference in hot flash frequency of 20% between raloxifene and another placebo-like agent with regard to hot flashes.

	PBO (N=18)	RLX (N=17)	PAX (N=6)
Hot Flash Frequency (adjusted mean (SE) % decrease baseline to week 12)	-37.4 (11.6)	-14.2 (11.6) (a)	-49.8 (19.1)
Hot Flash Severity Score (adjusted mean (SE) % decrease baseline to week 12)	-39.9 (14.3)	-9.6 (14.4) (b)	-36.6 (23.8)

a: Frequency: RLX vs. PBO p=0.152
b: Severity: RLX vs. PBO p=0.133

LB-5.

Current Opinions of American (New York City) Gynecologists on Indications and Contraindications for Hormone Therapy

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Objective: Historically, the American College of Obstetricians and Gynecologists (ACOG) recommended hormone therapy (HT) for vasomotor symptoms of menopause and advised against HT for those with a history of breast cancer, thromboembolism, and menorrhagia. Subsequent data from the Women's Health Initiative (WHI) suggested that HT increased risk for cardiovascular and Alzheimer's disease. These findings precipitously reduced global HT prescriptions. However, the WHI conclusions continue to be debated as they contradict the results of numerous antecedent observational studies. In particular, the difference in occurrence of illnesses between the treatment and placebo groups was not statistically significant. The mean age (63.3 years) of WHI participants was older than the age at which most women begin HT. Finally, women were offered conjugated equine estrogen and extrapolation to use of unconjugated estrogens may be flawed. As a result of the controversy regarding the WHI, physicians remain conflicted about indications and contraindications of HT use. Even so, several post-WHI European studies found that physicians have adopted WHI recommendations in their prescribing practices. Unconjugated estrogens are now more preferentially prescribed. Finally, the majority (96.7%) of those surveyed felt that another study was needed to definitively answer the questions of when HT is to be used in a clinical setting. We wished to investigate American gynecologists' reported prescribing practices with regard to the indications and contraindications for HT use in New York City and the surrounding metropolitan area, given the ongoing controversy regarding HT benefits. **Design:** A questionnaire concerning attitudes, management strategies, and use of HT was mailed out to eligible physicians in New York City. All 1,797 board-certified obstetrician-gynecologists in New York City and the surrounding metropolitan area, including Long Island and Westchester County were invited to complete the questionnaire. Demographic data was analyzed using chi-square statistics. Logistic regression was used to analyze differences in prescribing patterns, controlling for confounding variables (SPSS). **Results:** We received completed questionnaires from 12% (208/1,797) of NYC obstetrician-gynecologists. In the absence of contraindications, 18% (37/205) of respondents felt that all women should be offered HT. Prescription practices largely conformed with the findings from the WHI study (Table). Benign menorrhagia was an area of uncertainty, with 30% (60/197) of gynecologists categorizing it as an indication, 50% (99/197) as a contraindication, and 19% (38/197) finding it irrelevant in their clinical paradigm. For climacteric symptoms, most (71%; 132/186) recommended a HT course of <5 years and a minority (6%; 11/186) advocated long-term use. For osteoporosis prophylaxis, 37% (57/153) recommended using HT for <5 years and 25% (38/153) recommended long-term use. Women's preferences continue to dictate prescribing practices, with nearly 90% of physicians prescribing HT to those women who strongly wished to be on HT. **Conclusion:** The prescribing practices of NYC obstetrician-gynecologists are largely in line with the findings from the WHI study recommendations, despite the ongoing controversy surrounding the validity of those conclusions.

NY gynecologists self report of prescription practices of HT*

Symptoms/Conditions	Indicated N (%)	Contraindicated N (%)	Irrelevant N (%)
Hot flashes and/or sweats	204 (100%)	0	0
Mood swings	189 (92%)	0	16 (8%)
Vaginal atrophy	196 (97%)	0	7 (3%)
Benign menorrhagia	60 (30%)	99 (50%)	38 (19%)
History of venous thromboembolism	2 (1%)	204 (99%)	0
History of acute myocardial infarction	2 (1%)	202 (98%)	1 (0.5%)
Symptomatic ischemic cardiac disease	2 (1%)	202 (98%)	2 (1%)
History of cerebrovascular accident	1 (0.5%)	204 (99%)	1 (0.5%)
Family history of breast cancer	13 (6%)	141 (69%)	52 (25%)
History of radically treated breast cancer	5 (2%)	198 (96%)	3 (2%)
History of radically treated endometrial cancer	5 (2%)	179 (87%)	22 (11%)
Patient intensely desires postmenopausal HT	180 (88%)	3 (1%)	21 (10%)
Patient strongly rejects postmenopausal HT	16 (8%)	163 (80%)	24 (12%)

*** Some questions were left unanswered, with lower totals in subgroups.**

LB-6.

