

ASBMR- Annual Meeting
Atlanta, Georgia
September 16, 2016

Highlights of the ASBMR 2016 Annual Meeting

John P. Bilezikian, MD
Roland Baron, DDS, PhD

The ASBMR Program for 2016

- **Special Sessions**
 - Special Symposium: Bone-omics: Translating Genomic Discoveries into Clinical Applications (9/15)
 - Named plenary lectures (Gerald D. Aurbach
Lecturer: Michael Snyder-9/16; Louis V. Avioli
Lecturer: Sundeep Khosla-9/17)
 - Plenary Symposia
 - Symposia
 - Basic Science Evening: Brain Signaling in Bone- 9/17
 - Clinical Science Evening: Can We Close the Treatment Gap for Osteoporosis- 9/17

Larry Raisz (1925-2010)



- Founding Member of ASBMR, 1977
- Founding President of ASBMR, 1980-1981
- Leader Extraordinaire
- Founding Editor of JBMR, 1986
- Scientific Leader
- Mentor
- Friend
- The "guru" of this program for Health Professionals!
- In Memoriam (Bilezikian et al., J Bone Miner Res 2011;26:903-911)

The ASBMR Program for 2016

- **Special Sessions (cont'd)**
 - Clinical Debate (9/16 ASBMR-ECTS)
 - Grant Writing Workshop
 - ASBMR Clinical Breakfast: How Discoveries Lead to Treatment or Rare Bone Diseases (9/16)
 - ASBMR-IOF Co-sponsored Session: Fracture Risk Assessment to Target Treatment: Effectiveness and Cost-Utility- 9/17
 - Publications Workshop: Increase Your Chances of Getting Published: 9/18

Betsy McClung



Inspiration for and founder of
this session 1996-

**Betsy-
This
presentation
is
for you!**

The ASBMR Program for 2016

- **Special Sessions (cont'd)**
 - Clinical Debate ASBMR-ECTS 9/16
 - ASBMR Task Force Reports
 - Long Term Safety and Efficacy of Vertebral Augmentation- 9/18
 - Cell Based Therapies- 9/18
 - Career Development Session: Negotiating for Success- 9/19

The ASBMR Program for 2016

- **NEW! HANDS ON WORKSHOPS**
 - How to Get Most Out of the UCSC Genome Browser: 9-16
 - Interpreting the Influence of Genomics on Bone Mineral Density: 9-17
 - Computational Methods for RNA-Seq Data analysis and network Modeling: 9-18
 - Biomechanical Phenotyping: How to Get the Most Out of a Phenotype: 9-18
 - Histomorphometry: An Introduction to Guidelines, Applications and Protocols: 9-19

The ASBMR Program for 2016

- Meet The Professors (18 clinical/translational; 6 basic- Fri, Sat, Sun, Mon)
 - Working Groups (8: Fri, Sun eves)
 - Ancillary Program- Industry sponsored (1: Sun AM)
 - Oral abstracts **158** (13% of total 1211* vs 10.8% of total in 2015)
 - Late-breaking abstracts **89** (-23% vs 2015)
- 2016: Total (not including late breaking abstracts) = 1211 (-16.4% vs 2015)**

The ASBMR Program for 2016

- **Networking and Social Opportunities:**
 - Welcome Reception and Plenary Poster Session: 9-16
 - NIH Lounge
 - Young Investigator, Diverse Member and New Member Lounge
 - Young Investigator and New Member Reception 9-16
 - Young Investigator and Diverse Member Networking Hour 9-16
 - Women's Committee Networking Reception 9-16

Distribution of all abstract presentations (orals and posters)

- A. Osteoblasts **67 (5.5%)** **34%**
- B. Osteocytes **40 (3.0%) NC**
- C. Osteoclasts **60 (5.0%)** **15%**
- D. Bone, Cartilage and Connective Tissue Matrix & Development **32 (3.0%)** **62%**
- E. Modulators of Bone Remodeling
- F. Hormonal and Paracrine Regulators **69 (5.0%)** **20%**
- G. Energy Metabolism, Bone, Bone Marrow Niche **94 (7%)** **20%**
- H. Genetic Disorders of the Musculoskeletal System **5331 (5.0%)** **71%**
- I. Bone Tumors and Metastases **35 (3.0)- NC**

The ASBMR Program for 2016

- **Networking and Social Opportunities (cont'd):**
 - ASBMR Networking Breakfast 9-17
 - ASBMR Networking Event: 9-17
 - ASBMR Annual Town Hall Meeting and Reception: 9-18
 - Diversity Reception: 9-18
 - The ASBMR Discovery Hall
 - ASBMR Networking Center

Distribution of all abstract presentations (orals and posters)- cont'd

- J. Osteoporosis – Assessment **92 (8.0%)** **46%**
- K. Osteoporosis – Epidemiology **6892 (6.0%)** **26%**
- L. Osteoporosis – Treatment **101 (8.0%)** **33%**
- M. Osteoporosis – Pathophysiology **40 (3.0%)** **14%**
- N. Osteoporosis- Secondary causes **45 (4.0%)** **280%**
- O. Osteoporosis- Health Care Delivery **29 (2%)** **17%**
- P. Osteoporosis- Nutrition and Dietary Supplements **52 (4%)** **58%**
- Q. Osteoporosis in Special Populations
- R. Aging, Osteoarthritis and Muscle/Bone Interactions **82 (6.0%)** **21%**
- S. Biomechanics, Mechanobiology, and Quality **69 (5.0%)** **53%**
- T. Bone Acquisition and Pediatric Bone Disease **30 (2.0%)** **6%**
- U. Adult Disorders of Mineral Metabolism **39 (3.0%)** **43%**
- V. Muscle biology and bone **44 (3%)** **91%**
- W. Rare and Other Bone Diseases **61 (5%)** **5%**

