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Abstracts of Eighth International Symposium on Osteoporosis: Translating Research into Clinical Practice

POSTER SESSION I (PS1)

PS1.2 ADVERSE DENTAL OUTCOMES ASSOCIATED WITH INTRAVENOUS VERSUS ORAL BISPHOSPHONATE USE IN PATIENTS WITH OSTEOPOROSIS

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Background: Given prior research findings of adverse events with bisphosphonates (BP), the purpose of this study was to determine the association between adverse dental outcomes and intravenous (IV) or oral BP utilization in patients with osteoporosis.
Methods: This analysis utilized a patient-level database of over 55 million lives and 70 US health plans from 2000 to 2006. Patients with a diagnosis of osteoporosis were categorized into cohorts based on BP use: IV, oral, or none. Continuous enrollment for at least 6-months pre- and post-index diagnosis was required. Adverse outcomes were defined as: (1) inflammatory conditions of the jaw, including osteonecrosis; (2) major jaw surgery required due to necrotic or inflammatory conditions; or (3) jaw surgeries required due to malignancies. Propensity-scores and multivariate regression analyses used to determine adjusted odds ratios (OR) for outcomes based upon IV or oral BP use relative to no BP use, controlling for patient demographics, comorbidities, prior dental or oral surgery, physician likelihood of prescribing oral versus IV BPs, and antibiotic, hormonal treatment, or thalidomide use. Subgroup analyses excluding patients using oral corticosteroids were conducted.
Results: Overall, 2,321 patients utilized IV BPs versus 213,364 for oral BPs. IV BPs were associated with significantly higher odds of inflammatory necrosis of the jaw (OR=6.02, 95%CI [3.77–9.53]) and major jaw surgery required due to necrotic or inflammatory conditions (OR=8.67,95%CI [3.77–19.94]) relative to the no BP group. No significant association was observed with oral BPs for any adverse outcome. Subgroup analyses excluding oral corticosteroid use yielded similar findings.
Conclusion: After controlling for numerous demographic and clinical factors, this study indicated that a large and significant association between IV BP utilization and inflammatory conditions of the jaw or major jaw surgery required due to necrotic or inflammatory conditions. While no significant relationship was observed for oral BPs, continued research is warranted to assess the long-term association between BP use and adverse outcomes in patients with osteoporosis.

Multivariate-adjusted odds ratios for study outcomes among osteoporosis patients

	Osteoporosis patients including concomitant oral corticosteroid use		**Osteoporosis patients without concomitant oral corticosteroid use**	
	Intravenous bisphosphonates	**Oral bisphosphonates**	**Intravenous bisphosphonates**	**Oral bisphosphonates**
Inflammatory Necrosis of the Jaw [odds ratio, (95%CI)]	6.02 (3.77–9.53)	1.03 (0.86–1.23)	5.49 (3.21–9.37)	0.99 (0.81–1.20)
Surgery: Necrotic Process [odds ratio, (95%CI)]	8.67 (3.77–19.94)	0.95 (0.63–1.43)	7.74 (2.96–20.27)	0.92 (0.59–1.45)
Surgery: Malignant Process [odds ratio, (95%CI)]	0.49 (0.07–3.48)	0.81 (0.62–1.05)	0.61 (0.09–4.40)	0.86 (0.65–1.14)
Age [mean, years]	63.6	65.6	65.1	65.6
Sex [female, %]	73.3	93.5	75.9	94.5
Sample size [*n*]	2,321	213,364	1,910	196,686
Sample size, propensity-score matched osteoporosis group, no bisphosphonate use [*n*]	423,845	423,842	409,465	409,465

PS1.3 THE EFFECT OF THE WOMEN'S HEALTH INITIATIVE (WHI) STUDY ON BONE HEALTH IN A LARGE HMO IN SOUTHERN CALIFORNIA

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Background: Since the Women's Health Initiative (WHI) findings became available in July 2002, millions of women have discontinued postmenopausal hormone therapy (HT). The objective of this study was to evaluate the association between HT cessation and hip fracture risk in a large HMO in Southern California.
Methods: This was an observational study in a population of 80,956 women aged 60 or older who were on HT at the time the WHI findings were made public. The study groups consisted of women who continued taking HT (HT Continues Group) and those women who stopped taking HT during this period (HT Stops Group). The Kaiser Permanente Electronic Medical Record (EMR) was used to collect data on anti-osteoporosis medications, DEXA scan data, hip fracture occurrences, associated medical problems, and BMI in both study groups.
Results: There was a 35.6% reduction in the hip fracture rate in the HT Continues Group ($p<0.001$). This was in spite of the fact that 30.1% of the HT Stops group were on anti-osteoporosis medications compared with 18.7% of the HT Continues Group (this is a 61.2% higher rate in patients in the HT Stops Group $p<0.001$.)

The HT Stops group also had 63.1% DEXA scans compared with 52.6% in the HT Continues Group ($p<0.001$). The HT Stops group also had 20.0% Osteoporosis by DEXA scans compared with 14.2% in the HT Continues Group ($p<0.001$).
Conclusion: Consistent with the data from the WHI and other studies, the current study showed a 35.6% decrease in the incidence of hip fracture among women currently taking HT relative to women who stopped HT. It has been identified that the protection of received from hormonal use is unmatched by any other medication.

PS1.4 MEASURING THE EFFECTIVENESS OF AN OSTEOPOROSIS DISEASE MANAGEMENT PROGRAM IN AN INTEGRATED HEALTHCARE DELIVERY SYSTEM

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Background: Osteoporosis disease management programs are often implemented without the benefits of an integrated health care delivery system. This leads to inability to adequately identify, risk stratify, treat, and track patients at risk for osteoporosis and subsequent fragility fractures.
Methods: This was a prospective observational study that looked at the effectiveness of a Healthy Bones Program on the osteoporosis disease management of 650,000 patients at a large Health Maintenance Organization (HMO) in Southern California (SCAL) from the years 2002 to 2007 inclusively. An electronic medical record system was used to collect data on these patients that included anti-osteoporosis medication usage, DXA scans, and fragility fractures.
Results: The SCAL Healthy Bones Program was made up of members from a multi-disciplinary team. Since the SCAL Healthy Bones Program was adopted, we have seen our annual DXA scan utilization go from 21,557 a year in 2002 to 78,262 a year in 2007, a 263% increase. The DXA scan utilization in men in 2002 was 1,549 and increased to 15,700 a year by 2007, a 913.6% increase. The annual number of patients on anti-osteoporosis medication went from 33,208 a year in 2002 to 84,155 a year in 2007, a 153.4% increase. The annual number of men on anti-osteoporosis medication in 2002 was 2,663 and increased to 9,310 a year by 2007, a 249.6% increase. There was a large variation in the reduction in the hip fracture rate at our 11 medical centers in SCAL. The reduction in hip fracture rate varied from a 31.0% reduction to a 54.3% reduction. The average reduction of our hip fracture rate was 38.1%. That translated to preventing 970 hip fractures in the year 2007 (2,544 hip fracture were predicted and we had 1,574 hip fractures).
Conclusion: By aggressively identifying and managing patients with osteoporosis we were able to show a 38.1% reduction in the hip fracture rate at our HMO in SCAL. That translated to preventing 970 hip fractures in the year 2007 (2,544 hip fracture were predicted and we had 1,574 hip fractures). Men had the largest increase in osteoporosis disease management from 2002 to 2007.

PS1.5 EFFICACY OF BAZEDOXIFENE IN REDUCING THE INCIDENCE OF NONVERTEBRAL FRACTURES IN POSTMENOPAUSAL OSTEOPOROTIC WOMEN AT HIGHER FRACTURE RISK

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Background: Bazedoxifene has been shown to prevent bone loss and reduce bone turnover in a 2-year study of postmenopausal women at risk for osteoporosis. In a recent phase 3 trial, treatment with bazedoxifene for 3 years effectively reduced the risk of new vertebral fracture relative to placebo in postmenopausal women with osteoporosis. There was no significant effect on nonvertebral fractures (NVFs) in the overall population. Here we report the results of post hoc analyses of NVF incidence among women at higher risk for fracture in that study.

Methods: Generally healthy postmenopausal women (N=7,492; mean age, 66.4 years) with osteoporosis were randomized to daily therapy with bazedoxifene 20 or 40 mg, raloxifene 60 mg, or placebo; all subjects received supplemental elemental calcium (1,000–1,200 mg/day) and vitamin D (400–800 IU/day). Kaplan–Meier estimates of the incidence of NVFs at 36 months were evaluated for the overall population and for subgroups of women at higher fracture risk, based on known skeletal risk factors (low femoral neck [FN] T-score and/or prevalent vertebral fracture).
Results: The overall incidence of NVFs was similar among groups. In a subgroup of women at higher risk for fracture (FN T-score ≤−3.0 and/or ≥1 moderate or ≥2 mild vertebral fractures; n=1,772), NVF rates were 4.9%, 6.5%, 8.4%, and 9.1% with bazedoxifene 20 and 40 mg, raloxifene 60 mg, and placebo, respectively. Bazedoxifene 20 mg significantly reduced NVF incidence relative to placebo and raloxifene 60 mg (50% and 44%, respectively; p<0.05); a similar reduction was observed when NVF data for bazedoxifene 20 and 40 mg were combined (40% relative to placebo; p=0.03). Conversely, there were no significant between-group differences in NVF rates in the lower-risk subgroup (n=5,710). Further evaluation of NVF incidence in subjects with FN T-scores ≤−2.5 or ≤−2.0 and/or ≥1 moderate or ≥2 mild vertebral fractures showed a trend toward NVF risk reduction with bazedoxifene treatment, supporting the robustness of the results. The selection of subjects at higher fracture risk was also supported by Cox regression analyses, which showed that the treatment by risk category interaction was significant with bazedoxifene 20 mg (p=0.025) and was of borderline significance with bazedoxifene 20 and 40 mg combined (p=0.052).
Conclusion: Treatment with bazedoxifene significantly reduced the risk of NVF in postmenopausal osteoporotic women at higher risk for fracture.

PS1.6 ALENDRONATE+VITAMIN D THERAPY OR REFERRED CARE IN OSTEOPOROTIC WOMEN: RATIONALE AND DESIGN, INCLUDING MEASUREMENT OF PHYSICAL FUNCTIONS, FALLS, AND POSSIBLE GENETIC MARKERS

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Aim: Vitamin D is required for bone strength and also acts on muscle function. Vitamin D insufficiency is prevalent, and often overlooked by physicians. A planned study will examine the effects of a single tablet containing the bisphosphonate alendronate 70 mg plus vitamin D_3 5,600 IU (ALN+D) compared with referred care on serum vitamin D, falls, and physical function.
Methods: In an upcoming international, randomized, controlled trial of 6 months with a 6-month extension (under the same treatment assignments), approximately 800 women (≥65 years of age, osteoporotic, at increased risk of falls, with baseline 25(OH)-vitamin D of 8 to 20 ng/mL) will either receive ALN+D weekly or be referred to their primary care physicians (who are not investigators in the trial) for one of the usual osteoporosis therapies. Women in the ALN+D group with ≤1,000 mg daily calcium intake at baseline will receive 500 mg elemental calcium/day. The primary endpoint will be proportion of patients with serum 25(OH)-vitamin D <20 ng/mL. Secondary endpoints will include bone turnover markers. Exploratory endpoints will include the Short Physical Performance Battery (SPPB) and the relationships among genotype, RNA expression, total body composition, and SPPB. Endpoints of the trial extension will include 25(OH)-vitamin D, bone mineral density, and fall event rate. All falls will be reported by patients to their study site. Fall case report forms will include 15 questions concerning detailed description, location, and outcome of the fall. Falls due to fragility, but not due to a syncopic event or external force, will be included for data analysis. Fall case report forms will be adjudicated by an independent committee, blinded to patient-treatment group. Safety will be monitored.
Conclusion: This study may demonstrate relationships among osteoporosis/vitamin D therapy, falls, physical function, and molecular/genetic information.

PS1.7 ALENDRONATE REVERSES THE LOSS OF BONE MINERAL DENSITY AND BONE STRENGTH ASSOCIATED WITH ROSIGLITAZONE IN AGED OVARIECTOMIZED RATS

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Background: Evidence has recently emerged that diabetes treatments targeting peroxisome proliferator-activated receptor-γ (PPARγ), such as rosiglitazone (RSG) and pioglitazone, are associated with an increased risk of fracture. This study was designed to investigate the underlying mechanisms of RSG-associated fracture and to determine if changes in bone parameters associated with RSG could be prevented by combination treatment with an antiresorptive agent.
Methods: Nine-month old Sprague–Dawley rats underwent ovariectomy (OVX) or sham operation. OVX animals were randomized into eight groups of 12 each receiving vehicle, metformin (PO, 300 mg/kg/day), alendronate (SC, 0.03 mg/kg/twice weekly), 17β-estradiol (SC pellet, 0.01 mg), RSG at two different doses (PO, 3 or 10 mg/kg/day), RSG (10 mg/kg/day) +alendronate, or RSG (10 mg/kg/day)+17β-estradiol for 12 weeks. Bone mineral density (BMD), bone mineral content (BMC), and bone turnover markers were measured and biomechanical testing was performed.

Bone densitometry values by DXA/pQCT as percent change from baseline

		OVX		RSG (3 mg/kg/day)		RSG (10 mg/kg/day)		RSG (10 mg/kg/day) +alendronate	
		BMC (*N*=23)	BMD (*N*=23)	BMC (*N*=12)	BMD (*N*=12)	BMC (*N*=24)	BMD (*N*=24)	BMC (*N*=12)	BMD (*N*=12)
Whole body (DXA)	LSMean	5.678	−0.4024	4.016	**−3.0181****	**−1.732*****	**−4.4959*****	5.256	**3.051*****
	SELSM	0.926	0.4501	1.281	0.6231	0.906	0.4406	1.281	0.6231
Lumbar spine (DXA)	LSMean	−2.196	−4.6467	**−12.523*****	**−12.4844*****	**−17.060*****	**−15.3025*****	2.163	**−0.268*****
	SELSM	1.208	0.8623	1.672	1.1938	1.182	0.8442	1.672	1.193
Tibia metaphysis (pQCT, total)	LSMean	−8.658	−11.31	−11.463	**−16.01***	**−13.572***	**−16.53***	**−0.435*****	**−1.62*****
	SELSM	1.104	0.92	1.528	1.37	1.080	1.29	1.528	0.85

*$p \leq 0.05$, **$p \leq 0.01$, ***$p \leq 0.001$; Dunnett's t test; significantly different from OVX

Results: Over the study period, BMD and BMC (whole body, lumbar spine, and proximal tibia) significantly decreased for RSG-treated animals relative to OVX controls. The pQCT analysis indicated the decreases in BMD for RSG-treated animals were mostly trabecular bone loss. Slight decreases were noted in bone strength parameters at sites rich in trabecular bone (lumbar spine and calcaneus). No effects were noted on levels of osteocalcin for RSG-treated animals. Slight decreases in P1NP levels were noted relative to OVX controls. Combination treatment with alendronate completely prevented bone loss and bone strength reductions associated with RSG treatment, whereas 17β-estradiol treatment only partially attenuated the reductions in these parameters. Metformin treatment did not affect BMD or strength parameters compared with OVX controls.

Conclusion: The results indicate that oral administration of RSG exacerbates OVX-induced bone loss at sites rich in trabecular bone. However, concomitant treatment with alendronate is effective in preventing RSG-induced bone loss in this model.

PS1.8 EFFECTS OF ARZOXIFENE ON BONE TURNOVER AND SAFETY IN POSTMENOPAUSAL WOMEN WITH LOW BONE MASS: RESULTS FROM A 6-MONTH PHASE 2 STUDY

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Background: Preclinical studies suggest that arzoxifene (ARZ), a benzothiophene selective estrogen receptor modulator (SERM), has an improved bone efficacy and a similar endometrial safety profile to raloxifene (RLX) 60 mg/day. This 6-month, phase 2, multicenter, randomized, double-blind, placebo (PBO)- and active-controlled (RLX) study was designed to assess the effects of various doses of ARZ on bone turnover markers and overall safety in postmenopausal women with low bone mass.

Methods: Healthy postmenopausal women (*N*=219; mean age, 59 years) with a lumbar spine or femoral neck *T*-score between −1 and −2.5 were randomly assigned to ARZ 5 (*N*=34), 10 (*N*=33), 20 (*N*=34), or 40 mg (*N*=40), RLX 60 mg (*N*=37), or PBO (*N*=41). All women received daily oral calcium (400–600 mg). The primary endpoints were 6-month percent change in osteocalcin and overall safety; the primary analysis was ARZ compared with PBO. Secondary endpoints included other bone turnover markers, BMD as an exploratory endpoint, and hot flush occurrence (assessed by electronic diary). Endometrial safety was assessed by transvaginal ultrasound and endometrial biopsy.

Results: Baseline characteristics were similar across treatment groups. All ARZ doses significantly reduced osteocalcin levels vs PBO ($p<0.05$). At 6 months, median percent changes in serum osteocalcin were −24%, −30%, −45%, −39%, −45%, and −44% in the PBO, RLX, and ARZ 5, 10, 20, and 40 mg groups, respectively. Compared with PBO, ARZ also significantly reduced serum bone specific alkaline phosphatase, CTX, and P1NP at 6 months ($p<0.05$). The 6-month change in lumbar spine (LS) BMD was significantly greater with all ARZ doses vs PBO ($p<0.05$): 1.50%, 1.69%, 1.77% and 1.92% in ARZ 5, 10, 20, and 40 mg, compared to a 0.60% decrease in PBO. ARZ generally had greater effects on bone turnover and LS BMD than RLX at 6 months. The proportion of women reporting ≥1 adverse event (AE) did not differ significantly among treatment groups ($p>0.05$). Muscle cramps were reported more frequently with ARZ vs PBO, with a similar frequency to RLX (pooled ARZ 7.1%, RLX 5.4%, PBO 0%). The frequency and severity of hot flushes did not differ significantly between ARZ and PBO ($p>0.05$), except for an increase in the ARZ 5 mg group by some measures. Change in endometrial thickness was not statistically significant for any ARZ group compared with PBO or RLX ($p>0.05$), and no cases of endometrial hyperplasia or adenocarcinoma were observed.

Conclusion: In postmenopausal women with low bone mass, all doses of ARZ were well tolerated, suppressed bone turnover and increased LS BMD. Within the limitations of this small phase 2 study, the endometrial safety profile of ARZ was similar to RLX.

PS1.9 ASSESSMENT OF FRACTURE RISK AND RECOMMENDATION FOR OSTEOPOROSIS TREATMENT IN WOMEN UNDERGOING THEIR FIRST DEXA SCAN: A COMPARISON BETWEEN BMD, BONE DESTINY AND OSTEOPOROSIS CANADA GUIDELINES

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Objective: To assess, in women visiting the bone density clinic for the very first time, the proportion of women who are recommended for osteoporosis treatment based on three different assessment methods, bone mineral density (BMD), Bone DESTINY and Osteoporosis Canada (OC) guidelines.
Methods: Females ≥50 years of age who underwent their first DEXA scan between January 2007 and October 2008 were included in the analyses. Treatment recommendations were made based on BMD alone where those with a BMD ≤−2.5 are considered to be at risk for fracture, Bone DESTINY where five colour codes represent fracture risk and those who are at high or very high risk for fracture (red or purple) are recommended, and Osteoporosis Canada (OC) guidelines which categorize patients at low, moderate or high risk for fracture and those at high risk are recommended for treatment. Bone DESTINY's estimation of fracture risk combines BMD, age, steroid use, propensity to fall, previous history of falls, previous fragility fractures and BMI <20 kg/m^2 while OC guidelines included sex, BMD, age, previous history of fragility fracture and steroid use. The proportion of women recommended for treatment was compared between the three groups.
Results: Of 2,769 females included in the analyses, 1,288 were 50–59 years old, 745 were 60–69 years old, 457 were 70–79 years old and 279 were ≥80 years old. The percentage of women in each age group recommended for treatment is displayed in the table.

Percent recommended for treatment

	BMD	DESTINY	OC
50–59 years	12	13	4
60–69 years	16	22	16
70–79 years	27	37	44
80–89 years	46	70	67

Conclusions: Of women who underwent their first DEXA scan, bone DESTINY and OC guidelines recommend treatment in more than one-third of 70–79 year olds and over two-thirds of those over 80 years of age. When considering only BMD, the proportion of women recommended for treatment is significantly lower. These results emphasize the need to consider risk factors in addition to BMD when recommending osteoporosis treatment. The ease and efficiency of interpretation of the DESTINY tool make it an attractive option for estimating fracture risk and translating this information into treatment decisions for family physicians.

PS1.10 FRACTURE RISK ASSESSMENT AND TREATMENT RECOMMENDATIONS IN FEMALES WITH FRAGILITY FRACTURES ASSESSED BY BMD, BONE DESTINY AND OSTEOPOROSIS CANADA GUIDELINES

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Objective: To assess the proportion of female patients with a previous fragility fracture recommended for treatment based on three different assessment methods, bone mineral density (BMD), Bone DESTINY and Osteoporosis Canada (OC) guidelines.
Methods: All females ≥50 years of age who had previously sustained a fragility fracture and who underwent a DEXA scan between January 2007 and October 2008 were included in the analyses. Fracture risk and treatment recommendations were made based on (a) BMD alone, (b) Bone DESTINY (estimation of fracture risk combines BMD, age, steroid use, propensity to fall, previous history of falls, previous fragility fractures and BMI <20 kg/m^2) and (c) OC guidelines (included sex, BMD, age, history of fragility fracture and steroid use). According to guidelines, women with a BMD ≤−2.5, a DESTINY fracture risk in either the red or the purple categories or those at high risk for fracture according to Osteoporosis Canada guidelines are those who would be recommended for treatment. The proportion of women recommended for treatment was compared between the three groups.
Results: Of 3,914 females included in the analyses, 763 were 50–59 years old, 1,118 were 60–69 years old, 1,225 were 70–79 years old and 810 were 80–89 years old. The percentage of women in each age group with a previous fragility fracture recommended for treatment is displayed in the table.