Gynecologists' beliefs regarding hormone therapy for Alzheimer's dementia and depression

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Objective: We wished to evaluate New York City gynecologists' views on the efficacy of hormone therapy (HT) in preventing Alzheimer's dementia (AD) and alleviating depression. Early results of epidemiologic studies on HT use in preventing and treating AD have been conflicting. In 2002, the Women's Health Initiative Memory Study (WHIMS) found that conjugated estrogen plus progestin did not prevent mild cognitive impairment and increased the risk for probable dementia in postmenopausal women. The estrogen plus progestin arm of study was halted prematurely due to adverse cardiovascular and cancer risks in the parent Women's Health Initiative (WHI) study. The WHI and WHIMS findings have been debated as they differ from the results of past observational studies and lacked statistical significance, meeting pre-determined end points instead. Additionally, some WHIMS participants were noncompliant with their therapy. Nevertheless, these studies have affected prescribing practices world-wide, with a large decrease in the number of HT prescriptions. Recent findings from observational studies continue to reveal contradictory conclusions as well as variable effects of HT among older women, indicating a need for an additional study to unquestionably determine the effects of HT use when used in a clinical setting. Similarly, the efficacy of HT for treating depression in the menopausal transition is unclear. Variation in effects of HT use on depression symptoms are likely due to the complexity of the mechanisms involved and differences in response among women users. We wished to investigate American gynecologists' reported prescribing practices of HT use with regards to AD and depression in New York City and the surrounding metropolitan area, given the ongoing controversy regarding HT benefits in these conditions. **Design:** A questionnaire concerning attitudes, management strategies, and use of HT was mailed out to eligible physicians in New York City. Participants: All 1,797 board-certified obstetrician-gynecologists in New York City and the surrounding metropolitan area, including Long Island and Westchester County were invited to complete the questionnaire. Measurements: Demographic data was analyzed using chi-square and binomial statistics. Logistic regression was used to analyze differences in prescribing patterns, controlling for confounding variables (SPSS). **Results:** We received completed questionnaires from 12% (208/1,797) of NYC obstetrician-gynecologists. About a third of respondents felt HT use prevented AD (29%; 60/205), another third felt it was not useful in preventing AD (37%; 75/205) and another third were unsure (34%; 70/205). The beliefs of gynecologists do not appear to be greatly influenced by the WHIMS results with regard to the possibility of HT use as a risk factor for AD. Most gynecologists (69%; 141/204) felt that HT use can alleviate symptoms of depression ($p<0.05$). **Conclusion:** Despite the conclusions of the WHIMS, gynecologists remain divided in their attitudes towards HT as a risk factor for AD. The majority of gynecologists believe that HT use could alleviate depression.

NY gynecologists self report of opinions about HT*

Opinions about HT	Agree N (%)	Disagree N (%)	Don't Know N (%)	P value
Prevents Alzheimer's dementia	60 (29%)	75 (37%)	70 (34%)	NS
Can alleviate depression	141 (69%)	21 (10%)	42 (21%)	<0.05

*** Some questions were left unanswered, with lower totals in subgroups.**

LB-7.

Longitudinal Examination of Exercise and Self-Esteem in Middle-Aged Women

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Objective: To examine prospectively the relationships among the facets of multidimensional self-esteem and physical activity in middle-aged women using the Exercise and Self-Esteem Model (EXSEM: Sonstroem et al., 1994). **Design:** Middle-aged women (N =143) previously enrolled in a randomized controlled exercise trial completed measures of multidimensional self-esteem, physical activity, and self-efficacy at the end of the 4-month exercise trial and again two years later. To examine the EXSEM pathways, a longitudinal panel analysis was conducted within a structural equation modeling framework using Mplus Version 5.1. **Results:** The results indicated that across the 2-year period, enhancements in physical activity (PA) (β=.28, p<.05) and self-efficacy (β=.35, p<.05) and reductions in body mass index (BMI) (β=-.18, p<.05) were associated with improved subdomain esteem relative to physical condition, and reductions in BMI (β=-.31, p<.05) were associated with improved subdomain esteem relative body attractiveness. Over time, the effects of PA, self-efficacy, and BMI on changes in physical self-esteem and global esteem were mediated by changes in physical condition and body attractiveness subdomain esteem. Women reporting greater levels of PA, self-efficacy, and with lower BMI, also reported greater enhancements in subdomain self-esteem. **Conclusion:** The results of this longitudinal analysis support the hierarchical and multidimensional structure of self-esteem and indicate that middle-aged women may enhance condition and body-related physical self-esteem by participating in physical activity, increasing their self-efficacy, and maintaining healthy BMI levels.