All osteoporosis-related categories: **27% (2016); 26% (2015), 27% (2014), 31% (2013), 34% (2012)**

All Abstracts reduced by 4% in 2013; 6% in 2014; 2.7% in 2015; 16.4% in 2016 (not including late-breaking abstracts)

Trends and special emphasis that you may notice at the 2016 ASBMR meeting

- Therapeutics of Osteoporosis (including Randomized Clinical Trials)
- Epidemiology of Osteoporosis
- Vitamin D, Calcium and Nutrition
- Musculoskeletal Biology

Acknowledgements*

- | | |
|---------------------|------------------------|
| • Tuan Nguyen | • Bill Leslie |
| • John Eisman | • Nicola Napoli |
| • Thierry Chevalley | • Nick Harvey |
| • Rene Rizzoli | • Eric Orwoll |
| • Ego Seeman | • Claes Ohlsson |
| • Mike Lewiecki | • Liesbeth Vandenput |
| • Mike McClung | • Lisa Langsetmo |
| • David Dempster | • Felicia Cosman |
| • Rachel Wagman | • Jacques Brown |
| • Andreas Grauer | • Nicola Pannacchiulli |
| • Roland Chapurlat | • Courtney Kennedy |
| • Stephanie Boutroy | • Alexandra Papaionnou |

*Provided me with material relevant to their presentations

Trends and special emphasis that you may notice at the 2016 ASBMR meeting (continued)

- Secondary Causes of Osteoporosis
- Genetics as applied to clinical aspects of skeletal health
- Rare Bone Diseases

Topics to be covered

- EFF-ASBMR Fellows' Symposium
- Vitamin D, Calcium, Nutrition, Exercise
- Epidemiology and Outcomes Research
- Muscle, Sarcopenia, Frailty, Aging
- Clinical Applications of Advanced Imaging
- Therapeutics of Osteoporosis
- Diabetes, Obesity and Bone
- Rare Metabolic Bone Diseases
- Pediatrics/Adolescents/Development
- Clinical Genetics
- Others

Highlights of the ASBMR 2016 Annual Meeting*

Bilezikian:

Clinical Science Meeting Overview

Baron:

Basic Science Meeting Overview

*Data presented at this session in anticipation of the actual abstract presentations are embargoed until the time of the abstract presentations

10th EFF-ASBMR FELLOWS FORUM ON METABOLIC BONE DISEASES September 14-15, 2016



64 Attendees
14 countries represented
33% International
50/50 MDs and PhDs
3 Plenary Lectures and 8 workshops
11 Faculty
Fellows presented 54 abstracts!

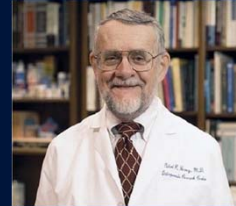
VITAMIN D, CALCIUM, NUTRITION, EXERCISE

Fri: 9/16 7:15-9:30 PM	Working Group: Nutrition and Bone (registration fee)	S. Shapses
Fri: 9-16 10:45-11:45 AM	MTP: Update on Nutritional Influences on the Musculoskeletal System	B. Dawson-Hughes
Sun: 9-18 8:00-9:30 AM	Symposium: Gut Microbiome and Bone Homeostasis	A. Uitterlinden, R. Rizzoli, R. Pacifici
Sun: 9-18 11 AM-Noon	What is the Optimal Dose and Administration of Vitamin D Supplements for Falls and Fracture Prevention?	K. Sanders

Abstracts of note: #s 1008, 1070, 1071, 1107, 1108, 1109, 1110, 1112, 1129

Why Calcium and vitamin D?

"a person needs both calcium and vitamin D to ensure sufficient net absorption of calcium for meeting various body needs"
(Heaney AJCN 2008)



Abs #1008: Nguyen et al. Calcium plus Vitamin D Supplementation, Fracture, and Cardiovascular Outcomes

Background and Question: Calcium and Vitamin D Supplementation: good or bad for fracture and/or cardiovascular outcomes

Design:

11 Primary RCTS (n=56569) on Fx risk; 7 post-hoc analyses of RTCs on CVD (n=46526);
Bayesian approach to analysis of the RCTS

Results:

Abs #1108: Harvey et al. Calcium and/or Vitamin D supplementation are not Associated with Ischemic Heart Disease

Background and Question: Calcium ± Vitamin D Supplementation: increased risk of MI?

Design: UK biobank cohort (n= 502,664) age 40-69; prospective over 7 yrs

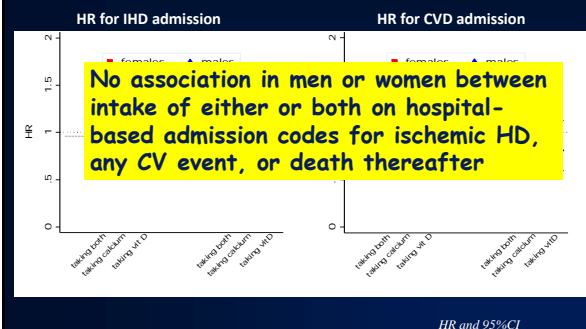
Results: # self-reporting calcium, 6.9%; vitamin D, 3.9%; both, 2.1%.