Percent of women recommended for treatment

	BMD	DESTINY	OC
50–59 years	19	39	36
70–69 years	27	79	81
70–79 years	37	89	96
80–89 years	56	96	98

Conclusions: Overall, Bone DESTINY suggests treatment in a much higher number of fragility fracture patients than BMD alone with an overall treatment recommendation in 78% of women assessed by bone DESTINY compared to 35% assessed by BMD alone. Like DESTINY, 80% of women would be recommended

for treatment based on OC guidelines. Based on the agreement in results between DESTINY and OC guidelines, the ease of interpretation make DESTINY an attractive option for reporting fracture risk and interpreting results by physicians.

PS1.11 ASSESSMENT OF FRACTURE RISK AND TREATMENT OF OSTEOPOROSIS IN POSTMENOPAUSAL WOMEN: A COMPARISON OF BMD, BONE DESTINY AND OC GUIDELINES

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Objective: To assess the proportion of women recommended for osteoporosis treatment based on three different assessment methods, bone mineral density (BMD), Bone DESTINY and Osteoporosis Canada (OC) guidelines, were compared in all female patients who visited the bone density clinic within a given time period.
Methods: All females ≥60 years of age who underwent a DEXA scan between January 2007 and October 2008 were included in the analyses. Treatment recommendations were made based on (a) BMD alone where those with a BMD ≤−2.5 are considered to be at risk for fracture; (b) Bone DESTINY where five colour codes represent fracture risk and those who are at high or very high risk for fracture (red or purple) are recommended and (c) Osteoporosis Canada (OC) guidelines which categorize patients at low, moderate or high fracture risk and those at high risk are recommended for treatment. Bone DESTINY's estimation of fracture risk combines BMD, age, steroid use, propensity to fall, previous history of falls, previous history of fracture and BMI <20 kg/m^2 while OC guidelines included sex, BMD, age, previous history of fragility fracture and steroid use. The proportion of women recommended for treatment was compared between the three groups.
Results: Of 14,812 females included in the analyses, 7,049 were 60–69 years old, 5,252 were 70–79 years old and 2,511 were 80–89 years old. The percentage of women in each age group recommended for treatment is displayed in the table.

Percent recommended for treatment

	BMD	DESTINY	OC
60–69 years	19	28	20
70–79 years	29	43	51
80–89 years	47	77	72

Conclusions: Given that bone DESTINY and OC guidelines account for fracture risk factors in addition to BMD alone, it is not surprising that there is a large discrepancy in the proportion of women who would be recommended for treatment between these groups. Differences between bone DESTINY and OC guidelines are likely a result of differences in the weightings of risk factors such as steroid use and previous fragility fracture and the impact of additional risk factors. Based on the agreement in results between DESTINY and OC guidelines, the visual ease of interpretation make DESTINY an attractive option for reporting fracture risk.

PS1.12 FRACTURE RISK ASSESSMENT AND TREATMENT RECOMMENDATIONS IN MALES WITH FRAGILITY FRACTURES ASSESSED BY BMD, BONE DESTINY AND OSTEOPOROSIS CANADA GUIDELINES

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Objective: To assess the proportion of male patients with a previous fragility fracture recommended for treatment based on three different assessment methods, bone mineral density (BMD), Bone DESTINY and Osteoporosis Canada (OC) guidelines.
Methods: All males ≥50 years of age who had previously sustained a fragility fracture and who underwent a DEXA scan between January 2007 and October 2008 were included in the analyses. Fracture risk and treatment recommendations were made based on BMD alone, Bone DESTINY and Osteoporosis Canada (OC) guidelines and results were compared. According to guidelines, men with a BMD ≤−2.5, a DESTINY fracture risk in either the red or the purple categories or those considered to be at high risk for fracture according to Osteoporosis Canada guidelines are those who would be recommended for treatment. Bone DESTINY's estimation of fracture risk combines BMD, age, steroid use, propensity to fall, previous history of falls and BMI <20 kg/m^2 while OC guidelines included sex, BMD, age, history of fragility fracture and steroid use. The proportion of men recommended for treatment was compared between the three groups.
Results: Of 572 males included in the analyses, 111 were 50–59 years old, 175 were 60–69 years old, 185 were 70–79 years old and 101 were 80–89 years old. The percentage of males in each age group with a previous fragility fracture recommended for treatment is displayed in the table.

Percent recommended for treatment

	BMD	DESTINY	OC
50–59 years	24	39	12
60–69 years	22	79	50
70–79 years	30	77	57
80–89 years	30	95	85

Conclusions: Overall, Bone DESTINY suggests treatment in a much higher number of fragility fracture patients than BMD alone or OC guidelines with an overall treatment recommendation in 73% of men assessed by bone DESTINY compared to 26% assessed by BMD alone and 41% by OC guidelines. These results suggest that both BMD and OC guidelines under-identify males with a fragility fracture who require treatment. This may be explained by the addition of the history of falls and propensity to falls in the DESTINY software which is not used in OC risk-stratification. These results warrant further investigation.

PS1.13 PHYSICIAN KNOWLEDGE AND OPINION OF THE CMS'S PHYSICIAN QUALITY REPORTING INITIATIVES (PQRI) AS THEY RELATE TO OSTEOPOROSIS

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Background: The 2006 Tax Relief and Health Care Act (TRHCA) (P.L. 109–432) required the establishment of a physician quality reporting system, including an incentive payment for eligible professionals who satisfactorily report data on quality measures for covered services furnished to Medicare beneficiaries. This system was implemented by the Centers for Medicare and Medicaid Services (CMS) in July 2007 on a voluntary basis and under the title of the Physician Quality Reporting Initiative (PQRI). It is a pay-for-performance program which creates incentives for physicians to adopt best practice guidelines for over 100 known clinical practices. Five of these practices relate to the recognition and treatment of osteoporosis. We hypothesized that most physicians in a position to treat patients with osteoporosis are either unaware or ill quipped to implement them into practice.
Methods: We created a 13 question survey to gauge physician practice patterns, awareness of PQRI initiatives as they relate to osteoporosis and opinions regarding ideal osteoporosis referral and treatment.
Results: 238 surveys were sent and 74 were completed for a response rate of 31%. 61% of responders treat musculoskeletal conditions almost exclusively. Nearly half of responders state that 21–40% of their patients are covered by Medicare and another 30% state that 41–60% are covered by Medicare. 73% stated that they were either "slightly familiar" or "not familiar at all" with PQRI guidelines. 64% and 68% respectively stated that they "did not know" how many initiatives applied to their practice or how many they adhered to currently. 60% cited increased time, manpower and paperwork as potential barriers to implementing these guidelines. Responses were mixed regarding which physician should be responsible for managing osteoporosis with answers favoring family care and rehabilitation specialists. Most agreed that orthopedic surgeons should initiate communication after fragility fracture to the primary care physician. And 97% felt that a medical physician such as family practitioner, endocrinologist or internist should manage bisphosphonate therapy, not a surgeon. Opinions were nearly evenly split regarding whether the 1.5% bonus was satisfactory or not to induce a change in behavior in physicians.
Conclusions: This survey study highlights a relative lack of awareness, significant perception of barriers to implementation and ambivalence regarding effectiveness of the PQRI incentive program as it pertains to osteoporosis performance improvement measures. Significant hurdles remain if such initiatives are to achieve the intended purpose of better standardized care and cost reduction. And it is unclear whether the program in its current state is sufficient to accomplish these goals.

PS1.14 IBANDRONATE HAS PHARMACOLOGIC CHARACTERISTICS THAT ENABLE EFFECTIVE MONTHLY ORAL AND QUARTERLY IV DOSING

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Bisphosphonates (BP) are the mainstay of treatment for post-menopausal osteoporosis and initially were formulated for daily oral administration. In the oral ibandronate Osteoporosis vertebral fracture trial in North America and Europe (BONE), daily ibandronate 2.5 mg reduced the risk of vertebral fractures by 52% in US patients, and in a high-risk subgroup reduced the risk of nonvertebral fractures (NVFs) by 69%. Longer dosing intervals were sought to improve convenience and adherence, and the IV regimen provides a longer dosing interval option for patients who cannot tolerate oral treatment. Weekly administration at the same total dose of BP can be considered pharmacologically equivalent to daily. However due to the ~2-week lifespan of osteoclasts and physiology, particularly of cortical bone, longer dosing intervals require higher total doses than daily or weekly regimens.

Ibandronate's strong binding affinity and potent inhibition of osteoclasts allows sustained reduction of bone turnover without return to turnover above premenopausal levels between doses. Extensive in vivo studies and modeling showed that increasing the total dose of ibandronate would enable extended dosing intervals. Monthly oral ibandronate 150 mg and quarterly IV 3 mg were selected for clinical study. In the Monthly Oral iBandronate In LadiEs (MOBILE), and Dosing IntraVenous Administration (DIVA) studies, these regimens provided significant BTM reductions and superior BMD improvements to daily ibandronate. Monthly oral and quarterly IV ibandronate are the only extended dose interval BPs for which it has been demonstrated that, with an appropriate dose increase, a BMD response can be obtained that is superior to the daily formulation of the same BP. A meta-analysis using individual patient data confirmed that higher-dose ibandronate administered at extended intervals (including the approved regimens), significantly reduced the risk of key NVFs (34.4% relative risk reduction, $p=0.032$) and all clinical fractures (28.8%, $p=0.010$) compared with placebo. Despite the higher dose, monthly oral and quarterly IV ibandronate have tolerability profiles consistent with other N-containing BPs.

Monthly oral ibandronate and quarterly IV ibandronate provide effective treatment with extended dosing intervals. As the only bisphosphonate approved for both oral and IV administration, ibandronate provides patients with the option of switching between oral and IV treatment while remaining on the same BP.

PS1.15 MONTHLY ORAL IBANDRONATE FOR REDUCTION OF FRACTURE RISK IN POSTMENOPAUSAL OSTEOPOROSIS: ANALYSIS OF DATA FROM META-ANALYSES, RANDOMIZED CLINICAL TRIALS, AND OBSERVATIONAL CLAIMS DATABASE

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Background: Monthly ibandronate (IBN) increases bone mineral density (BMD) and reduces fracture risk in women with postmenopausal osteoporosis (PMO), as seen in randomized clinical trials (RCTs). Translating these findings into 'real-world' effectiveness requires consideration of other data sources.
Objective: This review more fully evaluated anti-fracture risk efficacy and safety of monthly oral IBN in women with PMO, using multiple complementary data sources.
Methods: IBN data from three different sources were analyzed. The first comprised two meta-analyses: one of four prospective Phase III RCTs (BONE, IV fracture prevention, DIVA, and MOBILE) with ≥2 years of follow-up for fractures, and the other involving RCTs of ≥1 year duration. Patients were stratified based on IBN annual cumulative exposure (ACE): high (≥10.8 mg, including the monthly 150 mg oral and quarterly 3 mg IV dosing used in clinical practice, and the unlicensed 2 mg IV q 2 months), mid (5.5–7.2 mg), and low (2.0–4.0 mg). The second data source was a head-to-head, randomized, non-inferiority comparison (MOTION) of BMD changes with monthly IBN versus weekly alendronate treatment over 1 year. Lastly, a large claims database study (VIBE) assessed fracture risk over 1 year in women who received monthly IBN or weekly bisphosphonates (BPs).
Results: These analyses demonstrate that oral IBN significantly reduces fracture risk in women with PMO, and improves BMD as effectively as weekly alendronate. Meta-analyses revealed significant NVF risk reductions at high ACE levels versus lower ACE and versus placebo. In MOTION, mean relative BMD changes from baseline were similar between monthly IBN and weekly alendronate: 5.1% and 5.8%, respectively, for lumbar spine, and 2.9% and 3.0% for total hip, meeting the noninferiority criterion. VIBE data indicated no significant differences between monthly IBN and alendronate or weekly BPs in risk of hip fracture (adjusted relative risk 1.06; 95%CI 0.61–1.83, $p=0.840$), NVF (0.88; 95%CI 0.71–1.09, $p=0.255$), or any clinical fracture (0.82; 95%CI 0.66–1.00, $p=0.052$). IBN significantly decreased risk of vertebral fracture or any clinical fracture in patients >65 years compared to the weekly BPs combined and individually.
Conclusions: Evidence from multiple RCTs and practice-based data sources confirm that monthly oral IBN is effective and well tolerated for reduction of hip and vertebral fractures and NVF in women with PMO.

PS1.16 VERTEBRAL BONE MINERAL DENSITY (BMD) RESPONSES TO IBANDRONATE MEASURED BY QUANTITATIVE COMPUTED TOMOGRAPHY (QCT) AFFECT SUPERIOR, INFERIOR, AND SUBCORTICAL REGIONS

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Background: Three-dimensional BMD measured by QCT provides information about response to osteoporosis therapy not captured by areal BMD changes.
Objective: This randomized trial evaluated the effect of monthly oral ibandronate or placebo on total hip and lumbar spine QCT BMD in women with postmenopausal osteoporosis. The primary endpoint was integral total hip BMD; reported here is a post hoc analysis of extended vertebral subregions.
Methods: Ninety-three women with areal BMD *T*-scores ≤−2.0 and ≥−5.0 were randomized to monthly oral ibandronate (150 mg; $n=47$) or placebo ($n=46$) for 12 months. CT scans were done at baseline and month 12. Vertebral (L1–L2) QCT volumes of interest (VOIs) included total vertebral body, central 10 mm (midsection), and inferior and superior VOIs. Cortical, subcortical, trabecular, and integral BMD were evaluated in each VOI. Extended cortical BMD included cortical and subcortical BMD. Within-group mean percentage changes were determined, and treatment differences were assessed by center-adjusted analysis of variance. *p* values were post hoc, descriptive, and unadjusted for multiple comparisons.
Results: Forty-one ibandronate and 35 placebo patients had evaluable spine scans at both visits. Ibandronate improved integral BMD significantly versus placebo, with similar gains in the vertebral body (4.4%, $p=0.001$) and midsection (4.0%, $p=0.011$). Trabecular total vertebral body BMD showed a comparable and significant gain (4.3%, $p=0.024$). Superior and inferior trabecular BMD showed significant treatment differences (4.9%, $p=0.032$, and 4.6%, $p=0.055$, respectively), whereas midsection trabecular BMD increase was non-significant (2.3%, $p=0.244$). The extended cortical midsection had a significant treatment difference (3.9%, $p=0.014$) though the cortical midsection was not statistically significant (4.4%, $p=0.154$), likely due to higher variability in the smaller VOI.
Conclusions: Monthly oral ibandronate for 12 months increased integral and trabecular vertebral BMD versus placebo. Trabecular BMD especially increased in the inferior and superior vertebral regions. The cortical midsection BMD treatment difference was not significant but became so when subcortical BMD was

included (extended cortical BMD). Ibandronate-induced QCT BMD increases appeared greatest in the vertebral periphery.

PS1.17 5-YEAR EFFICACY AND SAFETY OF ORAL MONTHLY IBANDRONATE: RESULTS OF THE MOBILE LONG-TERM EXTENSION STUDY

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Background: The 2-year Monthly Oral Ibandronate in Ladies study (MOBILE) compared bone mineral density (BMD) with oral ibandronate monthly 100 or 150 mg or 50 mg (2 days monthly) to 2.5 mg daily in women with postmenopausal osteoporosis. The MOBILE long-term extension (LTE) rerandomized patients to the 100 or 150 monthly regimens and followed BMD changes for three additional years.

Objective: To assess lumbar spine (LS) and total hip (TH) BMD and long-term safety and tolerability with monthly oral ibandronate 100 or 150 mg continued 3 years after the 2-year core study.

Methods: Core MOBILE subjects were 55–80 years old and ≥5 years postmenopausal with LS BMD *T*-scores ≤−2.5 and ≥−5.0. Ambulatory patients completing the 2-year core study with ≥75% compliance were LTE-eligible. Those receiving 100 or 150 mg monthly oral ibandronate continued to do so; those originally receiving 2.5 mg daily or 50 mg/day for 2 days monthly were re-randomized to 100 or 150 mg monthly LTE treatment. The primary outcome was mean percent change in LS BMD at 36 months compared to LTE study baseline. Mean percent change in TH BMD 36 months after the LTE baseline was a secondary outcome. Additional pooled analysis (150 mg, n=171; 100 mg, n=173) assessed BMD changes from core MOBILE baseline to LTE completion (5 years). Adverse events were monitored throughout the study.

Results: In the intent-to-treat (ITT) population, mean percent BMD changes from LTE baseline and from core MOBILE baseline are shown in Table 1. Clinical osteoporotic fractures affected 8.9% of 150 mg patients (34 of 361) and 9.5% of 100 mg patients (37 of 358) in the LTE safety population. Discontinuation rates due to adverse events (AEs) were 4.4% (150 mg) and 5.3% (100) mg, reflecting primarily gastrointestinal AEs.

Conclusions: LS BMD continuously increased with both monthly 150 and 100 mg ibandronate during the 3-year LTE, and TH BMD gains from the 2-year core study were maintained with 150 mg. Clinical osteoporotic fracture incidences (captured as AEs) were similar between groups. Both monthly oral ibandronate doses were well tolerated.

Table 1 Mean percent BMD changes from MOBILE LTE or original MOBILE baselines

	Percent change from MOBILE LTE baseline (3 years of treatment), mean (95%CI)		Mean percent change from start of MOBILE baseline (5 years of treatment)	
BMD site	150 mg/mo (n=350)	100 mg/mo (n=348)	150 mg/mo (n=350)	100 mg/mo (n=348)
Lumbar spine	2.43 (1.90, 2.96)	2.18 (1.63, 2.73)	8.43 (7.49, 9.37)	8.17 (7.18, 9.16)
Total hip	−0.35 (−0.0715, 0.016)	−0.80 (−1.19, −0.42)	3.47 (2.83, 4.11)	2.99 (2.28, 3.70)

CI confidence interval

PS1.18 BAZEDOXIFENE REDUCES ALL CLINICAL FRACTURES AND MORPHOMETRIC VERTEBRAL FRACTURES IN POSTMENOPAUSAL WOMEN AT INCREASED FRACTURE RISK ASSESSED BY FRAX

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Background: In a phase III study, bazedoxifene significantly decreased the risk of vertebral fractures in postmenopausal women. No significant effect was noted on clinical fractures, but fracture risk reduction was reported in a post hoc subgroup analysis in a high risk group categorised on the basis of BMD and prior fracture. We re-evaluated the efficacy of bazedoxifene on fracture outcomes in the pivotal study and avoided subgroup analysis by examining bazedoxifene efficacy as a function of fracture risk using the entire study population.

Methods: For the present analysis, we compared the effects of two doses of bazedoxifene (20 and 40 mg daily combined) with placebo on the risk of all clinical fractures as well as morphometric vertebral fracture. The risk of a major osteoporotic fracture was assessed using the FRAX® algorithms, and the relationship between pre hoc 10 year fracture probabilities and efficacy examined by Poisson regression.

Results: This independent re-analysis confirmed that bazedoxifene significantly decreased incident morphometric vertebral fractures (hazard ratio HR=0.61; 95%CI=0.43–0.86; p=0.005) and was associated with a statistically non-significant 16% decrease in all clinical fractures compared to placebo treatment (hazard ratio HR =0.84; 95%CI=0.67–1.06; p=0.14). Hazard ratios for the effect of bazedoxifene on fractures decreased with increasing fracture probability. In patients with 10-year fracture probabilities at or above 16%, bazedoxifene was associated with a significant decrease in the risk of all clinical fractures (the 80th percentile of risk). For morphometric vertebral fractures, bazedoxifene was associated with a significant decrease in risk with 10-year fracture

probabilities above 7.3% (the 44th percentile of risk). At equivalent fracture probability percentiles, the treatment effect of bazedoxifene was greater on vertebral fracture risk than on the risk of all clinical fractures.

Conclusion: Bazedoxifene (20 and 40 mg doses combined) significantly decreases the risk of all clinical fractures and morphometric vertebral fractures in women at or above a FRAX® based fracture probability threshold. The efficacy increases with increasing fracture probability. These results, consistent with the previous sub group analysis, suggest that bazedoxifene should be targeted preferentially to women at increased fracture risk.

PS1.19 IMPACT OF VARYING BMD RESOURCES ON PREDICTION OF HIP FRACTURE USING FRAX

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Background: In many healthcare systems, including the NHS in the UK, access to DXA is limited and case-finding strategies are promoted. We aimed to examine the effects of the use of clinical risk factors (CRFs), BMD or the combination using the FRAX® tool for the detection of women at risk of hip fracture.

Methods: Data from ten prospective population based cohorts, in which BMD and CRFs were documented, were used to compute the 10-year probabilities of hip fracture calibrated to the fracture and death hazards of the UK using the FRAX® tool. The base case examined the effects in women at the age of 65 years. Simulation samples of 1,000 women were derived with BMD measurements undertaken in none, all or intermediate proportions of the population in order to identify women in whom the probability of hip fracture lay above the 10-year probability of hip fracture at which treatment became cost-effective using previously published UK data. For strategies with limited use of BMD tests, the tests were targeted to those lying nearest the intervention threshold in order to maximise the positive predictive value (PPV) and hence the NNT to prevent one hip fracture.

Results: When women aged 65 years were assessed with CRFs, increasing the number of BMD tests, from zero up to 100% of women, increased progressively the number of women categorised at high risk and decreased the NNT. The change in NNT was non-linear. NNT was 54 with the use of CRFs alone and fell to 43 when BMD was used in 10–30% of women. When BMD tests were undertaken in all women, the NNT decreased to 33. NNT with the use of BMD alone was 47.

Conclusion: The combined use of BMD and CRFs outperforms the use of BMD or CRFs alone. The input of BMD as part of a FRAX® assessment increases the performance characteristics of fracture risk assessment, so that the optimal use of the FRAX™ tool is with the concurrent use of BMD tests. Where resources are limited, the use of BMD tests are optimally targeted to 10–30% of women that lie closest to the intervention threshold.

PS1.21 PHYTOESTROGENS AND OSTEOPOROSIS: A VIABLE ALTERNATIVE?

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Background: Osteoporosis is a reduction in bone tissue resulting in brittle and fragile bone prone to fracture, usually occurring in postmenopausal women. Given the demonstrated risks to conventional hormone replacement therapy (HRT), many women and their practitioners have been in search of alternatives. Phytoestrogens are naturally occurring, plant based diphenolic compounds that are similar in structure and function to estradiol. Common and significant sources of phytoestrogens are soybeans (isoflavones), cereals and oilseeds (lignans) and alfalfa sprouts (coumestans). This study aimed at evaluating the role of phytoestrogens in bone conservation.