LB-8.

Menopausal status and diurnal blood pressure variation in middle-aged Mexican-American Women

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Objective: Diurnal blood pressure (BP) variation has been shown to predict CVD morbidity and mortality with non-dipping nocturnal BP (less than 10% variation from daytime mean value) or over-dipping nocturnal BP (20% or greater variation from daytime mean value) being associated with increased CVD risk. The mechanisms underlying diurnal BP variation are varied and include age, ethnicity, medical conditions, and lifestyle factors. Postmenopausal status has been associated with non-dipping nocturnal BP in African-American and Caucasian women. To our knowledge, no studies to date have examined the association between menopausal status and over-dipping BP. The purpose of the current study was to examine the relationship between menopausal status and the prevalence of non-dipping and over-dipping nocturnal BP in a group of middle-aged Mexican American women. **Design:** 247 women, aged 40-65, were randomly recruited from communities near the San Diego/Mexico border. Exclusionary criteria included hypertension (stage 3 and above) or antihypertensive treatment, history of cardiovascular disease, diabetes, kidney disease, or other serious illness, pregnancy, and taking medications with autonomic effects. Menopausal status was assessed via self-report and women were categorized into the following groups: premenopause (regular menstrual cycle over past twelve months), perimenopause (inconsistent menstruation over past twelve months), and postmenopause (no menstruation within the past 12 months). Ambulatory blood pressure was monitored during a 36 hour period within a typical work week. Based on participant's self-reported sleep/wake schedule, the monitor was programmed to take readings every 30 minutes during waking hours and 60 minutes during sleep. Participants were instructed to maintain a normal level of activity. All BP readings were reviewed and out of range values were identified and excluded from analyses. Average blood pressure during wake and sleep (based on self-reported actual sleep times) was estimated for each person via multi-level modeling analyses, to accommodate the nested structure of the data. Average daytime values accounted for momentary fluctuations in posture, temperature, physical activity, and substance and/or food consumption assessed via electronic diary. A percent dipping score for systolic (SBP) and diastolic (DBP) blood pressure was subsequently calculated (wake BP-sleep BP/wake BP) and used to categorize women into groups based on the following criteria: non-dippers (< 10% variation) and over-dippers (>20% variation). **Results:** On average, women were 49.51 years of age (SD = 6.64), 72.8% were born in Mexico, and 68.6 % reported an education level of high school or higher. Analyses regressing the prevalence of non-dipping BP on menopausal status indicated that stage of menopausal transition was not associated with the prevalence of non-dipping nocturnal SBP and DBP (all ps >.10). However, after accounting for age, recent use of hormonal replacement therapy, education, income, nativity, physical activity level, and BMI, postmenopausal women displayed greater odds of over-dipping nocturnal SBP as compared to their premeopausal [OR (95%CI) = 4.85(1.05, 22.5), p <.05] and perimenopausal [OR (95%CI) = 4.33(1.01, 18.76), p = .05] counterparts. Menopausal status was not significantly related to prevalence of over-dipping nocturnal DBP. **Conclusion:** In a sample of middle-aged Mexican-American women, menopausal status was associated with diurnal blood pressure variation with the prevalence of over-dipping nocturnal SBP being higher among postmenopausal women compared to other groups. Contrary to previous findings, menopausal status was not associated with the non-dipping nocturnal BP in this sample. These findings provide preliminary evidence for the significance of menopausal status in understanding diurnal blood pressure variation in middle-aged Mexican-American women. Over-dipping nocturnal BP is associated with cardiovascular events potentially due to hypoperfusion during sleep or an exaggerated morning surge of BP. Thus, over-dipping may represent one manifestation of menopause's effect on CVD risk.

LB-9.