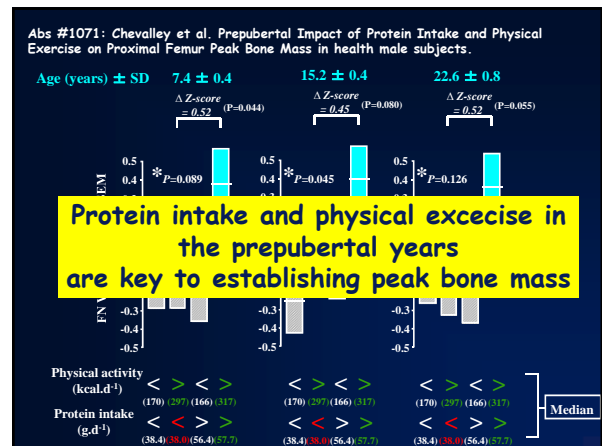
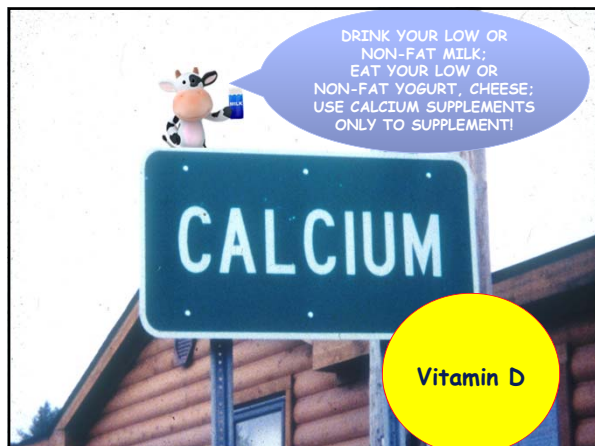
Abs #1008: Nguyen et al. Calcium plus Vitamin D Supplementation, Fracture, and Cardiovascular Outcomes

Results:

Outcome	5-yr incidence ¹	Relative risk	Utility ²	NNT or NNH
Total fracture	0.093	0.85	0.90	NNT = 68
Myocardial infarction	0.017	1.05	0.75	NNH = 1176
Stroke	0.018	1.03	0.72	NNH = 1851

Abs #1108: Harvey et al. Calcium and/or Vitamin D supplementation are not Associated with Ischemic Heart Disease





LAST YEAR: #1064: Coster et al. Increased Physical Activity in Childhood Reduces Fracture Risk- an 8-Year interventional Study in 3534 Children

Background: Exercise increases bone mass in children

Question: Does it influence fracture risk?

Design: 40' of exercise/school day x 8 yrs in 1339 children (6-8 yrs old). Control: 2,195 children in other schools 60 minutes/school week.

Results: RR for fx fell every year: at end RR reduction 0.48 (CI 0.25-0.91). Bone mass higher in the exercisers. Muscle strength greater

Conclusion: EXERCISE LEADS TO BETTER SKELETAL HEALTH IN CHILDREN.

Abs #1107: Langsetmo et al. Low Protein Intake Among Older Men is Associated with an Increased Risk of Fracture (presentation modified since abstract submission)

Background: Dietary protein is a potentially modifiable risk factor vis a vis fracture risk in older men.

Question: Is protein intake associated with fracture risk in older men? Related to BMD?

Design: Mr. OS (n=5,888, mean age 73.6y; range 64-100 in 2000-2002). 808 incident fxs over 15 years (63,500 person yrs)

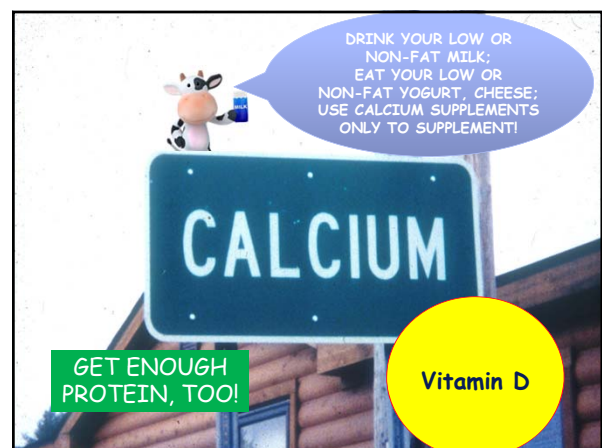
Conclusions: low protein intake was inversely associated with MOF, fragility fx, and hip fracture

Abs #1071: Chevalley et al. Prepubertal Impact of Environmental Factors on Proximal Femur Peak Bone Mass; the key role of protein intake on response to physical exercise in healthy male subjects.

Background: Protein intake (Prot-int) and physical activity (PA) are beneficial to skeletal health in childhood.

Question: Does this childhood effect last until peak bone mass (PBM) is achieved?

Design: 124 boys (7.4) followed until 22.6 years of age. PA and Prot-Int determined in youth. (no comment on whether these indices were maintained throughout childhood)

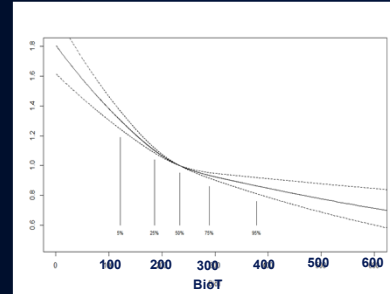


EPIDEMIOLOGY AND OUTCOMES RESEARCH

Fri: 9/16 10:45 AM	MTP: Using Medical Claims Data to Study Fracture Epidemiology	S. Berry, N. Wright
Sat: 9/17 11:00 AM	MTP: Utility and Limitations of TBS in Fracture Risk Assessment	W. Leslie
Abstracts related to Epidemiology 1021, 1029, 1032, 1073, 1074, 1075, 1076, 1077, 1078, 1107, 1108, 1109, 1111, 1127, 1128		
Abstracts related to Outcomes Research 1006, 1007, 1008, 1073, 1077, 1125		

#1127: Vandenput et al. Low Testosterone, but not Estradiol, Predicts Incident Falls in Older Men- the international MrOS Study

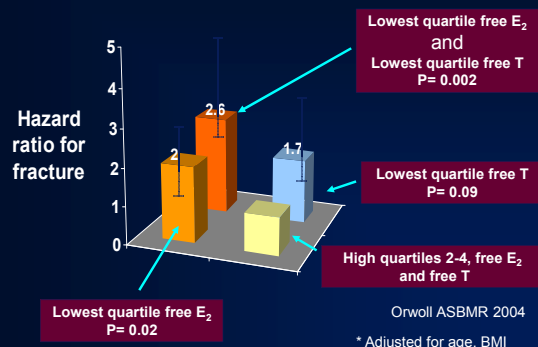
Fall Risk, HR



- > Fig describes a relationship to BioT
- > No relationship to E or bioE



Both E and T are needed for optimal male skeletal health*



#1078: Harvey et al. Falls Predict Fractures Independently of FRAX probability: The Osteoporotic Fractures in Men (MrOS) study

Background: Falls result in fractures; FRAX does not include information about falls.