Methods: Seventy-five postmenopausal women were recruited in this study. They were randomly divided into three equal groups; the first group served as the control (casein/nonfat dry milk) group, the second group was placed on a diet of 60 g of isoflavones (soy protein) and the third group was placed on a 100 g isoflavone enriched (soy protein) diet. Bone mineral densities (BMDs) at the lumbar spine (L1-L4) and hip region were measured at baseline and after 6 months of being placed on the diets using dual-energy X-ray absorptiometry (DEXA). Biochemical markers of bone turnover: osteocalcin and serum bone specific alkaline phosphatase [BAP] were assessed. Exclusion criteria included athletic individuals, smoking, those on HRT and those taking vitamin supplements and calcium.

Results: Our data point to a reduction in bone resorption in both groups that were placed on an isoflavone enriched diet when compared to the control group. For the group taking soy protein with a high concentration of isoflavone, compared to the control group significant increases were found in BMD in the lumbar spine but not in the hip region. In the group receiving the lower concentration of isoflavone a less significant increase was found in the lumbar spine and no significant change was found in the hip region. Significant differences in the lumbar spine BMD (0.825 ± 0.141 vs 0.698 ± 0.134 g/cm^2, $p<0.05$) were found between the higher and lower intake of isoflavone. In addition, after 6 months of therapy, significant improvement of bone biochemical markers was found. The group on the higher concentration of isoflavone had significantly lower levels of osteocalcin and higher levels of BAP when compared with those with the lower intake of isoflavone and with the control group respectively.

Conclusion: This study provides evidence that suggests that there is a positive association between consumption of isoflavone enriched diet and protection of bone mass in the spine area of postmenopausal women.

PS1.22 RISEDRONATE SODIUM RETARDS PROGRESSION OF SUBCLINICAL ATHEROSCLEROSIS IN POSTMENOPAUSAL WOMEN WITH OSTEOPOROSIS

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Background: Osteoporosis and cardiovascular disease represent major public health problems. These two conditions may be sustained by a common pathophysiological mechanism. Inflammation may be a common link between low bone mineral density and atherosclerosis. Accumulating evidence suggests that bisphosphonates, frequently used to treat osteoporosis, may display anti-atherogenic properties. Accordingly, the aim of the present work was to investigate whether risedronate sodium therapy is effective in retarding preclinical atherosclerosis in postmenopausal osteoporotic women.

Methods: Sixty-four primary osteoporotic women, mean age 66.5 years, were studied. Osteoporosis was assessed by dual energy X-ray absorptiometry (DEXA) of the hip and lumbar spine. Preclinical atherosclerosis was evaluated by carotid-intima media thickness (CIMT) using B-mode ultrasonography before and after 12 months therapy with 35 mg once a week of risedronate sodium. Levels of inflammatory markers including high sensitivity C-reactive protein (hsCRP), interleukin-6 (IL-6) and tumour necrosis factor alpha (TNF-alpha) as well as lipid levels (total cholesterol(TC), low density lipoprotein-cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C) and triglycerides (TG)) were assessed before and after therapy. All values were compared to 30 healthy age, sex and body mass index matched controls.

Results: Following 12 months of risedronate sodium therapy, there was a statistically significant reduction in CIMT (mean (SE)-0.036 mm (0.01 mm), $p<0.05$. Furthermore, the levels of hsCRP and of the proinflammatory cytokines IL-6 and TNF-alpha showed modest yet statistically significant reductions in comparison to the pretreatment values. There was a reduction in TC, LDL-C and TG levels but this reduction did not reach statistical significance. As expected, bone mineral density (BMD) in both lumbar spine and hip improved significantly after 12 months therapy with risedronate sodium.

Conclusion: Risedronate sodium retarded preclinical atherosclerosis in postmenopausal osteoporotic women. In addition, risedronate sodium improved the levels of hsCRP and pro-inflammatory cytokines, IL-6 and TNF-alpha suggesting that apart from improving BMD, it may also have an anti-atherogenic role via its effect on inflammatory mediators. These findings suggest that risedronate sodium displays pleiotropic effects partially through its effect on proinflammatory cytokine mediated inflammation. Further larger longitudinal randomized placebo-controlled studies are needed to verify these results.

PS1.23 PERCUTANEOUS DELIVERY OF A BI-PHASIC BONE SUBSTITUTE FOR THE TREATMENT OF VERTEBRAL COMPRESSION FRACTURES: EARLY CLINICAL RESULTS

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The advent of percutaneous material delivery has provided a viable treatment option that quickly improves the quality of life in patients with vertebral compression fractures. Injection of the material stabilizes the fracture thus preventing micro motion at the fracture site. Synthetic bone substitutes have advantages over alternative materials; they do not have the potential for disease transmission associated with allograft material, and may be selected to prevent the donor morbidity associated with the exothermic properties of PMMA bone cement. The injectable material is a bio-compatible, injectable ceramic bone substitute which has been cleared by the FDA as a bone void filler. It has recently been introduced off-label for the treatment of vertebral compression fractures (VCFs) to provide stability, reduce pain and lower the incidence of secondary fractures. The bi-phasic powder comprises a synthetic calcium sulfate (60% by weight) and a balance of sintered hydroxyapatite, mixed with a radio-opacity enhancing component which contains iohexol to produce a flowable and injectable paste. The resultant product increases cancellous bone mass in vertebral bodies and avoids the negative aspects of implanting inert (e.g. barium sulfate) material. The calcium sulfate resorbs with time producing porosity which allows for new bone ingrowth through occupation of osteoprogenitor cells and osteoblasts, while the hydroxyapatite acts as a long term osteoconductive matrix.

The ceramic bone substitute provides the appropriate mechanical environment for stability of the VCF and pain prevention. The material construction delivers a compressive strength similar to that of cancellous bone when implanted and this restores initial strength to aid pain prevention. The stiffness is also similar to that of cancellous bone to help prevent additional fractures in adjacent vertebrae. These biomechanical properties shall be discussed.

PS1.24 PATIENT PREFERENCE AND SATISFACTION WITH A 6-MONTH INJECTION VERSUS A WEEKLY PILL FOR TREATMENT OF POSTMENOPAUSAL BONE LOSS

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Background: The Preference and Satisfaction Questionnaire (PSQ) was designed to compare patient preference for and satisfaction with two treatments for bone loss: denosumab, an investigational fully human monoclonal antibody given every 6 months (Q6M) by subcutaneous (SC) injection, and alendronate, an oral pill taken weekly.
Methods: Healthy postmenopausal women, with a *T*-score ≤−2.0 at the lumbar spine or total hip, were enrolled in a phase 3 international double-blind, double-dummy study and randomized 1:1 to receive either a SC denosumab injection Q6M (60 mg)+oral placebo pill weekly or a SC placebo injection Q6M+oral alendronate weekly (70 mg). After 12 months of treatment, patients completed the PSQ to rate their preference for and satisfaction with each treatment. The prespecified endpoints of preference and satisfaction were assessed based on single items. Patients were asked to choose either: the pill, the injection, or neither in response to the questions for preference: "Which do you prefer?" and satisfaction: "With which frequency of administration have you been more satisfied?". Patients were also asked if they were bothered by the treatments.
Results: Enrolled patients (*N*=1189; mean age 64 years) had a mean lumbar spine *T*-score of −2.6. Most patients (92.5%) answered ≥1 item of the PSQ. Among those who reported preference/satisfaction, significantly more patients preferred and were more satisfied with the Q6M injection than the weekly pill, regardless of treatment group (Table). Some patients reported no preference (alendronate=19%; denosumab=17%) or satisfaction (alendronate=23%; denosumab=23%) for one treatment over the other. More patients reported that they were not bothered at all by the Q6M injection (91% for both groups) than the weekly pill (alendronate=61%; denosumab=65%).
Conclusion: Similar to published reports (Reginster et al., Bone, 38:S2, 2006; Simon et al., Clin Ther, 24:1871, 2002), patients in this study both preferred and were more satisfied with a treatment that was dosed less frequently.

Patient-reported preference and satisfaction with the Q6M injection or weekly pill

		Preference, *n* (%)	Satisfaction with frequency, *n* (%)
Q6M denosumab injection+weekly placebo pill (*N*=555)	Q6M injection	352 (77)	338 (79)
	Weekly pill	107 (33)	89 (21)
	Within group *p*-value	<0.0001	<0.0001
Weekly alendronate pill+Q6M placebo injection (*N*=545)	Q6M injection	339 (77)	331 (80)
	Weekly pill	101 (23)	83 (20)
	Within group *p*-value	<0.0001	<0.0001
Between group *p*-value		0.8329	0.9256

Among patients reporting a preference or satisfaction with one treatment over the other

PS1.25 IS CLINICAL MEASUREMENT OF 25-HYDROXYVITAMIN D STILL A PROBLEM?

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Background: The high prevalence of vitamin D deficiency, and importance of this vitamin in skeletal and general health has become well recognized. This has resulted in a dramatic increase in 25-hydroxy vitamin D [(25(OH)D] measurement by clinicians to assess patient vitamin D status. Several methodologies are available to measure circulating 25(OH)D concentration. Differences in approaches and lack of uniform standard calibrators historically have led to variability between laboratories in 25(OH)D results. Recent clinical observations raise concern that substantial variability continues to persist. The purpose of this quality assurance exercise was to investigate consistency in 25(OH)D results between current methods and clinical laboratories.
Methods: Twenty-five serum samples selected to contain 25(OH)D2 and 25(OH)D3 at concentrations ranging from undetectable to high total 25(OH)D concentrations were utilized. At this time, 25(OH)D results are available from four laboratories which utilize either high performance liquid chromatography (HPLC), liquid chromatography tandem mass spectroscopy (LC-MS/MS) or a chemiluminescent autoanalysis. Additional laboratories and methodologies are being investigated. The University of Wisconsin clinical laboratory HPLC results were arbitrarily selected as a referent to which the other three laboratories were compared.
Results: When compared to the HPLC result, substantial bias was observed for two laboratories; a mean of +4.2 ng/mL in one laboratory and −7.2 ng/mL in another. For the laboratory with the positive bias, 22/25 results were numerically higher (+15.7% on average [range +0.4% to +29.0%]) than those obtained by HPLC. Similarly, for the lab with the negative bias, 24/25 results were lower (−23.2% on average [range −2.7% to −39.8%]) than the corresponding HPLC values. As an example of this variability, the 25(OH)D results for one serum specimen ranged from 22.7 to 39.0 ng/mL.
Conclusions: Substantial variability in 25(OH)D results persists in clinical laboratories. Such variability currently confounds use of a single cutpoint approach, e.g., 30 ng/mL, for the diagnosis of hypovitaminosis D. Further work to reduce between-laboratory 25(OH)D assay variability is necessary.

PS1.26 EARLY REDUCTION IN BACK PAIN: INTERIM RESULTS FROM DANCE, DIRECT ASSESSMENT OF NON-VERTEBRAL FRACTURE IN COMMUNITY EXPERIENCE

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Background: The Direct Assessment of Non-vertebral Fracture in Community Experience (DANCE) study is a prospective observational study examining the long-term effectiveness, safety, and tolerability of teriparatide (TPTD) in a large heterogeneous population in a community setting

Methods: In this study, back pain was evaluated by a self-administered 10 cm Visual Analogue Scale (VAS). At each visit, subjects were queried about their pain and back pain experience. To understand early experience in back pain with TPTD use, 493 subjects (449 women and 44 men) who rated their pain as ≥4 cm on the VAS and identified the source as either mid or lower back at baseline were included in this analysis. This cohort completed a follow-up survey within 3 months (mean 1.7±0.67 months) at which time subjects were queried about their use of analgesic medications.

Results: The baseline mean VAS for these subjects was 6.6 cm; mean lumbar spine BMD *T*-score was −2.5; 38.7% (189/489) of subjects reported ≥1 prevalent vertebral fracture. At the time of follow-up, VAS score decreased by 1.8±2.9 cm ($p<0.001$); 39% (193/493) of subjects reported at least a 30% reduction in back pain by VAS. There was no difference in baseline back pain score or change in back pain score by prevalent vertebral fracture status. The overall proportion of subjects who took analgesics decreased significantly after TPTD initiation. Usage of NSAID/COX-2 inhibitor (17.8% baseline, 12.0% follow-up) and opioid-related agents (32.0% baseline, 27.0% follow-up) also decreased significantly ($p<0.05$ from baseline).

Conclusion: In this naturalistic study, TPTD reduced VAS back pain and analgesic consumption in patients with osteoporosis. Given the lack of a control group and the tendency of back pain to spontaneously remit over time, one cannot necessarily attribute the reduction in pain to TPTD therapy. Confirmation of these findings will require a controlled clinical trial.

PS1.27 AUTOMATIC CLASSIFICATION OF VERTEBRAL SHAPE BASED ON STATISTICAL SHAPE MODELLING

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Background: The purpose of this study was to test a classifier of vertebral fractures based on statistical shape modeling.

Methods: We previously described a method for annotation of vertebral shape using 95 points representing the circumferential vertebral borders on lateral spine X-rays (Brett et al., In Proc ASBMR, W227, Hawaii, Sept 2007). We used this method to manually annotate 2,503 vertebrae on lateral thoracic and lumbar spine X-rays from 237 subjects. Independently, these films were read by an expert radiologist (CH) who classified each vertebra according to the Genant SQ scoring scheme and provided differential diagnosis for non-osteoporotic vertebral deformities. 2,390 vertebrae were normal, 967 had non-osteoporotic deformities, and 113 were fractured: 44 fractures were mild (grade 1), 69 were definite (grade 2 or 3). Using "leave-one-out" methodology we built two-class classifiers to classify all osteoporotic fractures vs non-fractures and specific grade osteoporotic fractures vs non-fractures.

Results: Balanced error rate classifiers yielded equal sensitivity and specificity of 95.6% overall, 90.1% for mild fractures, and 97.4% for definite fractures with the area under ROC curve of 0.9872, 0.9712 and 0.9975 respectively. The Kappa Score between expert and classifier was 0.64 overall, 0.24 for mild, and 0.69 for definite fractures.

Conclusion: These initial results show that a classifier can be constructed to distinguish osteoporotic from normal or non-osteoporotic deformities with an agreement similar to or better than, results published previously for human observers. Our study showed high sensitivity and specificity to identification of osteoporotic fractures from a set of vertebrae that were either normal or deformed not by osteoporotic fracture. Our training set was characterized by relatively few fractures and a high degree of non-osteoporotic deformities. Building the classifier based on films further enriched for vertebral fracture would likely improve its performance. Combining this classifier with an efficient annotation tool may provide a useful work flow tool in clinical trials or a decision-making aid in a point-of-care setting (Brett et al., In Proc ASBMR, W227, Hawaii, Sept 2007).

Table 1 Agreement between expert radiologist and classifier

		Radiologist			Radiologist			Radiologist	
		All Fx	No Fx		Mild Fx	No Fx		Definite Fx	No Fx
Classifier	All Fx	108	106	Mild Fx	40	217	Def Fx	67	54
	No Fx	5	2,284	No Fx	4	2,173	No Fx	2	2,336
	Total	113	2,390	Total	44	2,390	Total	69	2,390

PS1.28 TREATMENT INITIATION OF OSTEOPOROSIS IN IMMIGRANT VIETNAMESE WOMEN

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Background: The purpose of this study is to compare DEXA-scan results to the projected hip fracture risk by using the new World Health Organization (WHO) on-line FRAX™ tool in a population of Vietnamese women. Specifically, the study seeks to

explore the differences between the two methods in initiation of medication therapy.

Methods: 57 postmenopausal, Vietnamese women, who were currently patients at the Community Health Centers (CHC), SLC, UT, were included in the study. IRB and CHC board approval was obtained. A chart review was completed, noting age, height, weight, smoking and alcohol history, glucocorticoid use, fracture history, family history of osteoporosis-related fracture, and recent DEXA-scan *T*-score if available. The data for each subject identified was then entered into the on-line FRAX™ tool and the 10-year projected risk for hip and other major osteoporotic fracture calculated.

Results: Of the 57 women, 30 had received a DEXA scan, 27 had not. For the group of women without DEXA scans, the 10-year fracture probabilities were calculated using the on-line WHO FRAX™ tool. The 10-year hip fracture probability ranged from 0.1 to 0.8 and the 10-year other major osteoporotic fracture probability ranged form 1.6 to 4.2. Per the new NOF guidelines, treatment was not initiated in this group of women. In the DEXA scan group, nine were found to be osteoporotic at the hip or spine, 18 were osteopenic, and three had normal bone mineral density. Three of the osteopenic subjects had their DEXA scan done in the past 3 months. Using the on-line FRAX™ tool, hip fracture probability in these three women was ≤3%, and per the new NOF guidelines an antiresorptive agent was not initiated. 15 of the osteopenic subjects were currently taking an antiresorptive agent. Their DEXA scans had been done within the last 4 years; had the FRAX™ tool been available at the time of the DEXA scan, nine of the 15 would not have been started on medication therapy.

Conclusions/Recommendations: Over half the women started on medication therapy could have continued lifestyle changes only as their calculated 10-year probability of fracture was low. The FRAX™ tool was easy to use and readily available. The tool allows the clinician to make evidence-based decisions in caring for women from varied backgrounds while considering individual clinical risk factors in initiating medical therapy for osteopenia and osteoporosis.

PS1.30 INITIATION AND ADHERENCE WITH OSTEOPOROSIS THERAPY

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Background: There are effective treatments to prevent osteoporotic fractures, but even when diagnosed, osteoporosis is undertreated. We evaluated the bone density consequences of the decision to initiate therapy and the number of days on therapy in the first year after diagnosis.

Methods: From February 2006 through March 2007, we identified consecutive female members of a managed care plan with pharmaceutical coverage who received a dual energy X-ray absorptiometry (DXA) evaluation and fulfilled WHO criteria for OP. Patients were excluded if they received OP prescription medications in the prior 6 months. Approximately 12 months after the date of the initial DXA, patients were asked to return for follow-up DXA to allow for an assessment of change in bone density. Administrative electronic health records were used to identify prescription drug use and health care utilization.

Results: Two-hundred and forty-three women returned research authorization forms out of 465 contacted for participation. 138 of the 243 (57%) initiated pharmacologic therapy for osteoporosis during the year after the initial DXA. 144 (59%) returned for a follow-up DXA. Women returning for a follow-up DXA had a slightly higher hip bone density (BMD) at baseline than those not returning for a follow-up DXA (p=0.04), but were similar with respect to age, mean spine BMD, and proportion receiving drug therapy in the 1 year following the initial DXA. Of the 144 women who returned for a follow-up DXA, 78 (54%) received OP drug therapy in the 1 year following the initial DXA. Women receiving OP drug therapy had higher mean increases in spine (+3.0% vs +1.0%) (p=0.006) and hip (+1.2% vs −0.7%) (p= 0.0009) than those who did not initiate treatment. For those women who started drug therapy, the mean percentage of days on therapy between the initial and follow-up DXA was 56% (SD 34%). Women with 66% or more days on therapy between the initial and follow-up DXA did not differ from those not receiving drug therapy or those receiving <66% days on therapy with respect to mean baseline hip or spine BMD, age, or days between the initial and follow-up DXAs. For those women with ≥66% days on therapy, the mean change in spine BMD was 4.5% compared with 1.9% for those with <66% (p=0.01). For those women with ≥66% days on therapy, the mean change in hip BMD was 2.3% compared with 0.2% for those with <66% (p=0.006).

Conclusions: In a population of previously untreated women with osteoporosis diagnosed as part of routine clinical care, only a little more than half initiated treatment in the subsequent year. Patients with more days on therapy had improved bone density response compared with those who obtained fewer days of therapy.

POSTER SESSION II (PS2)

PS2.1 EFFECT OF ZOLEDRONIC ACID COMPARED TO RALOXIFENE ON BONE TURNOVER MARKERS IN POSTMENOPAUSAL WOMEN WITH LOW BONE MINERAL DENSITY

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Change in bone turnover markers at month 6 in the ZOL and RAL groups

	Baseline (mean±SD)	Month 6 (mean±SD)	Change from baseline (mean±SD)	ZOL vs. RAL (LS mean difference) (95%CI)[a]	*p*-value[a]
NTX/creatinine ratio (nMBCE/mM)				−14.3 (−18.6, −10.0)	<0.0001
ZOL	49.1±20.5	23.7±11.9	−24.6±14.0		
RAL	44.5±23.3	34.2±16.5	−8.4±15.4		
BSAP (U/L)				−6.9 (−9.2, −4.7)	<0.0001
ZOL	30.1±10.9	19.2±5.5	−10.6±7.3		
RAL	27.1±9.4	25.0±8.0	−2.3±7.1		

[a] Using analysis of covariance with treatment, center, and baseline as explanatory variables
CI confidence interval, *LS* least squares

Background: Reduction in bone turnover markers has been shown to correlate with increases in bone mineral density and subsequent reduced risk of fractures in patients with osteoporosis. The primary objective of this study was to compare the effect of a bisphosphonate, I.V. zoledronic acid 5 mg (ZOL) and a selective estrogen receptor modulator, oral raloxifene 60 mg daily (RAL) on bone turnover markers.
Methods: This multi-center, double-blind, 6-month, active-controlled trial randomized postmenopausal women with low bone mass defined as a *T*-score ≤−1.5 at lumbar spine or hip. We compared the effects of a single dose of I.V. ZOL vs. daily oral RAL in reducing urine *N*-telopeptide of type 1 collagen/creatinine ratio (NTX) and serum bone-specific alkaline phosphatase (BSAP). Efficacy variables were the changes from baseline in NTX (primary variable) and BSAP (secondary variable). Primary analysis time point for NTX was at 6 months of treatment; other analysis time points were at months 2 and 4. BSAP was also evaluated at months 2, 4 and 6.
Results: A total of 110 patients (56 ZOL, 54 RAL) were randomized. Baseline characteristics of the ZOL and RAL treatment groups were well matched. Median age of the study population was 60.0 years (range 47 to 78 years). ZOL demonstrated a significantly greater reduction in NTX compared to RAL at months 2, 4 and 6 with a treatment difference of −26.1, −22.5 and −14.3 nMBCE/mM, respectively (all *p*-values <0.0001). ZOL also demonstrated a similar significantly greater reduction in BSAP with a treatment difference of −6.8, −8.0 and −6.9 U/L at months 2, 4 and 6, respectively (all *p*-values <0.0001). As expected, during the first 3 days after the ZOL infusion, more patients reported post-dose symptoms including nausea (10.7% ZOL vs. 0.0% RAL), pyrexia (10.7% vs. 0.0%), pain (7.1% vs. 0.0%), and influenza-like illness (5.4% vs. 0.0%).There were no differences in overall incidence of adverse events between groups after 3 days.
Conclusions: A single infusion of ZOL achieved greater reductions in biochemical markers of bone resorption and formation over 6 months compared to daily oral RAL.