Is There Any Role for Oral Estrogen Therapy? The Case for Transdermal Therapy as of 2009

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Objective: To provide information comparing oral and transdermal(TD) hormone therapy(HT)to test the hypothesis that TD estrogens are superior to oral HT. **Design:** Review of the literature **Results:** Characteristics that have an impact on estrogen function and risk include estrogen type,dose,route of administration, and certain patient risk factors. The most physiologic form of estrogen is TD estradiol-17beta(E2),the estrogen available in all patch, cream, gel, vaginal and spray applications. TD delivery avoids the first-pass effect, resulting in more stable serum E2 levels without supraphysiologic concentrations in the liver. Recent epidemiological data support the concept of an improved risk-benefit ratio with TD when compared to oral HT. These are broken down into effects on lipids; cardiovascular, inflammatory and thrombotic effects, sexual effects, effects on insulin resistance, IGF, and on metabolic syndrome(MBS), and effects on weight. Many of these effects are secondary to oral estrogen's "first-pass" effect on the liver, releasing increased amounts of CRP, IGF-1, clotting factors, and the 3 hormone binding proteins, sex hormone binding globulin (SHBG); thyroid binding globulin and cortisol binding globulin. Compared with oral estrogens, TD E2 exerts minimal effects on total and free concentrations of testosterone, T4, cortisol, and their binding proteins. Studies have shown that oral HT beneficially effects lipid profiles of postmenopausal women, resulting in increased HDL-C and lowered LDL-C, but increasing triglyceride levels (an independent risk factor for stroke). TD HT appears to have a favorable effect on triglyceride levels while maintaining, albeit to a slightly lesser degree, oral HT's beneficial effects on LDL and HDL-C. In addition to hormone binding globulins, clotting factors also are produced by the liver and are stimulated by the high estrogen levels needed to overcome first-pass metabolism. Oral estrogen appears to affect the activity of platelets and plasma coagulation factors, both key factors to clotting and thrombosis. WHI data suggest that orally administered estrogen/progestin HT given in women 50 to 79 years old was associated with a significant increase in coronary heart disease, thrombogenic stroke, and venous thromboembolism (VTE). Similar increases for stroke and VTE were found for estrogen only. Transdermally administered estrogen does not appear to be associated with the same cardiovascular, stroke and VTE risks as oral HT Biochemically, oral estrogen appears to increase inflammatory proteins and suppress their inhibitors, largely an hepatic effect influenced by dose and route of administration. Oral estrogen causes an increase in CRP levels, while TD E2 has been shown to have no effect in CRP. In obese postmenopausal women with MBS and who have increased CV risk, TD therapy did not effect the circulating MMP-9-to-TIMP-1 ratio, whereas this was increased with oral HT. These metabolic changes in the presence of significant atherosclerosis may have the ability to cause coronary artery plaque instability and may lead to plaque rupture and coronary occlusion. Oral HT of any type has been shown to increase SHBG by greater than 100%. However, studies have verified that TD E2 has little or no effect on SHBG levels. The lower SHBG and higher free testosterone levels associated with TD therapy appears to have clinical relevance, translating into improved orgasmic and sexual vigor scores. Several studies have been performed investigating differences in body composition comparing orally versus transdermally administered estrogen; most of these studies show an improved lean:fat mass ratio for TD estrogen. **Conclusion:** Significant differences exist between oral and TD HT in terms of hormonal bioavailability with significant implications in clinical efficacy, potential side effects, and risk profile of the different HT options. By avoiding first-pass hepatic metabolism, TD E2 maintains high effectiveness, even at lower doses, with greater tolerability. TD HT has a less pronounced effect on hepatic protein synthesis, such as markers of coagulation and fibrinolysis, while oral HT has more pronounced hyper-coagulant effects and increases synthesis of CRP and fibrinolytic markers. In all domains, TD E2 appears superior to oral therapy.

LB-10.

C - Reactive Protein Immunoassay Performance Characteristics in Sera of the Yucatan Micropig (*Sus scrofa domestica*): CRP Concentrations Differ Significantly with ELISA Manufacturer

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Objective: C- reactive protein (CRP), an acute phase serum protein, has emerged as an important cardiovascular risk biomarker of inflammation for clinical and research applications in people and animal models. Consequently several commercially prepared sandwich-type immunosorbent immunoassays (ELISAs) for both human and porcine serum CRP have become available. The goal of this study is to compare the performance characteristics of three (DSL-human, ICL-porcine, Tridelta-porcine (TRI)) serum assays from different manufacturers in order to validate their use in micropigs utilized in atherosclerosis research studies. **Design:** Sera of thirty-four ovariectomized female micropigs fed an atherogenic diet were assayed using each of the three kits for CRP concentrations under identical laboratory conditions, operator and equipment. Seventeen were dosed with 1.25 mg PO SID conjugated equine estrogens. **Results:** The correlation between the assays was good (r_s = 0.68 for TRI and DSL, r_s = 0.69 for ICL and DSL, and r_s = 0.76 for TRI and ICL) using Spearman rank correlation coefficient ($p < 0.00001$).