Question: Do past falls predict incidence fractures, independent of FRAX?

Design: MrOS (USA, Sweden, Hong Kong). Falls and FRAX probabilities available in 4,365 men; age 73.5 yrs. Follow up: 8.7 to 10.8 yrs.

Results: Across all 3 cohorts, past falls predicted fractures at any site, MOF, and Hip Fx, independent of FRAX.

#1127: Vandenput et al. Low Testosterone, but not Estradiol, Predicts Incident Falls in Older Men- the international MrOS Study

Background: Estrogen and testosterone sufficiency are important for optimal male skeletal health.

Question: How do these sex steroids relate to fall risk in older men (>65)?

Design: MrOS (Int'l). Sex steroids measured over 2.7 (Sweden); 11.2 (USA); 3.8 (Hong Kong) yrs. (n=5,897)

Results: T and BioT predicted fall risk, but E2 or bioE2 did not.

1078 Harvey et al. Independent predictive value of prior falls and high FRAX for incident fracture

		Any (n=1428)	MOF (n=839)
Falls at baseline adjusted for FRAX	HK	1.94 (1.39, 2.71)	2.04 (1.34, 3.09)
	SW	1.57 (1.24, 1.99)	1.47 (1.11, 1.95)
	US	1.63 (1.40, 1.90)	1.47 (1.19, 1.83)
	Total	1.64 (1.46, 1.85)	1.53 (1.31, 1.79)

Conclusion: Fall history adds to FRAX-specific information on MOF and Hip fracture probabilities in men

	US	1.52 (1.30, 1.76)	1.49 (1.17, 1.91)
	Total	1.46 (1.29, 1.65)	1.48 (1.26, 1.73)

MOF=Major Osteoporotic Fracture (Hip, clinical vertebral, wrist, proximal humerus)
HK=Hong Kong; SW=Sweden; US=United States of America

#1074: Cosman et al. Spine Fracture Prevalence in US Women and Men Aged 40 years and older: NHANES 2013-2014

Background: Vertebral fractures are of major clinical significance but do not often come to medical attention.

Question: What is VF prevalence by VFA?

Design: Cross-sectional; 3,330 US adults with evaluable VFA, BMD, and an osteoporosis questionnaire

Results: 5.4% prevalence overall; sexes equal (all VF grades included); increased with age from 5% (<60) to 11% (70-79) to 18% (>80). Higher in those that met NOF criteria for VFA (14% vs. 4.7%)

#1128: Napoli et al. A Single Assessment of BMD Can Strongly Predict Fracture Risk Over 25 Years in Post-Menopausal Women: (SOF)

Background: BMD's value as a predictor of fracture risk is well-established over a 5-10 year period.

Question: Can a single BMD measurement predict fracture risk over 25 years?

Design: SOF (n=7,959), > 67 y ('88-'89); follow up for 25 y (Hip Fracture), 20 years for wrist and non verts. FN BMD related to long term fracture risk.

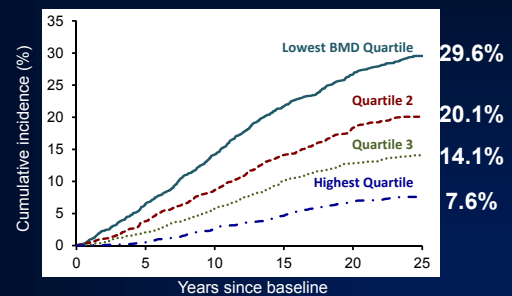
Results: highest vs lowest quartile of BMD; Risk for hip fracture 29.6% vs 7.6% (RH 4.9 CI 4.1-6.0)

#1074: Cosman et al. Spine Fracture Prevalence in US Women and Men Aged 40 years and older: NHANES 2013-2014

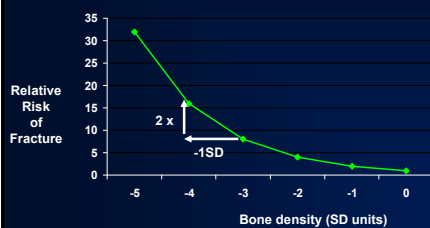
Fx by VFA	OP by DXA	NI by DXA
Yes (all)	26%	
Yes (>65)	38%	22%
No (>65)	14%	35%

Fx by VFA	Report of Spine Fx by Hx
Yes	8%
21%	Yes

#1128: Napoli et al. Cumulative Incidence of Hip Fracture over 25 Years by (Age-Adjusted) Femoral BMD Quartile

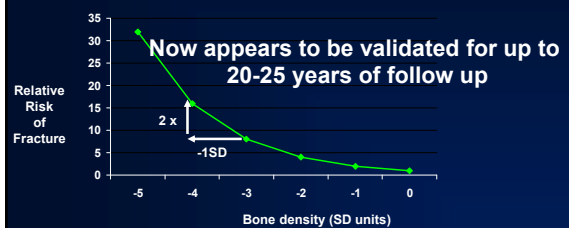


Relationship between BMD and fracture Risk



Adapted from Faulkner KG. *J Bone Miner Res.* 2000;15:183-187

Relationship between BMD and fracture Risk



Adapted from Faulkner KG. *J Bone Miner Res.* 2000;15:183-187

#1077: Lewiecki et al. Hip Fractures and Declining DXA Testing: At a Breaking Point?