PS2.2 REGIONAL DIFFERENCES IN THE MANAGEMENT OF OSTEOPOROSIS: THE GLOBAL LONGITUDINAL STUDY OF OSTEOPOROSIS IN WOMEN

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Aims: To compare use of diagnostic technology and osteoporosis medication in women 55 years and older in four geographic regions.
Methods: The Global Longitudinal study of Osteoporosis in Women (GLOW) is an observational follow-up study of women ≥55 years recruited by 615 primary physician practices (17 sites, ten countries). Practices typical of each region were identified by primary care networks organized for administrative, research or educational purposes. All non-institutionalized patients visiting the practice within the prior 2 years were eligible. Self-administered questionnaires were mailed, with a 2:1 over-sampling of women aged ≥65 years. Data collected included information on demographics; medical history; risk factors for osteoporosis-related fracture; fracture occurrence; self-report of diagnosis including bone mineral density testing and treatment with a bone medication (alendronate, calcitonin, etidronate, ibandronate, pamidronate, raloxifene, risedronate, strontium ranelate, teriparatide, tibolone, zoledronate).

Bone-density testing and bone medication by region

	Bone-density test (%)				Bone medication (%)			
	Australia	Canada	Europe	USA	Australia	Canada	Europe	USA
All women	76	87	54	81	28	30	19	33
Age >65 years	79	87	54	82	34	35	22	39
Age >75 years	76	84	47	79	41	41	24	42
Increased risk of fracture								
Fracture history	86	89	63	84	49	45	33	47
FRACTURE index ≥5	79	85	55	80	43	41	28	42
Self-reported diagnosis[a]								
Normal	63	79	37	69	11	8.8	6.8	10
Osteoporosis	95	97	87	95	67	66	56	76
Osteopenia	96	98	85	97	39	46	27	53

[a] Age-standardized to entire population

Results: Overall, 70% of the 60,393 women in the population reported having had a bone density test; frequency of testing ranged from 54% (Europe) to 87% (Canada). Reported use of bone medications (past or current) averaged 27% (range 19% in Europe to 33% in USA). Current use increased with age and with clinical risk: 37% of women with FRACTURE Index scores ≥5 (indicating a 5-year risk of non-vertebral fracture of 26%) reported taking bone-related medication. Frequencies ranged from 28% in Europe to 43% in Australia. When use was assessed by self-reported diagnosis of osteoporosis or osteopenia, frequency was 67% and 45%, respectively, with 8.6% of women without either diagnosis reporting use.

Conclusions: Management of osteoporosis in this population is not entirely consistent between Europe and other regions involved in GLOW. Use of bone-density testing and bone medications is lower in Europe than in other regions. Even in women with high FRACTURE Index scores, Europe appears to be more conservative than other regions in using medications.

PS2.3 ARZOXIFENE IN POSTMENOPAUSAL WOMEN WITH NORMAL OR LOW BONE MASS

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Background: Arzoxifene is a benzothiophene estrogen agonist/antagonist that is more potent and bioavailable than raloxifene (Palkowitz et al. 1997).

Methods: The study was a 24-month, phase 3, double-blind, multicenter trial of postmenopausal women with femoral neck or lumbar spine bone mineral density (BMD) *T*-score between −2.5 and 0 randomized to arzoxifene 20 mg/day (N=172) or to placebo (N=159). Elemental calcium 500 mg/day was provided. Primary endpoints were lumbar spine and total hip BMD change and endometrial safety.

Results: At baseline, subjects were well matched (Caucasian 83%, mean age 55 years, mean body mass index 28 kg/m^2, mean lumbar spine BMD 0.95 g/cm^2, total hip BMD 0.89 g/cm^2, median CTX 0.58 ng/L, and median PINP 52 μg/L). At 6 months and at subsequent assessments, BMD increases at all skeletal sites were significant (p<0.05) in the arzoxifene vs placebo group. At 24 months, BMD increases in the arzoxifene vs placebo group were lumbar spine 3.2%, total hip 2.3%, femoral neck 2.1%, and trochanter 3.0% (p<0.001 for all comparisons). No significant subgroup treatment effect at any skeletal site was observed (years postmenopausal [>2 and <5 vs ≥5 years], age [<55 vs ≥55 years], and ethnicity [Caucasian vs non-Caucasian]; all p>0.1). At 3 months and at subsequent assessments, CTX and PINP displayed a significant decrease in the arzoxifene vs placebo group (p<0.001), and at 24 months, CTX was decreased by 30% (p<0.001) and PINP was decreased by 31% (p<0.001) in the arzoxifene vs placebo group. There were no significant between-group differences in the incidence of endometrial hyperplasia or cancer as assessed by serial endometrial biopsy (placebo 2, arzoxifene 0) or in endometrial thickness assessed by transvaginal ultrasound. Adverse event monitoring showed no significant increase in adverse events in the arzoxifene group except for the MedDRA term "vulvovaginal mycotic infection" (placebo 0%, arzoxifene 4%, p=0.02). New or worsening hot flashes were not significantly different between the groups (placebo 11%, arzoxifene 12%, p=0.87). There were no deaths or venous thromboembolic events.

Conclusion: In postmenopausal women with normal to low bone mass, arzoxifene 20 mg/day increased BMD at the spine and hip and had a neutral effect on the uterus and endometrium.

PS2.4 EFFECT OF RALOXIFENE ON ALL-CAUSE MORTALITY ACROSS CLINICAL TRIALS

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Background: Raloxifene is a selective estrogen receptor modulator approved in the U.S. for prevention and treatment of osteoporosis in postmenopausal women and for reduction in risk of invasive breast cancer in postmenopausal women with osteoporosis or at high risk for invasive breast cancer. Understanding the effects of preventive treatments on mortality is critical to assessment of the overall risk and benefit. An analysis of all-cause mortality across raloxifene studies has not been reported.
Methods: We performed a pooled analysis of mortality data from large placebo-controlled clinical trials (>1,000 participants) of raloxifene 60 mg/day, including the Multiple Outcomes of Raloxifene Evaluation /Continuing Outcomes Relevant to Evista studies (MORE/CORE: 7,705 postmenopausal women with osteoporosis followed for 4 years and a subset of 4,011 followed for an additional 4 years; 110 deaths) and Raloxifene Use for the Heart (RUTH: 10,101 postmenopausal women with coronary heart disease (CHD) or multiple risk factors for CHD followed for 5.6 years; 1,149 deaths). Cause of death was assessed in all studies by adjudicators blinded to treatment assignment. Since there were no statistically significant interactions of the mortality outcomes in MORE/CORE and RUTH, we used Cox proportional hazards regression models to compare mortality by treatment assignment in a pooled analysis of data from these trials.
Results: All-cause mortality was lower in the raloxifene group than the placebo group. This was primarily due to lower rates of non-cardiovascular deaths, particularly those due to non-cancer causes (Table).
Conclusions: In a pooled analysis of older postmenopausal women, all-cause mortality was 10% lower in women receiving raloxifene 60 mg/day compared to placebo, due primarily to a reduction in non-cardiovascular, particularly non-cancer, death. A limitation of this analysis was the greater contribution of deaths from RUTH versus from MORE/CORE. The mechanism(s) whereby raloxifene might reduce the risk of non-cardiovascular death is uncertain.

Mortality in a pooled analysis of MORE/CORE and RUTH data

Endpoint	No. of events (percent)		Hazard ratio (95%CI)	*p*-value
	Placebo(*N*=7,633)	Raloxifene 60 mg/day (*N*=7,601)		
All cause mortality	660 (8.65)	599 (7.88)	0.90 (0.80, 1.00)	0.053
CV deaths	376 (4.93)	378 (4.97)	0.99 (0.86, 1.15)	0.930
Coronary	286 (3.75)	265 (3.49)	0.92 (0.77, 1.08)	0.303
Cerebrovascular	46 (0.60)	63 (0.83)	1.35 (0.92, 1.98)	0.120
Non-CV deaths	273 (3.58)	216 (2.84)	0.78 (0.65, 0.93)	0.007
Cancer	128 (1.68)	110 (1.45)	0.85 (0.66, 1.09)	0.200
Non-cancer	145 (1.90)	106 (1.39)	0.72 (0.56, 0.93)	0.011

PS2.5 UNDIAGNOSED HYPERPARATHYROIDISM AND HYPOVITAMINOSIS D IN STABLE AFRICAN AMERICAN HEART FAILURE PATIENTS: OVERLOOKED CAUSES OF OSTEOPOROSIS?

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Background: Patients with heart failure (HF) have been observed to be at risk for osteoporosis and bone fracture. As hyperparathyroidism (HPTH) has been noted in hospitalized pts with HF and African Americans have a high prevalence of hypovitaminosis D in the general population, we hypothesized that a high prevalence of these entities could be contributing to the development of osteoporosis in our population of indigent, AA pts with HF.

Methods: We studied 25-OH vitamin D levels, intact PTH (iPTH) and other clinical parameters in 43 randomly chosen stable pts from an inner City HF clinic (no admission to the hospital in past 30 days). No patient had been diagnosed with hyperparathyroidism previously.
Results: The population was 30% female, 100% AA, 28% employed, 68% greater than High School education, 61% income <20,000 per year. Mean age 62.1±11.8 years, cause of HF was ischemic (60%), hypertension (30%), other (10%), months since HF diagnosis 57.1±1.0, BMI 30.3±7.3, ejection fraction at most recent ECHO 34.1±14.4.88% (36) had hypovitaminosis D (25-OH level <40 ng/dL). HPTH was defined as >65 pg/mL. 42% of patients (n=18) had HPTH. Mean PTH was 48.4±2.6 for normals and 115.5±8.4 for HPTH. By t-test pts with HPTH were older (67.8±3.9 vs 58.2±2.0, p=0.011), had higher creatinine values (1.45±0.1 vs 1.09±0.00 mg/dL, p=0.01), and had worse NYHA Class (2.28±0.18 vs 1.8±0.15, p=0.048). There was no difference in 25-OH Vit D Levels (23.9±3.2 vs 27.9±3.0 ng/mL), ionized calcium (1.29±0.00 vs 1.27±0.00 mmol/L), and ionized magne-

sium (0.56±0.00 vs 0.59±0.00). By Chi squared there was no difference in CHF diagnosis or gender between the two groups.
Conclusion: (1) HPTH is highly prevalent in AA's with HF and is associated with older age, higher creatinine and worse NYHA Class. (2) Hypovitaminosis D is also highly prevalent but degree of deficiency was not associated with HPTH, perhaps because of the extremely high prevalence. (3) HPTH is not associated with gender, etiology of HF or ionized calcium or magnesium. (4) Pts with HPTH have higher creatinine values but would be still be considered as falling into the normal range, thus a major contributing factor to HPTH in this population may be hypovitaminosis D. (5) We suggest that routine screening for HPTH and Vitamin D status should be done in all AA pts w HF, with replacement attempted if deficient. (6) It is likely that HPTH and hypovitaminosis D contribute to the increased risk of osteoporosis and fracture in this population. Intervention studies should be designed in order to define the usefulness of Vitamin D replacement in the treatment of both HPTH and osteoporosis in AA's with HF.

PS2.6 BONE AND MINERAL METABOLISM IN ELDERLY PATIENTS WITH PARKINSON'S DISEASE

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Background: Parkinson's disease (PD) and osteoporosis are two common chronic disabling conditions in older adults that adversely affect quality of life. The aim of the present study was to study the relationship between bone changes and Parkinson's disease.
Methods: Eighty-two patients with established PD aged 65 years and above and 68 healthy volunteers were recruited. Exclusion criteria included other known causes of osteoporosis, history of corticosteroid, oestrogen, bisphosphonates, calcium or vitamin D intake. Data including demography, body mass index (BMI), diet, sunlight exposure, Hoehn and Yahr (H and Y) stage, disease duration, disease severity and history of previous falls and/or fractures were collected. Bone mineral density (BMD) was measured at the femoral neck and lumbar spine using dual energy X-ray absorptiometry (DEXA). Sera were analyzed for ionized calcium, phosphate, vitamin D, bone alkaline phosphatase (BALP) and urinary N-terminal telopeptide of type I collagen (NTx). Functional status and quality of life measures assessed included activities of daily living (ADLs), 6-min walk test and grip strength. Plain X-ray films were used to assess vertebral compression fractures (VCFs).
Results: The findings show that the BMD of all the PD patients was significantly lower compared to the controls, $p<0.005$. Twelve male (27.9%) and 19 (48.7%) female patients were diagnosed as osteoporosis. Osteopenia was detected in 16 male (37%) and 18 (46%) female patients. The BMD of the female PD patients was lower compared to the BMD of the male PD patients and to the BMD of the female controls. Significantly lower levels of serum calcium, 25-OHD and 1, 25(OH)2 D were found in PD patients compared to healthy controls. The levels of serum BALP and urinary NTx were significantly higher in patients compared to controls. Forty-six patients (11 males and 35 females) reported a fall(s) and 33 PD patients (seven males and 26 females) had experienced fractures or were found to have VCFs on X-ray. PD patients reported poorer health, less sunlight exposure (none to <15 min/week), greater impairment in ADLs, slower usual gait speed and weaker grip strength compared controls. There was a significant positive correlation between BMD and BMI, ionized calcium and 25-OHD and 1, 25(OH)2 D. A significant negative correlation was found between BMD and (H and Y) stage, disease duration, postmenopausal duration. The findings showed that PD patients with lower BMD, lower 25-OHD and 1, 25(OH)2 D levels, lower BMI, poorer functional status and more advanced (H and Y) stage had increased risk of falls and/or fractures.
Conclusion: PD is associated with an increased incidence of osteoporosis, falls and fractures. PD is thus a risk factor for osteoporosis and appropriate therapeutic interventions (e.g. vitamin D and calcium supplementation) should be initiated to slow or prevent disability.

PS2.7 RISEDRONATE TREATED SUBJECTS' RISK OF NONVERTEBRAL FRACTURE IS SIMILAR TO THAT OF UNTREATED PATIENTS 10 YEARS YOUNGER

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Age is a well recognized independent risk factor for fracture. Generally, older patients have lower BMD *T*-scores and greater risks for fracture. Nonvertebral fractures represent nearly 75% of all osteoporotic fractures, and greater than 90% of all osteoporosis-related fracture costs (Burge R, et al., J Bone Miner Res, 22:465–475, 2007). In this research, the objective was to examine the effect of risedronate on nonvertebral fracture risk as patients age. 3,229 osteoporotic PMO women in clinical trials (VERT, RON and ROE) who took at least one dose of placebo or risedronate 5 mg pill were included in the analysis. Patients ranged from 38 to 85 years in age and had a mean FN *T*-score of −2.2 SD. The fracture endpoint was the incidence of a new osteoporosis related nonvertebral fracture over a 3-year period. The impact of age on fracture risk was examined using Cox regression model with age and treatment as explanatory variables. Both treatment and age had a statistically significant impact on fracture risk. The interaction between treatment and age was included in the initial model but removed from the final model as it was not statistically significant ($p>0.05$). The association of the increased risk for fracture and age did not differ significantly by treatment groups ($p>0.05$ for the interaction term). Regardless of treatment group, for every one decade increase in age, patient risk for any osteoporotic non-vertebral fracture increased approximately 68% on average. It also suggested that the magnitude of the treatment benefit was

consistent regardless of age, i.e. risedronate reduced the fracture risk by 41% with $p<0.001$ after adjusting for age. When comparing 3-year fracture risk between risedronate and placebo patients, we found that fracture risk for patients who had been treated with risedronate 5 mg was estimated to be similar to the placebo patients who were 10.3 (95%CI=4.4, 20.2) years younger in age. 70-year-old patients in the risedronate 5 mg group had a risk of fracture similar to 60-year-old patients in the placebo group. In conclusion, every decade increase in age is associated with an increase in nonvertebral fracture risk by about 50%. In patients treated with risedronate, nonvertebral fracture risk was reduced to the risk seen in untreated patients who were 10 years younger in age.

PS2.8 RENAL SAFETY ACROSS A WIDE RANGE OF DOSING REGIMENS OF RISEDRONATE

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The incidence of osteoporosis and renal insufficiency increases with age; thus, the effect of osteoporosis treatments on renal function is a clinical concern. This retrospective analysis was conducted to study the influence of multiple dosing regimens of risedronate on the renal function of postmenopausal women with osteoporosis or osteoarthritis. Combined data from over 14,000 patients in the risedronate phase III clinical trials of post-menopausal osteoporosis (PMO) and osteoarthritis were analyzed across multiple dose regimens; 5 and 15 mg daily, 35 and 50 mg weekly, 75 mg on two consecutive-days-monthly or 150 mg monthly, or placebo. Median treatment duration was 2 years. Subgroups with baseline renal function impairment or renal risk factors were also examined. Serum creatinine (SCr), estimated serum creatinine clearance (CrCl—Cockroft-Gault) and renal function related adverse events (AEs) were analyzed. 94% of subjects were female, with a mean age of 70 years. The frequency distributions of changes in CrCl from baseline to endpoint value were not different between placebo and risedronate groups or between different dose/regimen groups, for each of the populations examined. Also, there was a similar frequency of patients who developed abnormal SCr or who developed SCr increases >0.5 mg/mL from baseline, within each of the active treatment group and placebo comparisons (Table 1). Patients with baseline renal impairment (CrCl ≤50 mL/min) or baseline renal risk factors (diabetes mellitus, hypertension, ACE inhibitor or NSAID treatment) also did not show treatment group differences. Renal function-related AEs were not different across groups, all ≤2%. While risedronate serum Cmax levels for 75 mg and 150 mg are approximately 11 and 29-fold greater than for 5 mg, there is no indication of adverse renal effects from these higher doses. Risedronate demonstrates a favorable renal safety profile across a wide range of doses, regimens and patient populations, without evidence of effect on renal function parameters.

Table 1 Renal safety endpoints in risedronate post-menopausal osteoporosis studies

Parameter	5 mg daily		75 mg two consecutive days (monthly)		150 mg once a month	
	Placebo (%)	5 mg daily (%)	5 mg daily (%)	75 mg/2CD (%)	5 mg daily (%)	150 mg monthly (%)
Serum Cr—treatment emergent abnormal[a]	8.0	8.4	1.7	1.4	1.7	0.8
Serum Cr—Δ from baseline >0.5 mg/dL at endpoint	0.7	0.7	0.3	0.2	0.0	0.3
Renal function adverse events	1.9	1.5	1.1	0.6	0.5	0.5
CrCl—Δ from baseline to endpoint, mean (SD)	−0.62 (10.14)	−0.42 (9.56)	−3.62 (11.13)	−4.12 (10.94)	−1.14 (7.59)	−1.45 (8.06)
CrCl—Δ from baseline to endpoint (baseline CrCl ≤50), mean (SD)	0.95 (6.36)	0.85 (6.40)	0.97 (8.51)	−0.26 (5.44)	−0.35 (4.79)	0.73 (5.96)

Number of patients varies depending on analysis but numbers of patients treated are the following: 5 mg daily studies (4,878 placebo and 4,846 5 mg daily), two consecutive days (613 5 mg daily and 616 75 mg/2CD), and once a month (642 5 mg daily and 650 150 mg monthly)
[a] Treatment emergent abnormal serum creatinine are patients with a normal baseline creatinine and one or more abnormal values after dosing

PS2.9 DIABETES MELLITUS AND THE RISK OF OSTEOPOROTIC FRACTURE

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Diabetes mellitus has been associated with an increased fracture risk. Interestingly, patients usually have a higher BMD than would be expected, especially those with type 2 disease. The primary objective of this research was to examine the impact of Diabetes Mellitus on the risk of fractures and the correlation with baseline BMD values among post-menopausal women with osteoporosis, in the placebo groups of the pivotal risedronate trials. Baseline

data of 6,072 patients with age of 79 or younger from the VERT trials and HIP were utilized in the analyses. Among those, approximately 5% of patients were identified as diabetic (306 in total) either via medical history or concomitant medication data. 55% (170/306) of the diabetic patients used oral hypoglycemic agents and none were on insulin. Although all were recruited based on BMD in the osteoporotic range, on average, the diabetic patients had a greater BMI relative to non-diabetic patients (27.9 for diabetic patients vs 25.4 non-diabetic patients, $p<0.0001$). The mean age for the diabetic patients (72 years) was similar to the non-diabetic patients ($p=0.6011$). The average years since menopause were statistically significantly different, although only by 1 year and thus not clinically relevant. Diabetic patients had statistically significantly ($p<0.001$) greater BMD values at baseline compared to non-diabetic patients (−2.4 vs −2.6 for mean FN *T*-score and −2.0 vs −2.6 for mean LS *T*-scores, respectively). Even though, the BMD *T*-scores were significantly higher for diabetic patients, prevalent radio-graphical vertebral and osteoporosis related non-vertebral fractures were not statistically significantly different between the diabetic and non-diabetic patients (61% vs 59% for prevalent vertebral fracture and 8% vs 10% for prevalent osteoporosis related non-vertebral fractures, respectively, $p>0.07$). The incidence of vertebral fractures was similar between the diabetic and non-diabetic patients. However, diabetic patients had a statistical significantly greater risk for non-vertebral fracture relative to the non-diabetic patients (RR= 1.69, $p=0.019$). In conclusion, BMD values were higher in the diabetic patients than the non diabetic patients at baseline yet their prevalent vertebral and nonvertebral fracture status was the same. Vertebral fracture risk was the same in osteoporotic postmenopausal women with diabetes and without. The nonvertebral fracture risk was higher in the diabetic patients. Physicians need to be aware of this higher nonvertebral fracture risk in these patients.