Background: Hip Fx incidence has fallen over the past 15 years. Reasons given: improvement in OP evaluation; DXA; treatments.

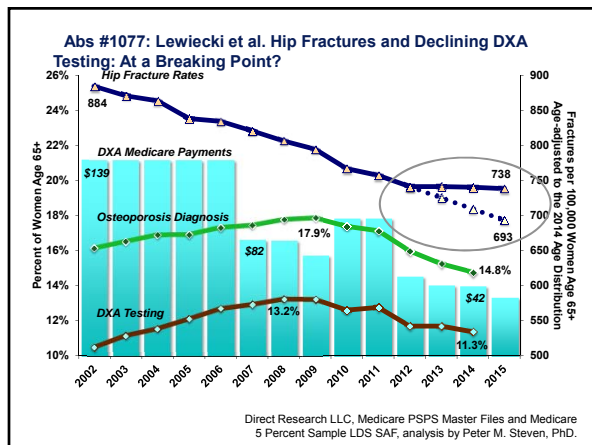
Question: What are the latest national trends in hip fracture rates?

Design: Health care claims enrollment data from Medicare. DXA service/ICD-9 code(s) for hip fracture

Results:

Muscle and Bone, Frailty, Aging

Fri: 9/16 10:45 AM	MTP: Updates on Nutritional Influences on the Musculoskeletal System	B. Dawson-Hughes
Fri: 9/16 7:15 PM	Working Group: Muscle and Bone	J. Willnecker
Fri: 9/16 7:15 PM	Working Group: Aging	S. Khosla
Sun: 9/18 11:00 AM	MTP: What is the Optimal Dose and Administration of Vitamin D Supplement in Falls and Fractures Prevention	K. Sanders



Muscle and Bone, Frailty, Aging

Mon: 9/19 11:00 AM	MTP: How to Evaluate Sarcopenia as a Risk Factor for Falls and Fractures	TBD
Mon: 9/19 2:30 PM	Plenary Symposium: Determinants of Skeletal Aging	S. Melov, A Wagers, B Alman
Abstracts of Note: #s 1067, 1078, 1110, 1111, 1126, 1127, 1130		

#1077: Lewiecki et al. Hip Fractures and Declining DXA Testing: At a Breaking Point?

HYPOTHESIS

Reduced DXA reimbursement

Fewer DXA providers

Fewer DXAs performed

Reduced number of patients diagnosed with osteoporosis

Fewer individuals being treated

Increasing incidence of hip fractures

Obesity and Frailty



#1126: Kennedy et al. Baseline Obesity is Predictive of More Rapid Frailty Onset: a 10-year Analysis of the CaMOS Study

Background: U-shaped relationship between BMI and frailty is known.

Question: Does obesity contribute to frailty onset or progression?

Design: CaMos frailty index (n=7,753, av age 66); 5- and 10-year follow

Results: Baseline obesity (esp. marked obesity) associated with faster rate of frailty development

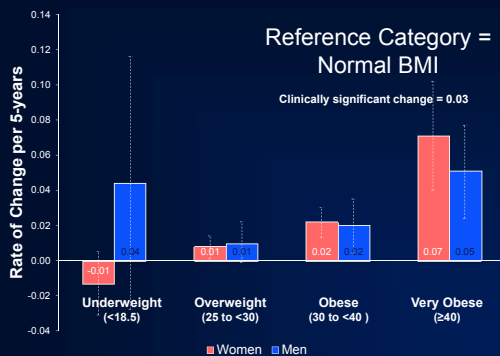
#1070: Boutroy et al. Measurement of Cortical and Trabecular Deterioration Identifies Women at Imminent Risk for Fracture: the OFELY Study

Background: Fracture risk is a function not only of BMD but skeletal microstructure

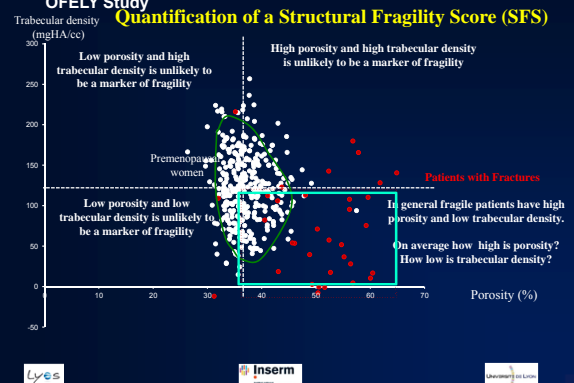
Question: Can a Structure Strength Index (SSI) based upon HRpQCT-determined cortical porosity and trabecular density (+ age) predict imminent fracture risk?

Design: OFELY (n=589 French PM women, 42-94 yrs); 9.4 years of follow-up; Comparators: FN BMD and FRAX (without BMD)

#1126: Kennedy et al. Baseline Obesity is Predictive of More Rapid Frailty Onset: a 10-year Analysis of the CaMOS Study



#1070: Boutroy et al. Measurement of Cortical and Trabecular Deterioration Identifies Women at Imminent Risk for Fracture: the OFELY Study



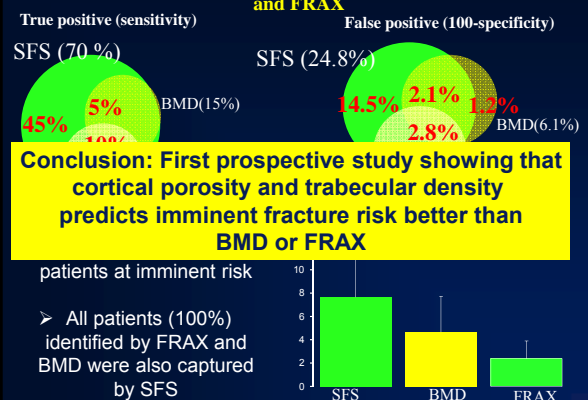
Clinical Applications of Advanced Imaging*

Fri: 9/16 Noon	Symposium: The Importance of Cortical Bone Through the Life Span	K. Engelke, S. Boyd, M. Leonard
Sat: 9/17 11:00 AM	MTP: Utility and Limitations of TBS in Fracture Risk Assessment	W. Leslie

Related Abstracts:
#s 1024, 1030, 1031, 1067, 1068, 1069, 1071, 1074, 1076, 1090, 1112, 1129

* Many abstracts also "fit" into other categories illustrating the rapid translational strengths of imaging technology to clinical disorders of bone

#1070: Predicting Imminent MOP fractures using SFS, FN BMD and FRAX



#1030: Seeman et al. Menopausal Bone Loss is Mainly Cortical, not Trabecular, and Does not Attenuate the Heritable of Variance in this Microarchitecture: a Prospective Study of Twins.

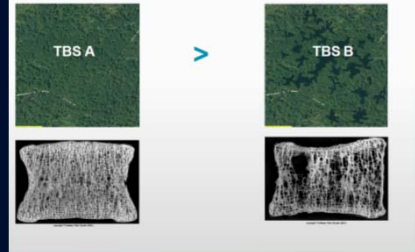
Background: The skeleton is 80% cortical bone, but remodeling occurs more rapidly in trabecular bone.

Hypothesis: Cortical bone loss accounts for most bone loss during the menopausal period

Design: HRpQCT of distal radius and tibia in monozygotic (n=199) and dizygotic twins pairs (n=125) over 3.4 (1.5-4.5) perimenopausal years

IMAGING: TRABECULAR BONE SCORE (TBS)

TBS Simplified Principle



#1030: Seeman et al. Menopausal Bone Loss is Mainly Cortical, not Trabecular, and Does not Attenuate the Heritable of Variance in this Microarchitecture: a Prospective Study of Twins.

State	Cortical Porosity Annualized increase	Trabecular Density (BV/TV) Annualized decrease
Premenopausal	+0.44 %	-0.17 %
Pre-peri MP	+0.80 %	-0.25 %
Peri-post MP	+1.40%	-0.31%
Post MP	+0.83%	-0.16%

Conclusion: Mean total bone loss at distal tibia:
Cortical: 74%
Trabecular: 26%

Clinical Applications of Advanced Imaging TBS Abstracts

Sat: 9/17
11:00 AM

MTP. Utility and Limitations of
TBS in Fracture Risk Assessment

W. Leslie

Related Abstracts:

#s **FR236**, FR 196

SA 190, **193**, 195, 196, 202, 214, **236**, 281, LB 376

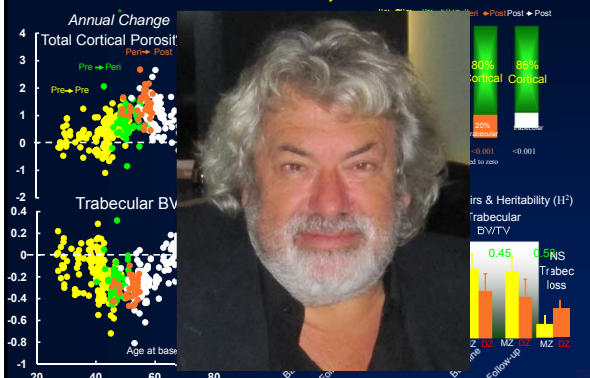
SU 035, 199, 200, 202, 203, 204, 211, 267, 280, 281, LB 368

MO 037, 188, 193, 199, 201, 226, 266, 278, 287, 346

FR 236 and SA 236: Wong et al. Low TBS correlates with AFFs but not with duration of antiresorptive therapy

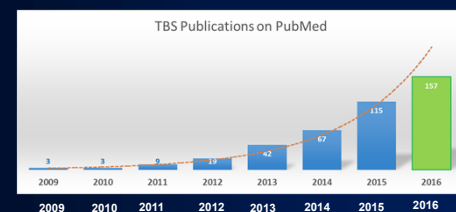
SA 193: Gong et al. TBS does not correlate with distal radial fractures

AB # 1030 Biomerem....Seeman Menopausal Bone Loss is Mainly Cortical & Does not Attenuate the Heritability of Microstructure



TBS reports at ASBMR and Publications since 2009...

- 2011 -- 1 abstract
- 2012 -- 19 abstracts
- 2013 -- 30 abstracts
- 2014 -- 34 abstracts
- 2015 -- 21 abstracts
- 2016 -- 34 abstracts