PS2.10 EFFICACY AND TOLERABILITY OF 75 MG RISEDRONATE DOSED ON TWO CONSECUTIVE DAYS A MONTH FOR THE TREATMENT OF POSTMENOPAUSAL OSTEOPOROSIS OVER 2 YEARS

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Risedronate 5 mg daily reduces the incidence of vertebral and nonvertebral fractures in patients with postmenopausal osteoporosis. Here we present 2 year results from a double-blind, randomized, active-controlled, parallel-group study that evaluated the efficacy and safety of 75 mg oral risedronate administered on two consecutive-days-a-month (2CDM) compared to 5 mg oral risedronate daily in women with postmenopausal osteoporosis. Postmenopausal women age 50 years or older with a lumbar spine (LS) BMD *T*-score of <−2.5 OR <−2.0 and at least one prevalent vertebral fracture (T4-L4) were enrolled in the study. All subjects received 1000 mg of elemental calcium and 400–800 IU vitamin-D daily. Non-inferiority of the 2CDM regimen to the daily regimen was evaluated based on percent change from baseline in LS-BMD at month 12. The key efficacy variable for year-2 was non-inferiority of the 2CDM regimen to the daily regimen as assessed by percent change from baseline in LS-BMD at month 24. 1,229 women from 61 study sites in 11 countries were randomized and received study drug. Baseline characteristics were well matched between the 2CDM and daily groups, except subjects in the 2CDM group were older (65 vs. 64 years). Mean LS *T*-score was −3.2, and 30% of subjects had prevalent vertebral fractures. At 24 months, mean (SE) LS-BMD had increased 4.2% (0.194) for 2CDM and 4.3% (0.194) for the daily regimen. The upper bound of the 95%CI for the mean difference (0.17%) was 0.679%, less than the predefined 2% non-inferiority margin. BMD differences between the two groups at months 6, 12 or 24 at LS, total hip and trochanter were not significant. The tolerability profile of the 2CDM regimen was generally comparable to the daily regimen. The 2CDM regimen of oral risedronate is a treatment option for osteoporosis in postmenopausal women.

PS2.11 ONCE-A-MONTH RISEDRONATE 150 MG REDUCES OSTEOPOROSIS-RELATED NONVERTEBRAL FRACTURE RISK VS. HISTORIC CONTROL AT 2 YEARS

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The anti-fracture efficacy of new osteoporosis therapies is evaluated in randomized placebo controlled trials. The inclusion of a placebo arm in subsequent studies of other dosing regimens may be limited by practical or ethical considerations. In these cases, an historical control group can be a viable alternative. In a recent active-controlled study, OAM risedronate 150 mg demonstrated increases in bone mineral density (BMD) that were non-inferior to those seen with risedronate 5 mg daily, which has proven anti-fracture efficacy. To assess the anti-fracture efficacy of this new regimen, fracture data collected in the active controlled study of 150 mg of risedronate was analyzed using matched historical control data from previous placebo-controlled trials with identical baseline characteristics. Women in the OAM study were matched with placebo patients in the historical control (HC) studies, Vertebral Efficacy of Risedronate Therapy (VERT) trials and the BMD-NA and BMD-MN trials, for LS BMD and prevalent vertebral fractures. Age and years since menopause were similar between the OAM study and the HC studies. An historical active treatment group was also constructed from the

5 mg daily arm of the VERT trials for comparison with the 5 mg daily and 150 mg OAM treatment groups in the OAM study. Over 2 years, osteoporosis-related nonvertebral fractures occurred in 2.2% of the risedronate 5 mg daily group from the OAM study (n=642) and 2.6% of the 150 mg OAM group (n=650), in 5.7% of the historical placebo patients (n=366, matched from 713) and 1.1% of the risedronate 5 mg daily patients (n=360 matched from 654) in the HC studies. Nonvertebral fracture risk at 24 months was reduced by 56% in the 150 mg OAM group compared with the historical placebo group (OR 0.44; 95%CI 0.22 to 0.89, p= 0.015). OAM risedronate appears as effective as the 5 mg daily dose in reducing the risk of nonvertebral fractures in the first 2 years of treatment when a historical placebo control group is used. The use of appropriate historical control data is an alternative to assess fracture effects in osteoporosis trials for which placebo-controlled data are not available.

PS2.12 VERTEBRAL FRACTURE RISK REDUCTION WITH RISEDRONATE 150 MG ONCE-A-MONTH

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Daily risedronate 5 mg has been shown to reduce vertebral and non-vertebral fracture risk in randomized controlled clinical trials. Other dose regimens of risedronate such as once-a-week, 75 mg on two consecutive days per month and once-a-month (OaM) risedronate 150 mg have been evaluated in non-inferiority trials with changes in bone mineral density as the primary endpoint. To assess the anti-fracture efficacy of some of these other doses, an analysis utilizing matched historical controls may be a useful method. Utilizing the historical control approach, we have recently shown the anti-fracture efficacy of the once-a-week and the 75 mg risedronate on two consecutive days a month doses. In the present work, we assessed the anti-fracture efficacy of the once-a-month risedronate 150 mg. Women in the once-a-month study were matched with placebo patients in the Vertebral Efficacy of Risedronate Therapy (VERT) trials for baseline characteristics, such as age, years since menopause, BMD and prevalent vertebral fractures. Vertebral fracture incidence was 1.4% (n= 650) and 5% (n=101, matched from 988) respectively in the 150 mg once-a-month and the historical placebo groups respectively. At 1 year, vertebral fracture risk was reduced by 72% in the once-a-month 150 mg group compared to the historical placebo group, (p=0.032), similar to that observed in the VERT trials (61–65%). The incidence of new vertebral fractures in the 5 mg historical group (n=99 matched from 979) was 2%, leading to a risk reduction of about 60% compared to the historical placebo group, providing internal validation. OaM risedronate 150 mg appears to reduce vertebral fracture risk to the same extent as the 5 mg daily dose. Use of matched historical controls may be an attractive approach to assess fracture effects of osteoporosis treatments when placebo controlled data are not available.

PS2.13 IBANDRONATE DOES NOT SHOW INCREASED RISK OF ATRIAL FIBRILLATION: RESULTS OF A POOLED ANALYSIS OF CLINICAL TRIALS

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Background: Results from a clinical trial with annual zoledronic acid infusion in PMO patients showed an increased risk of atrial fibrillation (AF) as a serious adverse event (SAE), raising concern that AF may be a class effect of bisphosphonates.
Objective: This pooled analysis examined the incidence of AF adverse events (AEs) and SAEs in the four pivotal ibandronate trials in women with postmenopausal osteoporosis (PMO) and assessed whether increased dose or duration of exposure affected AF incidence.
Methods: Data from the safety populations of the BONE, IV fracture study, MOBILE, and DIVA studies were included. Patients received oral or IV doses of ibandronate or placebo. BONE and the IV fracture study were 3-year placebo-controlled fracture trials and MOBILE and DIVA were 2-year active-controlled BMD studies. The incidence of AEs and SAEs of AF was assessed for all trials with ibandronate versus placebo, and by increasing ibandronate dose in individual trials. The effect of duration of exposure on AF events was assessed using Kaplan–Meier (KM) analysis. Ibandronate doses were grouped according to annual cumulative exposure (ACE): high doses (≥10.8 mg includes 150 mg oral monthly, 3 mg IV quarterly, and 2 mg IV every 2 months), mid doses (5.5–7.2 mg), and low doses (≤4.0 mg). ACE was defined as the drug strength (in mg) multiplied by the number of annual doses and the bioavailability (0.6% for oral and 100% for IV).
Results: In the pooled safety populations, a total of 75 patients reported AEs of AF (ibandronate 0.8% [57/6,830] and placebo 0.9% [18/1,924]). Of these, 36 patients reported AF as SAE (0.4% in both ibandronate and placebo groups). No cumulative effect of ibandronate treatment over time was observed. There was no increased incidence or dose response effect in all AEs or SAEs of AF with ibandronate by ACE dose category.
Conclusions: Results of this analysis of the four pivotal ibandronate studies indicate that, in women with PMO treated with ibandronate, there is no increased risk of AEs or serious AEs of AF, no dose-response effect, and no cumulative effect of treatment over time.

PS2.14 RISK FACTORS FOR FRAGILITY FRACTURE IN A MULTIRACIAL COHORT OF US WOMEN: THE GLOBAL LONGITUDINAL STUDY OF OSTEOPOROSIS IN WOMEN

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Aim: To identify risk factors for fragility fracture in a multiracial cohort of women from the USA.
Methods: GLOW is a prospective, multinational, observational study. Seventeen sites in ten countries in North America, Australia and Europe are participating. Practices typical of each region were identified through primary care networks organized for administrative, research or educational purposes. The present report is limited to data collected in US Caucasian, Black, and Asian women. All non-institutionalized women 55 years and older who visited the practices within the previous 2 years were eligible. Self-administered questionnaires were mailed, with 2:1 over-sampling of women aged 65 years and older.
Results: A total of 27,192 patients from 255 physician practices included 24,461 Caucasian, 2,271 Black, and 460 Asian women. Risk factors for fracture (established from studies of primarily Caucasian populations) varied among the three groups (Table). Caucasian women had highest prevalence of personal history of fracture, parental fracture, alcohol and steroid use. Black women reported more smoking, use of arms in rising, and rheumatoid arthritis. Asians had the highest prevalence of weight <125 lb (57 kg). Black women reported prior fracture rates that varied from 21% (rib) to 145% (upper leg) of Caucasians' prior fracture rates. Asian women tended towards intermediate values. Both Black and Asian women had hip fracture rates similar to those for Caucasians.

Age-standardized patient risk factors for fracture, by race

	Caucasian (n=24,461) (%)	Black (n=2,271) (%)	Asian (n=460) (%)
Weight <125 lb (57 kg)	15.4	4.8	47.6
Current smoker	7.3	12.4	4.0
Personal history of fracture	23.8	14.3	18.7
Parental fracture	17.3	7.2	11.2
Alcoholic drinks (>20 per week)	0.4	0.1	0.0
Arms used to assist from sitting	35.7	55.0	24.0
Steroid use	35.7	23.7	21.7
Rheumatoid arthritis	8.0	21.0	11.0
Secondary osteoporosis	16.0	25.2	15.6

Conclusions: Racial differences for prevalent fractures and clinical risk factors for fragility fracture were observed in this US cohort. Prevalence of prior fractures among both Black and Asian women, although less than that of Caucasian women, is substantial and places them at risk for future fracture.

PS2.15 EFFICACY AND SAFETY OF ZOLEDRONIC ACID 5 MG IN THE PREVENTION OF OSTEOPOROSIS IN POSTMENOPAUSAL WOMEN WITH OSTEOPENIA: THE HORIZON PREVENTION STUDY

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Background: Zoledronic acid (ZOL) prevents bone loss and reduces fracture risk in post-menopausal women with osteoporosis. As the majority of osteoporotic fractures occur in postmenopausal women with low bone mass (or osteopenia), this study was designed to evaluate the efficacy and safety of two ZOL I.V. regimens in the prevention of bone loss in postmenopausal women with low bone mineral density (BMD).
Methods: In this 2-year, randomized, double-blind, placebo-controlled study participants (aged ≥45) with low BMD (T-score <−1.0 and >−2.5 at lumbar spine [LS] and >−2.5 at femoral neck) received either ZOL 5 mg I.V. at randomization and month 12 (ZOL12), ZOL 5 mg i.v. only at randomization and placebo at month 12 (ZOL24), or placebo at randomization and month 12 (PBO). The primary efficacy endpoint was the percentage change in LS BMD from baseline to month 24. The secondary efficacy endpoints were the percentage changes in LS, total hip, femoral neck, trochanter and distal radius BMD at months 12 and 24 relative to baseline and changes in bone turnover markers (β-C-terminal telopeptides of type 1 collagen [βCTX], procollagen type 1 N-terminal propeptide [P1NP] and bone specific alkaline phosphatase [BSAP]).
Results: Baseline characteristics of all participants (n=531) were comparable. Majority were Caucasians (≥90%) and the mean age was comparable across the treatment groups. At month 24, both ZOL12 and ZOL24 regimens showed significant increase in LS BMD compared to PBO (mean percentage change [SD]=5.31 [3.269] and 4.55 [3.665] vs. −1.19 [3.889]; both p<0.0001). Similarly, both ZOL regimens were superior over PBO in increasing BMD at LS at month 12 and at total hip, femoral neck and trochanter at months 12 and 24 (all p<0.0001). Both ZOL regimens showed significant reductions in βCTX, P1NP and BSAP compared to PBO at months 12 and 24, (all p<0.0001), however these reductions were greater with ZOL12 compared to ZOL24 regimen during the second year (all p<0.001). The incidence of adverse events (AEs) was comparable in all groups (93.9%, 95.6% and 92.1%, in ZOL12, ZOL24 and PBO,

respectively). Post-dose symptoms were the most common AEs within 3 days after the first drug infusion in both ZOL regimens. There was no confirmed occurrence of atrial fibrillation, osteonecrosis of the jaw or differences between groups with respect to the long-term renal function. Serious AEs were similar across all treatment groups.

Conclusion: Both zoledronic acid regimens increased bone density and reduced bone turnover in postmenopausal women with low bone mass and were well tolerated. Intravenous zoledronic acid appears to be an effective strategy to prevent osteoporosis in postmenopausal women.

PS2.16 BONE MINERAL DENSITY AFTER HIP FRACTURE: VARIATIONS IN RESPONSE TO ONCE-YEARLY I.V. ZOLEDRONIC ACID 5 MG

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Background: Lyles et al. (N Engl J Med, 357:1799–1809, 2007) reported a 35% risk-reduction of all clinical fractures along with significant increases in total hip and femoral neck bone mineral density (BMD) with zoledronic acid (ZOL) compared to placebo. This retrospective analysis was conducted to identify the subgroup of patients who had greater or lesser BMD benefit following a hip fracture.

Methods: There were 2,127 recent hip fracture subjects who were randomized to receive once-yearly i.v. ZOL 5 mg or placebo. ANOVA models (with treatment, geographic region, subgroup, and treatment-by-subgroup interaction) for the percentage change in total hip and femoral neck BMD relative to baseline were used to evaluate the effects of ZOL within and across the subgroups. Treatment-by-subgroup interaction was considered significant if $p<0.10$. Subgroups included baseline levels of gender, age, body mass index, baseline femoral neck BMD, location of hip fracture, fracture history, and mental status by The Short Portable Mental Status Questionnaire.

Results: Overall, ZOL 5 mg consistently improved total hip and femoral neck BMD at months 12 and 24 compared to placebo across all subgroups. The table shows the subgroups that achieved greater statistically significant improvement in total hip or femoral neck BMD with ZOL compared to placebo.

Conclusion: ZOL consistently showed a reduction in fracture risk and mortality as well as an increased total hip or femoral neck BMD at months 12 and 24 relative to baseline across all subgroups. In addition, patients at highest risk for bone loss after hip fracture repair (aged ≥85 years, BMD *T*-score <−2.5, history of vertebral and non-vertebral fracture in addition to the baseline hip fracture) experienced greater increases in BMD than observed for the rest of the ZOL-treated population compared to placebo.

Subgroups with relatively increased total hip or femoral neck BMD

Subgroups	Variables	LS mean difference percent (*p*-value) month 12	LS mean difference percent (*p*-value) month 24
Aged ≥85 years	Percent change in TH BMD	6.5 (0.0045)	–
T-score <−2.5	Percent change in TH BMD	4.5 (<0.0001)	–
Fracture history (vertebral and non-vertebral)	Percent change in TH BMD	8.7 (0.0031)	13.4 (0.0692)
Fracture history (vertebral and non-vertebral)	Percent change in FN BMD	7.9 (0.0190)	13.4 (0.0692)

PS2.17 HIGH SENSITIVITY C-REACTIVE PROTEIN (HSCRP), SUBCLINICAL ATHEROSCLEROSIS AND BONE TURNOVER BIOMARKERS IN POSTMENOPAUSAL WOMEN WITH OSTEOPOROSIS: IS THERE A LINK?

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Background: Osteoporosis and atherosclerosis are common and important health problems. Accumulating evidence suggests an association between the two conditions. High sensitivity C-reactive protein (hsCRP), a marker of systemic inflammation, has been identified as a new independent risk factor for atherosclerosis. Low bone mass and osteoporosis has been related to increased cardiovascular morbidity and mortality. Accordingly, the aim of the present work was to assess the association between hsCRP, subclinical atherosclerosis and bone turnover markers in postmenopausal women with osteoporosis.

Methods: Sixty-eight newly diagnosed primary osteoporotic postmenopausal women, mean age 60.5 years, were studied. Bone mineral density (BMD) was measured at the femoral neck (FN) and lumbar spine (LS) using dual energy X-ray absorptiometry (DEXA). According to the WHO definition, osteoporosis was diagnosed at *T* score −2.5 at any site. Subclinical atherosclerosis was detected by carotid-intima media thickness (CIMT) using B-mode ultrasonography. Serum hsCRP, serum bone specific alkaline phosphatase (BALP) and urinary N-terminal telopeptide of type I collagen (NTx) were measured using enzyme-linked immunosorbent assay (ELISA). Serum lipids including total

cholesterol (TC), triglycerides (TG), HDL-C and LDL-C were measured. Values were compared to age-sex-body mass index (BMI) matched healthy volunteers.

Results: Serum hsCRP levels were significantly increased in patients with osteoporosis compared to control subjects, $p<0.005$. Both serum BALP and urinary NTx were significantly higher in patients compared to controls. Serum hsCRP levels correlated positively with increased serum BALP and urinary NTx levels and this significant correlation remained after adjusting for age and body mass index. CIMT was significantly increased in postmenopausal women with osteoporosis when compared to the healthy controls, $p<0.01$. There was a statistically significant correlation between hsCRP and CIMT, $p<0.05$; $r=0.558$. A significant negative correlation was found between CIMT and both FN and LS BMD. There was a modest increase in TC, TG and LDL-C levels in patients with osteoporosis versus controls, however this increase did not reach statistical significance. HDL-C levels in patients with osteoporosis were lower compared to controls, $p<0.03$.

Conclusion: The findings suggest that hsCRP, a marker of systemic inflammation, may be associated with an increased risk of both atherosclerosis and osteoporosis. Chronic inflammation may be the link between osteoporosis and atherosclerosis. The implication is that by controlling inflammation it may be possible to retard both atherosclerosis and osteoporosis.

PS2.18 FRAGILITY FRACTURES AND HEALTH STATUS IN A MULTINATIONAL COHORT: THE GLOBAL LONGITUDINAL STUDY OF OSTEOPOROSIS IN WOMEN

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Aim: To examine baseline self-rated health among women with and without prevalent fractures.

Methods: The Global Longitudinal study of Osteoporosis in Women (GLOW) is an observational follow-up study of women aged ≥55 years recruited by 615 primary physician practices (17 sites, ten countries). Practices typical of each region were identified through primary care networks organized for administrative, research or educational purposes. All non-institutionalized women visiting the practice within the prior 2 years were eligible. Self-administered questionnaires were mailed, with a 2:1 oversampling of women ≥65 years. Data on occurrence of prior fractures since age 45 at any of ten bone locations were collected. Respondents rated their overall health on a five-point scale, from "excellent" to "poor," and completed EQ-5D, a generic instrument that captures five dimensions of health status (mobility, self-care, usual activities, pain/discomfort, anxiety/depression).

Results: Among 57,141 women, 23% reported ≥1 fracture since age 45. Site-specific prevalence varied from 8.4% (wrist) to 1.06% (pelvis). Prevalence of "fair" or "poor" self-rated health was 20% for women without fractures vs 41% for those with multiple fractures (range 28% for wrist to 45% for spinal fracture). Mean EQ-5D scores were higher in women without fractures (0.78 vs 0.74 or 0.65 of a possible score of 1.00), and tended to indicate greater impairment for those who had had fractures to spine, hip, and upper leg.

Overall self-rated health status and fracture history (age standardized)

	No fracture (%)	Any 1 fracture (%)	Multiple fractures (%)
Subjects	77	17	6
EQ-5D: "any problems"			
Mobility	26	34	50
Self care	6	9	18
Usual activities	26	33	50
Pain	68	73	83
Anxiety	40	44	54
EQ-5D, mean (SD)	0.78 (0.06)	0.74 (0.05)	0.65 (0.07)
SF-36: "any limitations"			
Vigorous activity	79	82	88
Moderate activity	39	48	63
Bathe or dress self	11	15	24
Health "fair" or "poor"	20	27	41

$p<0.0001$

Conclusion: Women who have sustained fractures after age 45 reported poorer health status than contemporaries without fractures, particularly women with fractures of the spine, hip and pelvis.

PS2.19 SUBOPTIMAL OSTEOPOROSIS DIAGNOSIS AND TREATMENT IN PATIENTS WITH HIP FRACTURE BEFORE AND AFTER THIS SENTINEL EVENT

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Background: One in two women and one in four men over age 50 will have an osteoporosis-related fracture in her/his remaining lifetime. The most concerning complication of osteoporosis is hip fracture with significant morbidity and mortality. An average of

24% of hip fracture patients aged 50 and over dies in the year following their fracture. We hypothesized that osteoporosis is under-diagnosed and undertreated even after a sentinel event like fractured hip.

Method: We performed a retrospective chart review of 191 patients admitted with hip fracture to a hospital compiling data of demographics, diagnoses and medical therapy of osteoporosis, and GFR. By follow-up phone survey we successfully acquired data from 105 patients (55%) regarding their care from a doctor within the past 6 months, their awareness and treatment of their diagnoses of osteoporosis and subsequent fractures. 63 patients (33%) were confirmed deceased in the interim from discharge to the phone survey.12% could not be located. Data was analyzed using SPSS software.

Results: From the hospital chart review: 80% of patients were white females over 70. Only 30% of patients were taking calcium and 15% were taking Bisphosphonates. 25% were assigned diagnosis of osteoporosis and this correlated positively with both calcium and Bisphosphonates therapy (both $p<0.001$). Only 2% of patient had GFR less than 30, which might be a contraindication for bisphosphonates. From the phone survey: 105 patients contacted during phone survey reported seeing doctor within 6 months. Only 50% were aware of diagnosis of osteoporosis. About 50% were taking calcium and 40% were taking vitamin D. Only 28%were taking bisphosphonates. Intake of bisphosphonates correlated positively with the diagnosis of osteoporosis ($p=0.024$). 14%of accessible patients had a subsequent fracture.