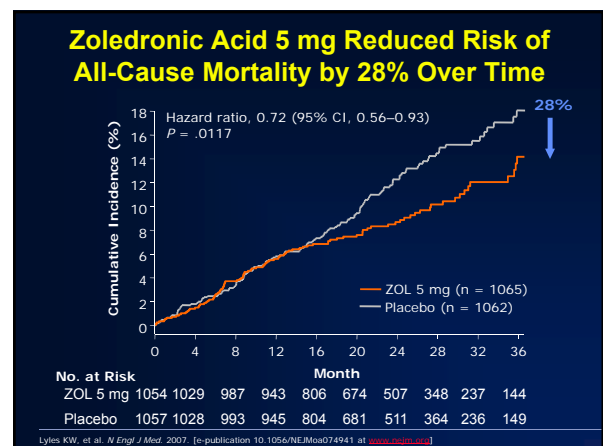
OSTEOPOROSIS THERAPEUTICS		
Fri: 9/16 3:00 PM	Clinical Debate- ASBMR-ECTS: Microdamage is Good for Bone: For: Mitch Schaffler Against: Ralph Mueller	C. Gluer M. Bouxsein
Sat: 9/17 8:00 AM	Louis V. Avioli Lecture Sex Steroids, Coupling, and Age-related Bone Loss	S. Khosla
Sat: 9/17 11:00 AM	ASBMR-IOF Co-Sponsored Session: Fracture Risk Assessment to Target Treatment: Effectiveness and Cost Utility	C. Cooper M. McClung

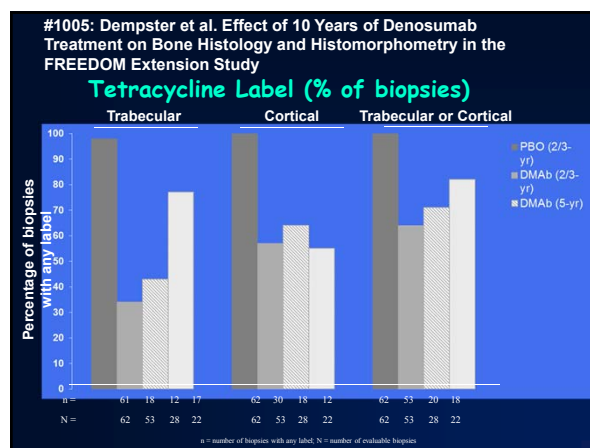
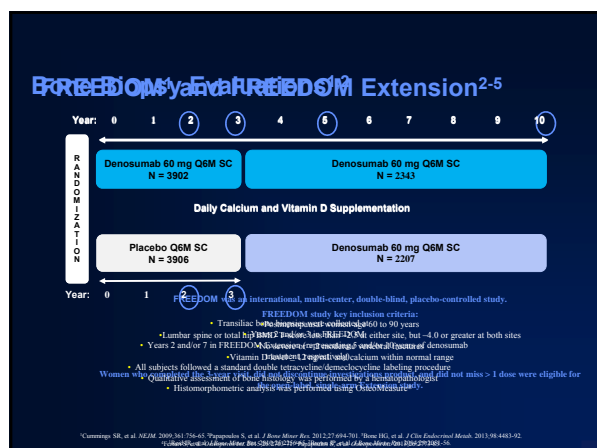
OSTEOPOROSIS THERAPEUTICS		
<p>Antiresorptives Bisphosphonates Denosumab Odanacatib</p> <p>Osteoanabolics: Romosozumab Abaloparatide</p>		

OSTEOPOROSIS THERAPEUTICS		
Sat: 9/17 11:00 AM	MTP: Sequential and Combination Therapy for Osteoporosis. Where are we now?	F. Cosman
Sat: 9/17 6:30 PM	Clinical Evening: Can We Close the Treatment Gap for Osteoporosis?	J. Compston D. Black S. Greenspan
Sun: 9/18 6:00 AM	Ancillary Symposium: New Horizons for Osteoporosis	J. Bilezikian M. Lewiecki P. Miller
Sun: 9/18 11:00 AM	MTP: Fracture Risk of Osteoporosis Therapy	M. McClung

<p>#1006: Axelsson et al. Alendronate Treatment is Associated with Reduced Fracture Risk and Maintained Safety in the Oldest Old</p> <ul style="list-style-type: none"> ➢ Swedish data base of 110,190 age 82.4 from 2008-2014 with prior fracture ➢ Alendronate use: reduced hip fx HR 0.72 (CI 0.61-0.85) ➢ Absolute risk reduction greater with age ➢ Side effects similar across quartiles of age <p>#1007: Bluc et al. The Effect of Bisphosphonates on All-Cause and Post-Fracture Mortality Risk in CaMOS</p> <ul style="list-style-type: none"> ➢ Canadian database of 7689, > 50 y over 15 yrs ➢ Mortality risk current BP users: HR 0.70 (CI 0.49-0.94); past BP users: HR 0.49 (CI 0.34-0.70) ALN and RIS but not Etidronate ➢ Not related to reduced subsequent fxs

OSTEOPOROSIS THERAPEUTICS		
Sun: 9/18 11:30 AM	ASBMR Task Force Reports	M. Bouxsein P. Ebeling
<p>Noteworthy Abstracts:</p> <p>Bisphosphonates: 1006,1007,1022, 1158, LB-1159, Denosumab: 1005, 1100, 1157, LB 1163 Odanacatib: 1090, 1097, 1099, 1155, 1156 Romosozumab: 1024,1096 Teriparatide: 1157 Abaloparatide: LB1162</p>		





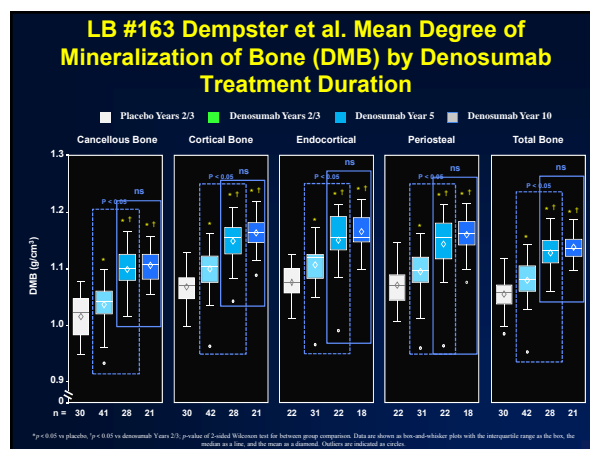
#1005: Dempster et al. Effect of 10 Years of Denosumab Treatment on Bone Histology and Histomorphometry in the FREEDOM Extension Study

Background: By bone bx, marked reductions in dynamic parameters after 5 yrs of denosumab

Question: Are these reductions maintained after 10 years?