Conclusion: Our study shows that even after fracture, many patients still remain uneducated and untreated for Osteoporosis. There is a need for increased patient education and treatment for osteoporosis. A standardized system which improves recognition and treatment of predisposing osteoporosis during the hospitalization for a sentinel hip fracture should be developed. Patient education about osteoporosis should be enhanced during hospital stays by case managers, physicians, residents. We have developed an Osteoporosis protocol for our hospital for any osteoporotic fracture to ensure that the treatment for osteoporosis is implemented before the discharge.

PS2.20 DENOSUMAB FOLLOWING LONG-TERM ALENDRONATE IN POSTMENOPAUSAL WOMEN WITH LOW BONE MINERAL DENSITY

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Background: Previous studies showed the RANKL inhibitor denosumab reduced fractures, increased BMD, and decreased bone turnover in postmenopausal women with osteoporosis. Although numerous therapies exist to treat osteoporosis, patients switch between therapies, and it is important to investigate the outcomes after changing therapies.

Methods: In this international, randomized, double-blind, double-dummy study, postmenopausal women ≥55 years old with a lumbar spine or total hip *T*-score of ≤−2.0 and ≥−4.0 who had received alendronate therapy equivalent to 70 mg/week for ≥6 months were eligible. All subjects received open-label branded oral alendronate 70 mg once weekly for 1 month, then were randomized (1:1) to continue receiving branded alendronate weekly plus subcutaneous placebo injections every 6 months (Q6M) or to receive subcutaneous denosumab injections (60 mg Q6M) plus oral placebo weekly. Randomization was stratified by length of prior alendronate therapy (6 to <12; 12 to 24; >24 months). All subjects received daily supplements of calcium and vitamin D. The primary endpoint was percent change in total hip BMD at 12 months.

Results: A total of 504 subjects with a mean age of 67.6 years and mean lumbar spine *T*-score of −2.63 were enrolled. Subjects had taken bisphosphonate therapy for a median of 36 months. In subjects transitioning to denosumab, total hip BMD increased by 1.90% at 12 months compared with a 1.05% increase in subjects continuing on alendronate ($p<0.0001$). BMD changes at the total hip with denosumab were largest in subjects with 6 to <12 months of prior ALN exposure (DMAb 2.34%; ALN 1.19%;) and smallest in subjects with >24 months of prior alendronate exposure (DMAb +1.69%; ALN 0.97%), ($p<0.05$ vs alendronate for both), which may reflect a reduced number of remodeling spaces after long-term bisphosphonate use. Denosumab also produced greater BMD gains than alendronate at the lumbar spine (3.03% vs 1.85%), femoral neck (1.40% vs 0.41%), trochanter (2.95% vs 1.90%), and 1/3 radius (0.87% vs 0.15%) ($p<0.0125$ for all). Subject incidence and types of adverse events and serious adverse events were similar between the two groups. Nasopharyngitis and back pain were most common.

Conclusion: In these postmenopausal women previously treated with alendronate, denosumab produced greater increases in BMD at all measured skeletal sites than did continued alendronate, with a similar safety profile in both groups. These results may reflect the different mechanisms of inhibiting bone turnover between the two drugs.

PS2.21 LOWER TRABECULAR BONE MINERAL DENSITY AND THINNER CORTICES AT PERIPHERAL BONES IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Introduction: It is well established that peripheral areal bone mineral density (aBMD) measured by dual X-ray absorptiometry (DXA) and the juxta-articular BMD metacarpal index (ratio of cortical area/total bone area) assessed by plain radiographs are reduced in patients with RA compared to the general population. Using peripheral quantitative computed tomography (pQCT), the aim of the present study was to compose a more detailed assessment of trabecular and cortical bone involvement in RA.
Methods: Consecutive RA patients seen at the Department of Rheumatology of the Inselspital Bern were recruited. PQCT measurements were performed at the distal epiphyses and mid-shafts of the radius, tibia and third metacarpal (additional measurement was placed at one third of bone length from the distal end of the third metacarpal). At the epiphyses bone mineral content (BMC), total BMD and trabecular BMD of the central 45% of the bone cross sectional area (CSA) were determined. At the shafts, total bone CSA (including medullary CSA), cortical bone CSA (excluding medullary CSA), cortical wall thickness, and cortical BMD were determined. Bone parameters were compared to those recently measured in a healthy reference population in our department by means of independent *t*-tests.
Results: Twenty-six RA patients and 133 reference participants were analysed for this abstract. RA patients and reference population were comparable with regard to age, sex and weight, but were 3.6 cm smaller than the reference group. Trabecular and total BMD were lower in RA patients than controls at the distal radius, distal tibia and distal metacarpal bone (95% confidence intervals not overlapping). At all measured shafts, cortical wall thickness was thinner in RA patients. At the third metacarpal bone, at both 30% and 50% from the distal bone end, total bone CSA was greater in RA patients (with a concomitantly thinner cortex), implying that recurring inflammation causes periosteal bone formation drift. In addition, trabecular BMD at the third metacarpal tended to be lower in patients with erosive RA than in patients without erosive changes.
Conclusions: In peripheral bones, total and trabecular BMD is lower and shaft cortices are thinner in RA patients compared to healthy controls.

PS2.22 HYPONATREMIA-INDUCED OSTEOPOROSIS

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Background: There is a high prevalence of chronic hyponatremia, defined as serum Na <135 mmol/L, in the aging population, frequently due to the inappropriate secretion of antidiuretic hormone (SIADH). Although this condition is often asymptomatic, recent reports have shown adverse effects on cognitive function and gait stability, leading to an increased risk of falling, which alone represents a risk factor for fractures. Here we tested the hypothesis that prolonged hyponatremia also contributes metabolically to bone loss by activating bone resorption to release stored sodium from bone.
Methods: We therefore initiated studies to evaluate if chronic hyponatremia represents a secondary cause of osteoporosis using a rat model of SIADH and analysis of a representative human database. We adapted our rat model of hyponatremia to 22 months old male F344 Brown Norway hybrid rats (F344BN), a well-known model of aging. Hyponatremia was maintained for 3 months by infusing desmopressin via mini-pumps (5 ng/h) and feeding a liquid diet. Normonatremic control rats also received desmopressin, but were pair-fed with a solid diet of equivalent composition to the liquid diet.
Results: Biweekly measurements of BMD by DXA demonstrated that hyponatremia induced more profound progressive bone loss (AP spine −20%, total femur −17.5%, proximal tibia −20% per month) than aging alone (AP spine −3%, total femur −2%, proximal tibia −0.7% per month). In another experiment on 12 months old male F344BN rats, hyponatremia for 3 months induced a similar 30% decrease in femoral BMD, whereas liquid diet alone in controls did not change BMD. Hyponatremia caused severe trabecular and cortical bone losses, as documented by micro-computed tomography (μCT), and histomorphometry. Histomorphometry and in vitro osteoclastogenesis studies indicted that the bone loss was due to increased bone resorption. Analysis of data from the Third National Health and Nutrition Examination Survey by multiple linear regression models demonstrated that among hyponatremics, serum [Na^+] explained 14.7% of the variation in total hip BMD; for every 1 mmol/L decrease in serum [Na^+], total hip BMD decreased by 0.037 gm/cm^2. Moreover, hyponatremia was independently associated with increased odds of osteoporosis (*T*-scores<−2.5) at the hip (odds ratio=2.85; 95% CI 1.03–7.86, $p<0.01$). All models were adjusted for age, sex, race, BMI, physical activity, serum 25(OH)D levels, and history of diuretic use and smoking.
Conclusion: Our results represent the first demonstration that chronic hyponatremia causes substantial bone mineral loss, a metabolic effect increasing fracture risk. Cross-sectional human data showing that hyponatremia is associated with significantly increased odds of osteoporosis are consistent with the experimental data in rodents, and suggest that bone quality should be assessed in all patients with chronic hyponatremia.

PS2.23 FAILURE TO PERCEIVE INCREASED RISK OF FRACTURE IN WOMEN 55 YEARS AND OLDER: THE GLOBAL LONGITUDINAL STUDY OF OSTEOPOROSIS IN WOMEN

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Aim: To compare self-perceived risk of osteoporotic fracture among women 55 years and older with reported risk factors.
Methods: The Global Longitudinal study of Osteoporosis in Women is an observational, longitudinal study of women 55 years and older recruited by 615 primary physician practices (17 sites, ten countries). Practices typical of each region were identified by primary care networks organized for administrative, research or educational purposes. All non-institutionalized patients visiting the practice within the prior 2 years were eligible. Self-administered questionnaires were mailed, with a 2:1 over-sampling of women ≥65 years. Data collected included information on demographics; medical history; risk factors for osteoporosis-related fracture; fracture occurrence; self-report of prevention, diagnosis and treatment of osteoporosis. Respondents rated their perceived risk of fracture vs women of the same age using a five-point scale from "much lower" to "much higher."
Results: Of the women with no risk factors, 89% believed their risk was the same as or lower than that of women of the same age, whereas the majority of women with risk factors failed to appreciate their increased risk of fracture (Table). Among women diagnosed with osteoporosis, 55% believed they were not at increased risk. One quarter of the 17,938 women with a FRACTURE Index ≥5 perceived themselves at higher risk.

Perceived risk of fracture compared with women of same age

Risk factor	*N*	Perceived risk of fracture	
		Lower or the same as (%)	Higher (%)
No risk factor	25,301	89	11
History of fracture	13,760	64	36
Maternal hip fracture	7,199	74	26
Parental hip fracture	8,941	75	25
Weight <125 lb (57 kg)	9,142	74	26
Smoker	5,299	80	20
Alcohol >20 U/week	287	77	23
Current steroid use	1,797	61	39
Rheumatoid arthritis	6,111	71	29
FRACTURE index ≥5	17,938	75	25
Diagnosis			
Osteoporosis	12,429	55	45
Osteopenia	9,974	75	25
Normal BMD	36,031	92	8

Conclusions: Most women at elevated likelihood of osteoporotic fracture do not perceive themselves to be at increased risk.

POSTER SESSION III (PS3)

PS3.1 DISTRIBUTION OF RISK FACTORS FOR FRACTURE IN WOMEN WITH AND WITHOUT A FRACTURE HISTORY: A REGIONAL COMPARISON. THE GLOBAL LONGITUDINAL STUDY OF OSTEOPOROSIS IN WOMEN

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Aim: To compare the prevalence of risk factors for fracture in three geographic regions in women with and without report of prior fracture, in a large cohort of women 55 years and older.
Methods: The Global Longitudinal study of Osteoporosis in Women (GLOW) is an observational follow-up study of 60,393 women aged 55 years and older recruited through 615 primary physician practices (17 sites, ten countries). Practices typical of each region were identified. All non-institutionalized patients visiting the practice within the prior 2 years were eligible. Self-administered questionnaires were mailed, with 2:1 over-sampling of those aged ≥65. Reminder postcards and second surveys were sent to enhance participation; in some sites patients were followed-up by telephone. Follow-up questionnaires will be sent at 12-month intervals for 5 years.
Results: Among women who reported a history of fracture after age 45, 45% required their arms to rise from sitting versus 30% of those without a history of fracture. Overall, 28% of women with a history of fracture reported cortisone use vs 24% in those without a fracture history. Women in the US with a fracture history were more likely to report being on cortisone (40%) than European women with a fracture history (17%) (Table). Of the women in Australia and Canada without a fracture history, 0.9% reported drinking >20 alcoholic drinks per week vs 0.5% of European women and 0.3% of US women. When comparing the three regions, all variables were highly significantly different ($p<0.004$) except for weight <125 lb in women with a fracture history ($p<0.0147$).

Age-standardized prevalence of risk factors for fracture

Risk factor (%)	History of fracture (n=11,893)			No history of fracture (n=38,333)		
	Can/Aust (n=1,448)	Europe (n=5,494)	USA (n=4,951)	Can/Aust (n=4,936)	Europe (n=16,965)	USA (n=16,432)
Maternal hip fracture	15	13	16	12	11	12
Weight <125 lbs (57 kg)	18	19	15	15	18	14
Current smoker	8.6	11	9.3	8.5	11	7.6
Arms used to assist from sitting	41	37	46	31	29	34
Parental fracture	18	17	20	15	13	15
Cortisone (ever taken)	28	17	40	24	13	33
Alcoholic drinks (>14/week)	1.3	0.5	0.4	0.9	0.5	0.3
Rheumatoid arthritis	12	14	11	9.0	11	9.0

Conclusions: In this international "real-world" population of women, self-reported risk factors for fracture varied widely by both geographic region and by history (vs no history) of fracture.

PS3.2 USING QUANTITATIVE ULTRASOUND TO DETERMINE PREVALENCE OF LOW BONE DENSITY IN A MULTIETHNIC ELDERLY POPULATION

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Background: Prevalence of osteoporosis among white women has been extensively investigated. However, for a very advanced elderly population, there is limited data on the prevalence of low bone mineral density (BMD) especially among men and ethnic minorities (Broussard and Magnus, Osteoporos Int, 15:349–360, 2004; Dawson-Hughes, J Clin Endocrinol Metab, 93(7):2463–2465, 2008).
Methods: In this study, we use quantitative ultrasound (QUS) of the calcaneus to determine whether these gender and ethnic disparities in low BMD exist when studying a diverse, frail elderly population. This study also obtained results the FRAX algorithm, developed by the World Health Organization (Dawson-Hughes, J Clin Endocrinol Metab, 93(7):2463–2465, 2008), to assess if there is additional benefit in either screening tool. In this IRB approved study, patients (age ≥65 years) were recruited from an urban outpatient geriatric practice in the Bronx to complete a short questionnaire and receive a free heel ultrasound test. Patients provided informed consent. Data were entered and analyzed using SPSS 15.0. Descriptive statistics was used to define the population. Significance testing between racial groups was assessed with ANOVA for continuous variables and with χ^2 tests for categorical variables. A p-value of ≤0.05 was considered significant.
Results: A total of 144 patients underwent QUS screening. Of these, 39 patients had a DXA within 5 years of the test and were excluded. The remaining 105 subjects had either never had a DXA (92), or had a DXA greater than 5 years prior to the study (13). Of these 105 subjects, 30 were white (29%), 42 were black (41%), and 31 were Hispanic (30%). The mean age of the study population was 80.8 years. Over a quarter of these patients reported prior fracture, and a minority of patients were taking a multivitamin or were being treated with calcium, vitamin D, or bisphosphonates. There was a significant difference between the rates of osteoporosis and osteopenia in men and women (p=0.003) but no significant difference by racial/ethnic background (p=0.148). The intra-rater reliability of the QUS was 0.94. Both the QUS and FRAX algorithm identified 20% to be at high risk for hip fracture and to have osteoporosis. The FRAX algorithm identified additional 34% at high risk for hip fracture and warranting osteoporosis, whereas the QUS identified an additional 9% with osteoporosis and warranting osteoporosis therapy.
Conclusion: These results suggest that although sex differences exist, very old age may confer equal risk for developing low bone density irrespective of racial/ethnic identity. The heel ultrasound detected an additional 9% with osteoporosis who would not have been identified as high risk by the FRAX algorithm.

PS3.3 REAL-WORLD EFFECTIVENESS OF BISPHOSPHONATES FOR THE REDUCTION OF CLINICAL FRACTURES

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In the United States, three oral bisphosphonates (alendronate, risedronate, ibandronate) have been available for the treatment of

osteoporosis for several years. Now, there is an opportunity to observe if the effectiveness of each bisphosphonate for fracture reduction in clinical practice is consistent with the efficacies established in the prospectively planned analysis of their respective randomized controlled trials. In this observational study, cohort of women aged ≥65 years starting treatment with any of the three bisphosphonates were followed within two databases of healthcare utilization records inclusive of years 2000–2006. To describe the fracture risk at the time of initiating a bisphosphonate, up to a 5-year history period was available to obtain measures of co-morbidities, medication history and a FRAX® probability of fracture. To estimate the effectiveness of each bisphosphonate, a pre-post study design was used to assess if the clinical fracture incidence decreased with adherence to an individual bisphosphonate. 'Pre' was defined by the fracture incidence during a wash-in phase of 3 months after starting therapy and 'post' was defined by the fracture incidence in the subsequent 1-year follow-up on therapy. Of the 210,157 patients initiating bisphosphonate therapy, those initiating ibandronate were younger, had less fracture history, greater prior bisphosphonate use, and a lower FRAX® probability of fracture than those initiating either risedronate or alendronate. Relative to the wash-in phase, the incidence of clinical fractures was lower in the subsequent year of therapy at all fracture sites with both alendronate and risedronate. No difference in fracture incidence was observed at non-vertebral or hip sites with ibandronate (Table). Overall, these data show that the effectiveness of bisphosphonates in real-world practice is consistent with results from phase III clinical trials.

Fracture per site	Nonvertebral sites	Hip	Vertebral sites
Alendronate [n=116,999]	–	–	–
Fracture risk reduction (%)	−28	−18	−57
Relative fracture risk	0.72	0.82	0.43
95% confidence interval	0.67–0.78	0.70–0.97	0.38–0.47
Risedronate [n=78,865]	–	–	–
Fracture risk reduction (%)	−22	–28	−54
Relative fracture risk	0.78	0.72	0.46
95% confidence interval	0.70–0.86	0.59–0.87	0.41–0.52
Ibandronate [n=14,293]	–	–	–
Fracture risk reduction (%)	−3	(−20)	−32
Relative fracture risk	0.97	1.20	0.68
95% confidence interval	0.76–1.23	0.72–2.02	0.50–0.92

PS3.4 INTERNATIONAL COST AND UTILITIES RELATED TO OSTEOPOROSIS FRACTURE STUDY IN USA (ICUROS-US); STUDY DESIGN AND METHODS

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Osteoporotic fracture results in significant cost burden in the United States with direct costs estimated at 16 billion dollars and loss of quality of life. While considerable data exist about the cost of hip fracture, less is known about the cost and disutility following clinical vertebral, wrist and nonvertebral fractures. ICUROS (International Cost and Utilities Related to Osteoporotic Fracture Study), an international observational follow-up study in nine countries including the United States, examines the consequences of three major osteoporosis-related fractures (hip, forearm and clinical vertebral) in terms of costs and disutilities. ICUROS will collect both direct and indirect cost data in the first 18 months following fragility fracture as well as utility data. Self-report data on both direct, and indirect costs and utilities will be collected at baseline, months 4, 12 and 18 with a recall of prefracture utility at baseline. Participating countries include: Austria, France, Germany, Italy, Lithuania, Russia, Spain, UK and the USA. ICUROS US will collect data on 50 incident hip and wrist fractures, 200 clinical vertebral fracture and 100 nonvertebral fractures of the pelvis, tibia or proximal humerus and will confirm the self-report data of direct costs with use of electronic claims databases. An age and propensity score-matched control will be identified for each case to enable an estimate of incremental direct costs of fracture. ICUROS US will therefore provide data on incremental direct costs of major osteoporotic fractures in the US as well as self-report data on indirect costs and information on disutilities.

PS3.5 SELF REPORTED PREVALENCE OF OSTEOPOROSIS AND ITS RISK FACTORS IN MACAO ADULTS—RESULTS FROM MACAO HEALTH SURVEY (MHS)2006

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Background: In U.S., the Asian people and non-Hispanic Caucasian were found the highest prevalence of osteoporosis compared with other ethnic groups. How is the situation outside the U.S.? This report based on the data from a random household health survey (MHS2006). Prevalence of osteoporosis and its risk factors will be presented in this Chinese dominant population.
Methods: A total of 3,119 Macao residents aged 18 and above were recruited. Osteoporosis was defined by answering "yes" to the question that "Has a doctor ever told you that you had Osteoporosis?" Other variables were collected in three ways: health assessment, questionnaire and lab tests. The data analysis was done by SPSS.
Results: The prevalence of osteoporosis was 7.2% for all adults age 18+ after adjusted age and sex. Specifically, the prevalence was 26.25% for females and 5.26% for males in the age 50+ group. People with osteoporosis were found more females, low income and education people, older in age, higher mean values in blood urea nitrogen, Low-density lipoprotein, Body mass index, Systolic blood pressure and Diastolic blood pressure but low mean values in Red blood cell, Hemoglobin, Hematocrit and White blood cell. They were also significantly higher prevalence in bronchitis, arthritis, migraine, kidney stone, glaucoma, depression, anxiety, cardiovascular diseases, cancer, drinking alcohol, hyper-

tension, diabetes, metabolic syndrome, obesity and hyperlipidemia. In a logistic model with osteoporosis status as dependent variable and all significantly related variables listed above were used as independent variables, we found that variables of age, sex, individual income, migraine and obesity could significantly predict osteoporosis status.

Conclusion: The prevalence of osteoporosis was 7.2% in Macao Adults aged 18+. The Rate ratio was 4.99 between females and males in people aged 50+. Older age, females, lower incomes, higher urea nitrogen, suffered with migraine and obesity could significantly increase the risk of osteoporosis.

PS3.6 CHANGES IN BONE DENSITY OVER 1 YEAR OF AROMATASE INHIBITOR THERAPY IN WOMEN WITH POSTMENOPAUSAL BREAST CANCER AND OSTEOPENIA

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Background: Studies demonstrate that women treated with aromatase inhibitors (AIs) such as anastrozole, letrozole and exemestane for treatment of hormone-sensitive breast cancer are at risk of bone loss and osteoporotic fractures. The ATAC trial showed that women with normal bone density do not become osteoporotic within 5 years of AI treatment; however, it is unclear whether there is significant risk of early bone loss in women with preexisting osteopenia.

Methods: A retrospective chart review of over 100 women seen in our Cancer and Bone Health Clinic for evaluation of bone status in the setting of aromatase inhibitor treatment was performed. We report the 1-year data on bone mineral density of the spine and femoral neck (FN) and vitamin D status in 61 osteopenic women who were evaluated over 1 year within the first 2 years of AI therapy.

Results: Of 104 women seen during AI therapy, 29% had a normal bone mineral density (BMD); 59% had osteopenia and 12% had osteoporosis at baseline (BL). Of the 61 women with osteopenia, the mean age was 58±6 years and the BMI was 27± 6 kg/m^2. The range of duration of AI therapy was 0 to 2 years at baseline. At BL, 11 of 61 women (18%) were receiving bisphosphonate treatment; 45 of 61 women (74%) were taking calcium plus vitamin D; 33 of 61 (54%) were on a multivitamin. After 1 year of follow-up on AI therapy, L-spine BMD (N=39 pairs) showed a mean decrease from BL of 1.5% (range −11% to +14%), p=0.06. Eighteen of 39 women (46%) lost ≥3% at the spine. At the FN, (N=36 pairs) there was a mean decrease from BL of 2.0% (range −14%to +11%), p=0.006. Seven of 36 women (19%) lost ≥5% at this site. Four women lost both ≥3% at the spine and ≥5% at the FN. Overall two of 36 women with L-spine and FN data became osteoporotic: one at the spine and one at the FN. At BL, 25 of 61 (41%) of women were vitamin D insufficient (25-OH D levels 20–30 ng/mL) and 15 of 61 (25%) were vitamin D-deficient (<20 ng/mL); nine of 61 (15%) remained D-insufficient and two subjects remained vitamin D deficient at 1 year despite recommendation of supplementation with vitamin D_3.

Conclusion: In women receiving AIs for treatment of hormone-sensitive breast cancer, we demonstrated significant bone loss at the spine and hip over 1 year of follow-up on AI treatment. Further analysis of factors influencing bone metabolism is required to determine whether rapid bone loss can be predicted in this population of women at risk.

PS3.7 IDENTIFICATION OF INFLAMMATORY GENE VARIANTS AS BIOMARKERS OF OSTEOPOROSIS RISK IN ASIAN WOMEN

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Background: Identifying risk factors for predisposition of osteoporosis (OP) is important for predicting, managing, and in the development of therapeutics for the disease. The goal of this study was to determine genetic markers that may be used to identify individuals at high risk for osteoporosis in Asian women. Chronic inflammation is thought to be an important underlying cause of OP. In mouse models blocking the interleukin1 (IL1) inflammatory pathway abolishes ovariectomy-induced bone loss. Functional SNPs can alter the level and/or activity of the gene product and the biological processes that the gene product controls; this has been demonstrated for the IL1 gene family.

Methods: Allelic association studies using SNPs within the IL1 and other inflammatory genes were examined in two cross-sectional studies in Asian women. These studies included one that measured bone biomarkers levels in 400 Japanese women within 36 months post menopause and another case–control study that analyzed vertebral fracture and bone biomarkers in 838 Korean women between the ages of 60–84.

Results: Variants of the IL1A, IL1B, IL1RN, or IL10 genes were associated with clinical phenotypes of OP, such as low bone mineral density (T allele/IL1RN rs315952; p=0.01), biomarkers for high bone turn over and vertebral fracture. High serum CTX and NTX levels were associated with the ILIA (T allele/IL1A rs17561; p=0.046) and the ILIB (T allele/IL1B rs4848306; p value 0.002–0.035) genes. Increased risk of vertebral fracture was associated with the IL-10 gene (C allele/IL10 rs1800872, OR=1.8, p=0.013). Interestingly, the genetic markers for OP identified between Asian and Caucasian women are in different inflammatory genes. A variant of IL1B gene (T allele of IL1B rs16944) was associated with increased risk for vertebral fracture in a previous study of 1,473 Caucasian women (OR=1.56, p=0.013), whereas in this study of Asian women polymorphisms within the IL10 gene were associated.

Conclusion: In summary, we have identified genetic risk factors for OP in Asian women and demonstrated that there are differences in the markers for OP between Caucasians and Asians.

PS3.9 RELIABILITY AND VALIDITY OF A MODIFIED VERSION OF THE SAFE FUNCTIONAL MOTION TEST—SHORT FORM FOR ASSESSING MOVEMENT PATTERNS IN INDIVIDUALS WITH LOW BONE MASS

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Background: Measures of quality of motion during daily activities which may increase functional risk of osteoporotic fracture are lacking. The short form of the Safe Functional Motion Test (SFM-SF) is comprised of seven tasks which are typically performed by older adults. The quality of the performance on each task is scored on an ordinal scale and scores are generated which relate to domains relevant to functional risk of fracture: spine compression, balance, flexibility and strength. The objective of this study was to establish the test–retest and inter-rater reliability of the SFM-SF and convergent validity of the balance domain within the SFM-SF in individuals with low bone mass.
Methods: Thirty-six community dwelling older adults with low bone mass (mean age (SD)=68.7 years (8.08 years), 31 females) completed the SFM-SF on two occasions separated by 8.7 days (5.9 days). On one occasion, performance on the SFM-SF was scored by two raters and the Berg Balance Scale Test (BERG), Timed Up and Go (TUG), and Community Balance and Mobility Scale (CBMS) were administered. Test–retest and inter-rater reliability was evaluated using type 2, one intraclass correlation coefficients (ICC), standard error of the measurement (SEM), and Bland Altman plots. Convergent validity was determined using Spearman rho correlations between the score in the balance domain of the SFM-SF and BERG, TUG, and CBMS scores.
Results: Reliability for the total score of the original SFM-SF was excellent (test–retest: ICC (95%CI)=0.90 (0.812, 0.948), SEM=1.85; inter-rater: ICC (95%CI)=0.95 (0.902, 0.974), SEM=1.27). However, the test–retest reliability was poor for the spinal compression domain (ICC (95%CI)=0.59 (0.324, 0.766)). Deletion of one task contributing scores to the spinal compression domain resulted in good test–retest (ICC (95%CI)=0.79 (0.621, 0.885); SEM=0.51) and inter-rater reliability (ICC (95%CI)=0.86 (0.751, 0.929); SEM=0.43). This modification improved reliability of the total score (mSFM-SF test–retest: ICC (95%CI)=0.93 (0.863, 0.962), SEM=1.47; ICC (95%CI)=0.96 (0.925, 0.98), SEM=1.07). Bland Altman plots indicated no systematic difference for the total score and scores for the spinal compression domain across occasions and raters. The balance domain of the mSFM-SF demonstrated good to high convergent validity (BERG: r=0.76; TUG: r=−0.69; CBMS: r=0.83).
Conclusion: The mSFM-SF is highly reliable in individuals with low bone mass. There is 95% certainty that the score on any given occasion is within three points of the true value. The balance domain correlates appropriately with established performance-based clinical measures of balance. Longitudinal studies to determine responsiveness to change and discriminative and/or predictive ability with respect to osteoporotic fracture are warranted.

PS3.10 POST-FRACTURE OSTEOPOROSIS INTERVENTION STRATEGY

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Background: The Ontario Osteoporosis (OP) Strategy is a multifaceted initiative mandated and funded by the Ontario Government, Ministry of Health. The Post-Fracture OP Program is one of five components and was implemented by Osteoporosis Canada (OC) on behalf of the Ministry. The goals of this program are to improve OP diagnosis and treatment in this population, prevent future fractures, and improve OP knowledge among health professionals and patients. As such, this program is aimed at orthopaedic surgeons, family physicians (FP), and individuals 50 and over with fragility fractures.
Methods: From January 3, 2007 to January 8, 2008 OC deployed 19 OP Screening Coordinators (OSCs) in 31 medium to high volume fracture clinics in Ontario. The OSC identifies fragility fracture patients, educates them on OP and their risks, and suggest follow up with the FP for further investigation and treatment of their bone health. OSC's also facilitate communication between the FP and surgeon by way of a standardized form letter recommending OP assessment with their patient. Quality assurance self-report data is collected on all patients and includes OP risk factors, prior OP treatment and adherence, prior bone mineral density (DXA) testing, OP knowledge and beliefs and socio-demographics characteristics. Patient review is conducted at 3 and 6 months. Data collection from January, 2007 to April, 2007 was completed on paper and starting in May, 2007 data was collected using tablet PC's.
Results: From May 2, 2007 to January 11, 2008, 97,386 fracture clinic patient visits were screened, of which 16,525 were identified for OP screening and 9,737 were seen by the OSC. Out of those identified for screening, 4,445 did not meet inclusion criteria, 4,950 completed baseline screening and 265 refused intervention. Follow up with the FP was suggested for 4,557 patients, with 3,291 FP's receiving the standardized form letter. Discussion about having a bone mineral density (DXA) test completed by their FP was suggested to 4,006, and 28 DXA's were ordered by the orthopaedic surgeons. The most common fracture sites were

the wrist, ankle, shoulder and hip. Among the target population, 97.8% of patients were suggested to take 1,500 mg of calcium and 800 IU Vitamin D daily and 97.5% of patients were provided with 1-800 number for information on OP.

Conclusion: Approval from each hospital's Research Ethics Board is currently underway to use the quality assurance data collected for research purposes. Data gathering methods will be modified depending on initial quality assurance analyses. Expansion of follow-up to include patients previously diagnosed and treated for OP to evaluate adherence will be initiated in the future. Linking to Ministry of Health and Long-Term Care billing data for drug prescription patterns and future fracture rates will be completed for those patients who have consented.

PS3.11 VITAMIN D LEVELS FROM A NEW ENGLAND ACADEMIC MEDICAL CENTER; THE INFLUENCE OF AGE, RACE, GENDER AND SEASON

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Background: Increasing awareness of the importance of vitamin D to health has led to greater interest in measurement of vitamin D in varied populations. Studies indicate that low vitamin D levels are a worldwide problem. Vitamin D "deficiency", defined as 25-hydroxyvitamin D (25-OHD) level ≤20 ng/mL (50 nM/L), and 25-OHD "insufficiency", defined as 25-OHD level 21–30 ng/mL (75 nM/L) are both felt to be sub-optimal. Previous studies have demonstrated that there is a higher prevalence of 25-OHD deficiency in the elderly and in the winter season.

Methods: We conducted a retrospective analysis of 25-OHD to assess the prevalence of "deficiency" and "insufficiency" in a southern New England population seeking care at the University of Connecticut Health Center (UCHC). A total of 5,898 patients had their initial 25-OHD assay performed using the DiaSorin radioimmunoassay, which equally detects vitamin D3 and D2 from June, 2005 to April, 2008. The de-identified samples were analyzed for the effect of age, sex, race and season of the year on 25-OHD levels.

Results: Approximately one third of the assays were ordered for patients attending an osteoporosis center where 25-OHD is routinely measured at the initial visit. Assays ordered from other specialty clinics may have been for specific indications, but the results were not significantly different. The distribution of 25-OHD levels by racial group confirmed previous reports of lower levels in Black, Hispanic and Asian populations, compared to Caucasians (Table). Among Caucasians, only 50% had sufficient 25-OHD levels while 27% were deficient. In the Black, Hispanic and Asian populations only 18–31% of the 25-OHD levels were sufficient and 41–64% of levels were deficient. Seasonal variation was significant with a mean 25-OHD level of 32 ng/mL in the summer and 27 ng/mL in the winter ($p<0.001$). The 25-OHD levels did not decline in the older patients but the levels in women were higher than in men ($p<0.001$).

Conclusion: There is a high prevalence of vitamin D deficiency and insufficiency in southern New England among patients seeking care at UCHC, especially in non-Caucasian racial and ethnic groups. Low 25-OHD levels can persist during the summer months, especially in these groups. Further studies are needed to determine the full impact of 25-OHD levels not only on skeletal health but also on neurological and cardiovascular function, immune response and cancer prevention. New guidelines are needed to address the prevalence of Vitamin D deficiency in the US population.

25-OHD levels by racial group

	Caucasian n=4,913	Black n=392	Hispanic n=473	Asian n=120
Mean 25-OHD (ng/mL)	31	20	23	25
Percent in range				
Sufficient (≥30 ng/mL)	50	18	26	31
Insufficient (21–30 ng/mL)	23	19	25	28
Deficient (≤20 ng/mL)	27	64	50	41

PS3.12 PREVENTIVE EDUCATION FOR OSTEOPOROSIS IN MID-LIFE PERSONS WITH SEVERE MENTAL ILLNESS

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Background: Persons with severe mental illness (SMI) are an under-recognized subgroup at high risk for osteoporosis. Little is known about their knowledge of bone health, and whether they respond to preventive education about osteoporosis. The purpose of this study was to evaluate the use of a web-based, personalized, patient-centered educational intervention in a cohort of middle-aged psychiatric inpatients with SMI.

Methods: Subjects aged 40–60 were recruited from three acute care inpatient units in an academic metropolitan psychiatry department into an osteoporosis screening and preventive education study. Subjects completed the 20-item Facts on Osteoporosis Quiz (FOOQ)© before and after the web-based educational site *Tone Your Bones* (http://www.toneyourbones.org). The site was personally viewed with each subject by a psychiatric nurse leader or research coordinator. The six educational site components consisted of: self-evaluation (including a risk factor checklist and dietary calcium calculator), bone density testing, the role of specialty examination, nutrition and dietary supplements, the

importance of strength, balance and posture with related exercises and safety tips, and a personalized treatment plan for better bone health.

Results: Thirty of 47 ethnically diverse men and women approached completed the FOOQ pre- and post-assessment following the Tone Your Bones educational program. Time administering the program ranged from 20 to 45 min. Ninety percent demonstrated an increase in osteoporosis knowledge, with mean pre- and postscores on the FOOQ 13.2 (+3.1) and 17.4 (+2.3) (two-sided $p<0.0001$) Participants uniformly found the program useful.

Discussion: The FOOQ appears to be a useful questionnaire for examining baseline knowledge and change in knowledge following education about osteoporosis in those with SMI. This study also confirms that persons with SMI are motivated for, can comply with, and benefit from bone health education. The web-based Tone Your Bones intervention provided personalized bone health assessment and education to SMI patients, and actively engaged them in their own health as part of their overall inpatient treatment. Future research outcomes should include effects on self-efficacy to advocate for osteoporosis prevention with health care providers.

PS3.13 FALL AND FRACTURE PREVENTION: WHAT ARE THE PERCEPTIONS OF THE ELDERLY TO HEALTH PROMOTION MESSAGES?

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Background: Falls and fractures are among the most common and serious problems facing elderly persons. Approximately one-third of elderly persons aged 65 years and older fall each year, and falls and fear of falling are associated with increased morbidity, mortality, depression and reduced mobility and activity. It is thus important to educate elderly individuals about fall and fracture risk and to instigate fall and fracture prevention measures. Accordingly, the aim of the present work was to gain insight of older people's views of fall and fracture risk prevention advice and determine ways of encouraging them to take action to prevent falls and fractures.

Methods: A total of 125 people aged 60–92 years were recruited from diverse settings (leisure centres, old age homes, religious centres, retirement clubs and local community) in order to ensure representation of both healthy and frail men and women with a wide age range and different living circumstances. Interviews and group discussions were carried out. Participants were queried about previous falls/fractures and previous experiences of communications regarding falling and fractures from health professionals. Furthermore, participants were queried about their perceptions of various health promotion messages aimed at fall and fracture prevention.

Results: Analysis showed that only six of 125 (4.8%) of the participants had received communications concerning fall and fracture prevention from their health professional. The vast majority of the participants linked the concept of fall and fracture prevention to hazard reduction approaches and restriction of mobility. Only three of 125 (2.4%) were aware that fall and fracture risk could be reduced by exercise aimed at improving strength and balance. Most of the participants refused to accept that they should be defined or behave as potential "fallers" (as this stigmatized them as being "old" and having to adapt to limitations due to their age) and in turn rejected health promotion messages aimed explicitly at "falls prevention"; that they needed to be given advice about how to adapt to "ageing" and to constantly anticipate limitations in their physical abilities and put safety before their identity, dignity and independence. Fall and fracture prevention advice was on the whole regarded as useful (even though it was largely lacking) and particularly welcomed when the positive benefits of exercise for balance and mobility were explained.

Conclusion: Our findings suggest that older people tend to reject explicit fall and fracture prevention advice since they see it as a potential threat to their freedom and independence. Health promotion messages emphasizing musculoskeletal strength and balance improvement rather than hazard reduction seems to be more acceptable, increase confidence and have a positive effect on physical function.

PS3.14 IDENTIFICATION AND ASSESSMENT OF FALL AND FRACTURE RISK FACTORS AND THE IMPLEMENTATION OF A FALL-PREVENTION INTERVENTION PROGRAM IN COMMUNITY-DWELLING ELDERLY INDIVIDUALS

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Background: Falls are common, 30% of community-dwelling elderly individuals fall at least once a year. Falls are the leading cause of injury deaths among people 65 years and older. Moreover, fall-related fractures are the third leading cause of years lived with disability. Accordingly, the aim of this work was to identify and assess specific risk factors for falls and fractures in community-dwelling elderly persons and to offer an individualized fall and fracture-prevention intervention program.

Methods: One hundred elderly persons with a history of a "fall" or with injury/fracture sustained as a consequence of a "fall" were. Participants received a comprehensive consultation including interrogation for a history of a previous fall, fracture, comorbid illness, housebound status, intake of calcium-rich diet and medications used. Bone densitometry by dual-energy X-ray absorptiometry (DXA) and fall risk assessment were performed. A thorough clinical examination was performed including neurological and musculoskeletal examination. Cognition, balance, visual acuity (VA) and hearing were also assessed. Physical performance assessment included quadriceps and grip strength, 6-min walk, "Get up and Go Test", ADLs and frailty assessment.

Laboratory testing included: serum calcium, phosphorus and vitamin D3. Following the fall risk evaluation, all subjects received fall risk education, nutrition counseling, environmental hazards (EH) education, medication review and an individualized exercise prescription. Effects of this intervention on participants were examined using a follow-up survey 1 year after the baseline survey.

Results: The mean age of the study group (66 women and 34 men) was 66.5 years. Thirty-seven (74%) had a history of previous a fall. Thirty-four sustained a fracture (commonest being fracture of neck of femur, followed by fractures of the wrist, humeral neck and pelvis). BMD measurements revealed osteoporosis in 25% of the subjects. Vitamin D deficiency was found in 33% of the participants. Logistic regression analysis identified the following predictors in the risk profile of falls and fractures: weak grip and quadriceps strength, functional limitations, low BMD, Vit D deficiency, poor balance, OA, DM, PD, dizziness, fear of falling, EH, polypharmacy, reduced VA and high frailty score. The incidence of falls over 1 year decreased significantly from 44% to 27% ($p<0.005$)at follow-up survey.

Conclusion: This study demonstrated that fall and fracture-related risk factors are common in the elderly and are due to multiple interacting factors. Fall risk assessment is thus essential in older adults to determine fracture risk and an individualized fall and fracture-prevention intervention program should be instigated to reduce this risk and to increase self confidence, sense of well-being and quality of life.

PS3.15 EFFECTS OF A TAILORED INTERACTIVE COMPUTERIZED INTERVENTION TO INCREASE SELF-MANAGEMENT BEHAVIORS

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Background: Aim was to describe differences in knowledge, calcium self-efficacy, outcome expectancy, goal congruence, and calcium intake between participants using a tailored interactive computerized intervention (TICI) or printed information (PI). The Integrated Theory of Health Behavior, a self-management theory, was foundational to development of the intervention and research method.

Methods: In this repeated measures experimental design 145 women were randomly assigned to TICI or PI. Data were obtained at baseline, 8 and 14-weeks, and 6-months. Healthy women between the ages of 40 and 60 were recruited via newspaper, television, radio, and company internal communications. Eligible women had inadequate calcium consumption, did not have osteoporosis, and were not taking bone-remodeling drugs. After signing a written consent women were randomly assigned to either the TICI or PI group. PI is commonly used health booklet containing general information about osteoporosis, risk factors, and recommended health behaviors. TICI contains general and tailored information and is delivered electronically. Content of the web site was matched to theory constructs, and designed to enhance knowledge and facilitate health beliefs. The web site was used at least once but could be used as often as desired. TICI group received a hand held computer for the duration of intervention. The hand held computer was designed to enhance self-management skills and used a minimum of three times per week for 8-weeks. Measures of osteoporosis knowledge, calcium consumption self-efficacy, outcome expectancy, goal congruence, and calcium intake were obtained at baseline and at 8-weeks. To minimize burden, participants received packets of data collection forms at enrollment and telephone or email reminders to complete data three times over the 6-month data collection time.

Results: There were no significant differences between the TICI and PI groups with respect to age, education, or marital status. The TICI group had more African American participants ($\chi^2=10.88$, $p=0.04$). Instruments all had high estimates of internal reliability (Chronbach's alpha coefficient: self-efficacy=0.93; outcome expectancy=0.97, and goal congruence=0.94). Knowledge increased for women in both groups with no interaction between time and group ($F=0213$, $p=0.647$, $df=1$). There was a significant time by group interaction for self-efficacy ($F=7.07$, $p=0.009$, $df=1$) and goal congruence ($F=5.59$, $p=0.021$, $df=1$). There was no difference in outcome expectancy.

Conclusion: In only 8-weeks changes in self-efficacy were observed. Increases in self-efficacy, as occurred with TICI, have potential for mediating long-term change. New and alternative theories and delivery methods are needed to further enhance health behavior change required to increase regular engagement in healthy behaviors to enhance bone health.

PS3.16 BONE DESTINY: A ONE-STEP GLOBAL FRACTURE RISK PREDICTOR FOR CLINICIANS

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Objective: BMD alone is an inadequate predictor of overall fracture risk and results expressed in *T*-scores often do not "synapse" a treatment response. Many patients with significant fracture risk are not on treatment because the risk is assessed by BMD alone. Thus, the objective was to create a one-step global fracture risk predictor for clinicians that combines bone mineral density (BMD) with other risk factors in an easily interpretable model.

Methods: "Bone DESTINY" was created as an integrated model: a one-step fracture risk predictor that analyses BMD and other fracture risk factors to produce an overall fracture risk. DESTINY risk factors are age, BMD, previous fragility fracture, family history of hip fracture, current steroid use >3 months, history of falls and propensity to fall. The model uses five global fracture

specific colour risk zones that are easily recognizable and treatment-impelling to healthcare professionals. (1) While conducting DEXA scans, technicians input all fracture risk factors into a hand-held computer. A software program produces a diagrammatic DESTINY report. (2) The DESTINY report is colour coded by fracture risk where green equals very low fracture risk, yellow equals low risk, orange equals moderate risk, red equals high risk, and purple equals very high risk. (3) The reporter sees both BMD and DESTINY results when dictating.
Results: Destiny was designed over a 2-year period as a one-step, cost neutral program that integrates data into a hand-held computer with BMD results from a DEXA scanner to express overall fracture risk. It has been used successfully in over 25,000 patients in the Hamilton area. The reports convey a global fracture risk. DESTINY reports are easily understood by family physicians and other clinicians who can arrange appointments and treatment based on treatment colour zones. Patients are also shown their treatment risk zone so that they will initiate appropriate follow up.
Conclusion: DESTINY, a one-step fracture risk predictor tool, has been used successfully in over 25,000 patients in the greater Hamilton area. DESTINY reports convey global fracture risk and are both simple to interpret and well received within the medical community. Recent reports suggest that DESTINY gives a fracture risk prediction similar to guidelines. The DESTINY software can be easily recalibrated to reflect changes in knowledge.

PS3.17 AN ANALYSIS OF SERUM CALCIUM, PARATHYROID HORMONE, AND 25-OH VITAMIN D LEVELS IN POST-MENOPAUSAL FEMALES WITH OSTEOPOROSIS

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Background: Osteoporosis is a very common, yet significantly underdiagnosed and undertreated condition with an estimated prevalence >10 million (out of these eight million women) in USA. Primary hyperparathyroidism and vitamin D deficiency are two important risk factors for osteoporosis, and affect older women more than other population groups. Furthermore, patients may have substantially symptomatic primary hyperparathyroidism (with bone disease) without elevated serum calcium (normocalcemic).
Methods: Data from 473 post-menopausal osteoporotic women (age >50 years, Bone DEXA *T*-score <−2.5) that visited our outpatient medicine and endocrine clinics from January, 2007 to June, 2008 was reviewed to determine what percentage of them got tested for serum 25-OH vitamin D and intact PTH levels. The prevalence of vitamin D inadequacy and primary hyperparathyroidism (including normocalcemic) was calculated from available data (i.e. the patients tested).
Results: Only 13.5% of the study population (n=64) got tested for serum 25-OH vitamin D levels, of which 76.6% had vitamin D levels <30 ng/mL (vitamin D inadequacy). 11.8% of patients (n=56) got tested for intact PTH levels, of which 39% had high PTH levels (>60 pg/mL). Patients with high PTH levels were screened for renal disease (Cr >1.4). 78% patients with high PTH levels and no renal disease were tested for serum 25-OH vitamin D levels. After further excluding vitamin D inadequacy in this group, it was found that 12.5% of the patients tested for PTH levels had primary hyperparathyroidism (biochemical). Surprisingly, of these patients with primary hyperparathyroidism, majority (71%) never had elevated serum calcium (albumin corrected) levels ("normocalcemic").
Conclusion: A large proportion of high-risk patients fail to get screened for two very important and treatable causes of secondary osteoporosis. Our study indicates that vitamin D deficient states and primary hyperparathyroidism may be commoner than usually considered, especially in an urban multi-ethnic immigrant population like ours. Given the high morbidity and mortality associated with hip fractures (and the tremendous health care costs), aggressive measures should be adopted to popularize screening for these two parameters in all osteoporotic individuals (regardless of serum calcium levels), with heavy emphasis on physician and patient education.

PS3.18 PERIMENOPAUSAL WOMEN'S INTENDED AND ACTUAL VITAMIN D INTAKE IN RESPONSE TO SELECTED BONE HEALTH INTERVENTIONS

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Background: Osteoporosis affects more than ten million people in the United States; an additional 34 million have low bone density, of which 80% are women. Adequate vitamin D intake is related to calcium absorption and bone density. To date, focus has been on post-menopausal women and related osteoporosis risks or treatment options. Few women are tested for bone density before menopause, and are unaware of osteoporosis risk until after the rapid bone density loss associated with perimenopause. Understanding women's motivation toward behaviors is needed in bone health promotion research and practice.
Purpose: To determine effects of bone health testing among perimenopausal women using dual energy X-ray absorptiometry (DXA) on outcomes of intent to engage in and actual bone health behaviors, focusing on vitamin D intake.
Methods: A longitudinal repeated measures experimental design randomly assigned 150 women, ages 35–55, to an intervention group (n=75, DXA and bone health information) or to a comparison group (n=75, bone health information). Baseline demographic data were collected; the Prevention Intentions Questionnaire and Behaviors Questionnaire were developed and administered to participants at baseline, 2 weeks, and 2 months after interventions.
Results: 149 women completed the study. 32% (n=24) intervention group women had low bone density. Intervention of DXA and bone health information showed near-significance (p=0.068) over intervention of bone health information alone in affecting women's intentions to improve overall bone health behaviors. DXA *T*-scores were inversely related to intentions to improve bone health behaviors ($r(74)=-0.23$, p=0.046) at 2 weeks after DXA and bone health information, and were inversely related to vitamin D intake ($r(73)=-0.25$, p=0.03) at 2 months after DXA and bone

health information. Although both intervention and comparison groups demonstrated increased vitamin D intake during the study, there was no significant difference in average vitamin D intake between groups. However, intervention group women with low bone density demonstrated a significant increase in vitamin D intake, compared to women with normal bone density, at 2 weeks ($p<0.05$) and at 2 months ($p<0.05$) after DXA and bone health information. At study's end, only women with low bone density met the recommended average vitamin D intake of at least 800 U/day.

Conclusion: Interventions focusing on perimenopausal women should include providing bone health information and updated information on adequate vitamin D intake. However, information alone may not be enough for appropriate behavioral change. Early detection and intervention of perimenopausal bone loss via DXA testing may improve bone health behaviors, may reduce osteoporosis morbidity, and improve women's quality of life, thus reducing financial consequences to individuals, families, communities, and the nation.

PS3.20 VALIDITY OF THE STRENGTH AND FLEXIBILITY DOMAINS COMPRISING A NOVEL PERFORMANCE-BASED MEASURE OF FUNCTIONAL RISK FOR OSTEOPOROTIC FRACTURE

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Background: Loss of strength and flexibility in older adults may increase the risk for injurious falls resulting in osteoporotic fracture. The Safe Functional Motion test (SFM), of the Bone Safety Evaluation, was developed to assess functional risk for fracture. This test is comprised of six domains: upper body (UB) flexibility, lower body (LB) flexibility, UB strength, LB strength, balance, spine compression). Performance during ten standardized tasks is observed and rated on an ordinal scale.

Purpose: To determine convergent construct validity of the four domains of the SFM related to flexibility and strength.

Methods: A cross sectional study of 30 older adults with low bone mass was conducted. Performance on the SFM was scored. Goniometry measures of range of motion (ROM, UB: shoulder and elbow flexion; LB: hip extension, external rotation, flexion with knee flexed, flexion with knee flexed, and ankle dorsiflexion) and measures of UB muscle strength (manual muscle testing of UB shoulder and elbow flexors on a ten-point scale; dynamometry measures of isometric grip strength) were acquired bilaterally. Functional LB muscle strength was assessed using the Timed up and Go (TUG). Duplicate measures of ROM and strength were averaged. Right and left grip strength measures were combined. Overall values for UB and LB ROM and UB muscle strength on manual testing were generated. Convergent construct validity was assessed using the Spearman rho correlations of the scores on the SFM domains related to flexibility and strength with comparable clinical measure. Overall scores for flexibility and strength domains were also compared. Statistical analyses were conducted using SigmaStat version 3.5.

Results: LB, but not UB, flexibility domain score is associated with LB ROM, UB ROM, composite ROM and TUG (Table 1). The expected associations for muscle strength were observed (Table 1).

Conclusions: SFM strength and LB flexibility domains have acceptable validity. Validity of the UB flexibility domain could not be established using goniometry measures of shoulder and elbow flexion. UB and LB strength domains can be combined into a single domain as an estimate of global strength and mobility. The contribution of these domains to prediction of risk for falls and osteoporotic fracture requires investigation.

Table 1 Associations between SFM domain scores and clinical measures

Clinical measures	UB	LB	UB+LB
SFM test: flexibility domain scores			
UB ROM	−0.179	0.515**	0.424*
LB ROM	0.097	0.636***	0.582***
Composite ROM	0.033	0.655***	0.581***
TUG	−0.158	−0.601***	−0.576***
SFM test: strength domain scores			
UB MMT	0.446*	0.247	0.418*
Grip Strength (lb)	0.324	0.409*	0.377*
TUG (s)	−0.734***	−0.581***	−0.732***

*$p<0.05$; **$p<0.01$; ***$p<0.001$

PS3.21 A NOVEL PERFORMANCE-BASED MEASURE OF FUNCTIONAL RISK FOR OSTEOPOROTIC FRACTURE HAS EXCELLENT RELIABILITY AND GOOD CONVERGENT CONSTRUCT VALIDITY

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Background: There are few performance based tests of mobility and function for older adults, such as the Physical Performance Test (PPT). Typically these are timed measures and loads on the spine are not considered. Thus these are not ideal for identifying functional risk for osteoporotic fracture. The Bone Safety Evaluation (BSE) was developed to provide a comprehensive assessment of individuals with low bone mass predictive of fracture risk and helpful in making decisions regarding treatment for osteoporosis. A component of the BSE is a performance-based test, the Safe Functional Motion (SFM) test, comprised of ten tasks which older adults typically do every day. The tester uses standardized verbal instructions and requests the patient to perform each task as they normally would at home. Six different domains (spinal compression, balance, upper limb flexibility, lower limb flexibility, upper limb strength, lower limb strength) are rated on an ordinal scale according to observed performance to

generate a score between 0 and 60. As a first step, the measurement properties of the SFM need to be established.
Purpose: To determine test–retest reliability and convergent construct validity of the SFM.
Methods: For test–retest reliability, 29 older adults with low bone mass were recruited from the northeast Georgia area. Performance on the SFM was rated by a single tester on two occasions between 3 and 7 days apart. Reliability of the total score and each domain was determined using the type 2, one intraclass correlation coefficient (ICC) and standard error of the measurement (SEM). Convergent construct validity was assessed using the Spearman rho correlations of the SFM total score and each comparable domain with the total PPT score for 31 subjects recruited from the same site. Statistical analyses were conducted using SPSS version 16.
Results: Test–retest reliability of the SFM is excellent (ICC=0.89, SEM=2.0). The SFM and PPT scores were correlated (r=0.559) and moderate to good correlations were observed for each domain which had comparable items in the PPT (r=0.394 to 0.638) with the exception of the upper limb flexibility domain (r=0.309, ns).
Conclusion: The SFM test is reliable and we have 95% certainty that the total score on a given day is within four points of the true value. The strength of the associations with PPT confirms that these tests measure different components of function. For example, the SFM assesses quality of movement rather than speed, includes a spine compression domain, and differs in the numbers of items scored for domains that are comparable. Notwithstanding these differences, the appropriate association with PPT is observed.

PS3.22 LESSONS LEARNED FROM SHARED MEDICAL APPOINTMENT FOR OSTEOPOROSIS MANAGEMENT

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Background: We have designed an innovation osteoporosis clinic by implementing shared medical appointments (SMA) for women and men with osteoporosis. Our goal is to improve our patient adherence and compliance to treatment recommendations, by fully understanding their disease and treatment regimen. It has been reported that a significant proportion of osteoporosis patients do not adhere to their treatment as prescribed. We have also noticed that there is insufficient understanding of osteoporosis, FDA approved medications and importance of calcium and Vitamin D supplementation and exercise in our patient population. SMA has been used by multiple clinics in the country especially in the care of patients with chronic diseases, such as diabetes, and has provided favorable outcomes to patients and providers.
Methods: Our clinics were held twice monthly for 90 min duration each. We chose an afternoon time for the convenience of elderly and or working patients' schedule. This clinic was run by an osteoporosis nurse practitioner as the provider and a rheumatologist as the facilitator. The nurse practitioner interviews and briefly examines each patient individually and while the provider is examining and documenting in the patient record, the facilitator presents to the patients valuable educational information regarding osteoporosis, understanding of bone density and laboratory testing and up to date recommendations regarding optimal management. In addition, adequate time was made available to address all patient questions. Patients signed a shared medical visit waiver form and consented to discuss their personal medical information at those visits.
Results: We share the pros and cons of our experience from these shared visits. Pros include prompt access to appointments, cut down on waiting list, more patients to fit in a busy schedule, improved physician productivity, educational information presented once to all group and multiple repetitions to each patients were not required, patient satisfaction was almost universal, most patients reported learning more than at any other visit, most patients reported that enough time was spent with them, patients learned from questions of others and their personal experience, overall impression of improved patient adherence and compliance to treatment, however, we have no actual statistical evidence to support that. The cons include not all patients are candidates for those visits, patients requested smaller groups per visit and shorter duration, need to ensure focus stays on osteoporosis, there was tendency for certain patients to deviate from osteoporosis topic and request attention for their rheumatologic disease problems.
Conclusion: We have learned that with careful planning and patient selection, the SMA was very helpful and provided the means to offer world class care to our osteoporosis patients and better management of their disease.

PS3.24 OLDER MEN'S KNOWLEDGE OF AND RISK FACTORS FOR OSTEOPOROSIS

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Background: Osteoporosis research conducted in the past has focused almost exclusively on women. There are many reasons for this seeming neglect of men. Among them are the following facts: After the age of 65 years, 80% of women develop osteoporosis or its precursor, osteopenia. In comparison, only 40% of men experience low bone density, which typically develops at a later age in men than in women. Prior research on men's knowledge about osteoporosis suggests that as few as 54% of men even know they can develop osteoporosis. Limited research has examined men's knowledge about osteoporosis and risk factors.
Methods: All men (n=4,274) attending senior centers and/or living in two continuing care retirement community in the one county were mailed an anonymous osteoporosis survey packet. The packet consisted of a demographic questionnaire, the Facts on Osteoporosis Quiz (FOQ), the Risk Factors questionnaire and the Men's Osteoporosis Knowledge Quiz (MOKQ). The MOKQ was

designed for this survey and consisted of six questions specifically about men and osteoporosis.

Results: Of the original 4,274 surveys sent out, 1,535 usable surveys were returned (36.2% of original sample). In response to the 26 knowledge questions, the average number answered correctly was 13 (50%). An examination of the six questions designed specifically for men revealed that an average of two of the questions (33%) was answered correctly. For comparison purposes, six items were identified as questions specific to women. The average number of these questions answered correctly by men about women was three (50%). 11% of the men reported a current diagnosis of osteoporosis or low bone mass and 16% reported a fracture after the age of 50 years. However, only 5.4% of the men reported taking a prescription medication to treat osteoporosis while 28.8% reported calcium supplementation and 47.8% reported Vitamin D supplementation.

Conclusion: In this study, men were asked osteoporosis knowledge questions specific to men. The results on overall knowledge are consistent with what others have found, with men scoring about a 50%. However, men knew less about their own risk factors (33% correct) than they did about women's risk factors (50% correct). This has important implications for patient education, practice, and policy, as outlined via an in-press manuscript.

PS3.25 PATIENT PERCEPTIONS OF OSTEOPOROSIS

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The purpose of this study is to determine the osteoporosis knowledge level of patients belonging to a multispecialty group in a moderately sized urban center. We want to identify items that may require more education and instruction. Interestingly, this population is quite savvy in their medical knowledge, possibly related to the excellent education provided by the physicians in the practice and the widespread use of Internet in this high tech, university city. This voluntary survey was sent to a computer generated random sample of 500 patients. 250 had received the diagnosis code for osteoporosis. The 250 patients without a diagnosis for osteoporosis were taken from well visits. Return rate on the surveys was 54% (134/250) for the patients with the diagnosis code for osteoporosis and was 29% (72/250) for the patients without the diagnosis. As expected, more patients with the diagnosis returned their surveys; but both groups had a better than average response rate. There was a higher response rate in the patients with some level of personal exposure to osteoporosis. Therefore, these responses may be coming from patients with slightly higher interest and education in this area and may account for the impressive knowledge shown here. In particular, the awareness of male osteoporosis and ethnicity differences was interestingly high. Not surprisingly, there was a high rate of medication usage in patients with the disease. However, the fact that non-osteoporosis patients have a 10% use of medication was surprising—this may be related to prophylaxis, or to an absent diagnosis code. Both groups had a good rate of using calcium and vitamin D on a regular basis. The fact that patients over 50 years old had more faith in the pharmacist was intriguing. Possibly it is because of the relationships they have had in the past, versus so many patients now using mail order medications. Perhaps the pharmacist relationship has weakened in younger patients. It is reassuring that 100% felt that it is the physician's responsibility to educate. It was surprising that so many respondents did feel that the media should play a role in education. We did not define media, so it is uncertain whether television, radio or print is felt to be the most significant area. There is speculation that direct to consumer marketing may increase awareness of conditions, without actually impacting which treatment is used. Most patients felt following a regular routine was the best way to improve their adherence.

PS3.26 RAPID PULSE TRANSDERMAL DELIVERY OF PTH (1–34) (ZP-PTH) IS EFFECTIVE IN INCREASING BONE MINERAL DENSITY OF LUMBAR SPINE AND HIP IN POSTMENOPAUSAL WOMEN WITH OSTEOPOROSIS

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Background: The treatment of osteoporosis with an anabolic agent, rhPTH (1–34) delivered by subcutaneous daily injections is effective in reducing incident fractures, but lack of patient acceptance of daily injection might limit its use. A transdermal patch providing a rapid, pulse delivery of hPTH (1–34) may provide an alternative treatment option. In this phase 2 study we determined the efficacy and safety of ZP-PTH compared to both placebo and Forteo® (rhPTH 1–34) in postmenopausal women with osteoporosis.

Methods: 165 postmenopausal women (aged 50–81 years, mean 64 years) with osteoporosis defined as lumbar spine (LS), femoral neck (FN) or total hip (TH) bone mineral density (BMD) *T* score of ≤ -2.5 or a *T* score of ≤ -2.0 with a prevalent vertebral fracture were enrolled in a 24-week, randomized, placebo-controlled, positive control, double-blind, multi-dose study. ZP-PTH placebo, 20, 30 or 40 μg hPTH (1–34) coated patch was self administered for 30 min daily or Forteo 20 μg daily by subcutaneous injection for 24 weeks. The primary efficacy measure was mean percent change in LS BMD from baseline. Prespecified secondary endpoints included change in TH/ FN BMD (0–24 weeks), serum procollagen 1 N-terminal propeptide (sP1NP) (0, 4, 24 weeks), serum C-terminal cross-linking telopeptide of type I collagen (sCTX) (0, 12, 24 weeks). Safety assessment included serum and urine calcium, topical effects assessment and pharmacokinetics.

Results: 155 (94%) of the randomized study subjects completed the trial. ZP-PTH increased mean percent change LS BMD in a

dose dependent manner (mean±SD; ZP-PTH Pbo=−0.33±3.4%, ZP-PTH 20=+2.96±3.5%, ZP-PTH 30=+3.47±3.5%, ZP-PTH 40=+4.97±4.1%) at 24 weeks. All three active patch treatments were significantly different from placebo ($p<0.001$) and the ZP-PTH 40 group was comparable to Forteo (3.55±3.7%). The ZP-PTH 40 treatment produced a significant increase in TH BMD (+1.33%) compared to placebo and Forteo ($p<0.05$). Bone turnover markers (sP1NP and sCTX) increased in a dose dependent manner and were all significantly different from placebo ($p<0.001$). Overall the treatments were well tolerated. There were no drug related SAEs and no AEs different than Forteo. Neither a sporadic nor a sustained hypercalcemia was observed in any treatment group. Across the ZP-PTH treatment groups, patch-related topical adverse events were mild to moderate and transient. There were no reports of skin infection, delayed type hypersensitivity or evidence of antibody formation to PTH in the patch treated groups.

Conclusion: Rapid, pulse delivery of hPTH (1–34) daily by transdermal patch (ZP-PTH) in postmenopausal women with osteoporosis for 24 weeks resulted in a significant gain in lumbar spine BMD. The ZP-PTH 40 dose was comparable to Forteo in lumbar spine BMD gains but it also increased total hip BMD. Additional studies will further define the efficacy and safety of this novel transdermal delivery system.

PS3.27 IMMUNOFLUORESCENT ANALYSIS OF VITAMIN D RECEPTOR LOCI AND MYOSIN HEAVY CHAIN ISOFORMS IN HUMAN SKELETAL MUSCLE FIBERS

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Introduction: Vitamin D receptors (VDR) have been identified in human skeletal muscle tissue using different techniques. In muscle, the active form of vitamin D, 1,25-dihydroxyvitamin D, acts through a nuclear VDR to induce de novo protein synthesis affecting cell growth and differentiation and through a cell surface VDR to trigger several genome-independent, rapid, second-messenger pathways involved in cellular processes. We developed a method using immunofluorescent detection to investigate VDR and myosin heavy chain (MHC) isoform expression in skeletal muscle of older female subjects.

Methods: Serial sections (7 μm) were cut from frozen samples obtained by needle biopsy of the vastus lateralis. Samples were fixed in 3% neutral buffered formalin, blocked in PBS/2% goat serum, and then probed overnight (4°C) with a primary mouse/anti-human VDR/NR1I1 monoclonal antibody (Perseus Proteomics). Subsequently, sections were probed with goat/anti-mouse ALEXA Flour-568® secondary antibody conjugate. Slides were mounted with DAPI-containing mounting medium to stain myonuclei. Unfixed sections followed a similar protocol to identify type I (A4.951; A4.840), type IIa (N2.261; SC.71), and type IIx (212F) muscle fibers. A rabbit antibody raised against laminin was used to facilitate identifying individual muscle fibers. Alexa Fluor® secondary antibodies were used for detection. Digital imaging was performed at 100× and 400× magnification. Adobe Photoshop®, Nikon NIS-AR and NIH Image J software were employed for data acquisition.

Results: Immunohistochemistry and fluorescent microscopy were used to identify VDR and MHC isoforms in the whole muscle section. Ten 400× fields comprising 46% of the muscle fibers in the whole section were randomly selected. This sub-sample had a similar type I/type II muscle fiber ratio (32:68%) to the whole section. There were distinctive nuclear and non-nuclear VDR staining patterns. VDR co-localized with DAPI. From those images, we measured the relative number of VDR positive myonuclei (Table). Immunohistochemical staining of VDR was confirmed by Western blotting using the same antibody.

Conclusion: Immunofluorescence identified VDR-positive myonuclei providing evidence of nuclear-specific VDR expression. With this technique, there is evidence of non-nuclear VDR staining which may represent cytoplasmic or cell-surface VDR in muscle tissue. MHC profiles provide information on the relationship between fiber subtypes and VDR expression.

Relative number of VDR-positive myonuclei in ten 400× fields comprising 46% of the muscle section

Muscle fiber type	Number of VDR-positive nuclei	Total number of nuclei	Ratio (VDR/total)
Type I	165	178	0.93
Hybrid I–IIa	14	14	1.00
Type IIa	155	180	0.86
Type IIx	147	170	0.86
Hybrid IIa–IIx	70	83	0.84
All type I	179	192	0.93
All type II	372	433	0.86
Total	551	625	0.88