Methods: 22 evaluable bxs; 21 for histomorphometry

Results: No pathologic findings (e.g. osteomalacia, woven bone or marrow fibrosis)



#1005: Dempster et al. Effect of 10 Years of Denosumab Treatment on Bone Histology and Histomorphometry in the FREEDOM Extension Study

Results (cont'd)

Tetracycline label*	Trabecular	Cortical
Year 2-3	34%	57%
Year 5	43%	64%
Year 10	77%	55%

* Double label in 32% at 10 years

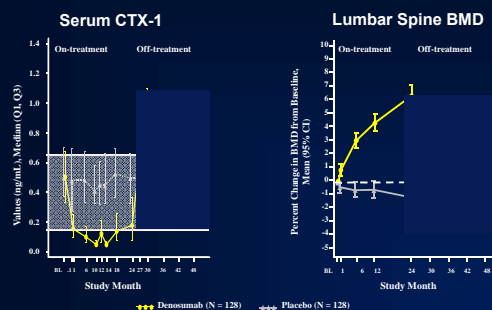
#LB1163: Dempster et al. Effects of Up to 10 Years Of Denosumab Treatment on Bone Matrix Mineralization: Results from the FREEDOM Extension Study

- Mineralization peaks at 5 yrs (at 10 yr = 5 yr)
- Heterogeneity index lowest at 5 yrs (at 10 yr = 5 yr)

Abs #1005 and #LB163. Dempster et al. Conclusions

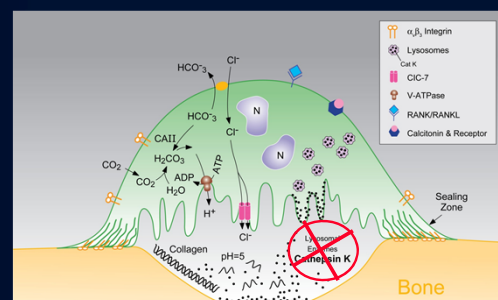
- After 10 years of denosumab, normal bone architecture, lamellar appearance, and mineralization
 - Cancellous and cortical bone structure maintained
 - The antiresorptive effects of denosumab maintained
 - No progression of low remodeling
 - Progressive increase in trabecular site tetracycline labels
 - Bone mineralization density increases through yr 5 but not thereafter
 - Heterogeneity index falls through yr 5 but not thereafter
 - No safety signals through 10 years

#1100: Brown et al. Discontinuation of Denosumab and Associated Fracture Incidence: Analysis from FREEDOM and Its Extension



Includes subjects who enrolled in the off-treatment phase
Reference: Bone HG, et al. J Clin Endocrinol Metab 2011
CTX-1: collagen type I C-terminal; Q1, Q3: first, third quartile; BMD: bone mineral density; CI: confidence interval

THE CONCEPT OF ODANACATIB: ANOTHER WAY TO TARGET THE OSTEOCLAST



Rodan & Dending BoneKey 2008

Cathepsin K is highly expressed in the osteoclast, where it is localized in the lysosomes and released during bone resorption.

#1100: Brown et al. Discontinuation of Denosumab and Associated Fracture Incidence: Analysis from FREEDOM and Its Extension

Background: When denosumab is discontinued, BTM rise and BMD falls acutely

Question: Is fracture incidence also increased upon discontinuation of denosumab?

Design: At least 2 doses; followed for > 7 mos; original Rx and crossover arms included (n=1001)

Results:

- New Vert Fx incidence increased in those with and without prior fractures when denosumab was discontinued

#1155: McClung et al. Olanacatib Efficacy and Safety in Postmenopausal Women with Osteoporosis: 5-year Data from the Extension of the Phase 3 Long-Term Olanacatib Fracture Trial (LOFT)

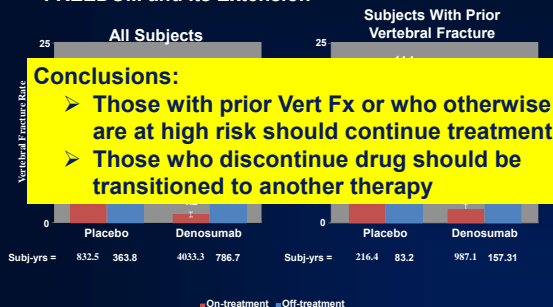
•Age: 72.8
•T-score <-2.7 (LS); -2.4 (TH); -2.7 (FN);
prior radiographic VFX (46.5%)
•N= 16,071; 387 centers; 40 countries

Current Study: average follow up: 44 (18) mos (n=6047 completers)

•RR Reductions in:
▪ Vert Fx 54%
▪ Hip Rx 47%
▪ Non-Vert: 23%

RR Reductions in:
Vert Fx: 52%
Hip Fx: 48%
Non-Vert: 26%

#1100: Brown et al. Discontinuation of Denosumab and Associated Fracture Incidence: Analysis from FREEDOM and Its Extension



Conclusions:

- Those with prior Vert Fx or who otherwise are at high risk should continue treatment
- Those who discontinue drug should be transitioned to another therapy

#1156: Papapoulos et al. Safety of Olanacatib in Postmenopausal Women with Osteoporosis: 5-Year Data from the Extension of the Phase 3 Long-Term Olanacatib Fracture Trial (LOFT)

Index	Placebo	Olanacatib
AEs	88.2%	88.3%
SAEs	30.4%	30.3%
Deaths (ITT)	8.2%	8.5%
Fem Shaft Fxs	0.1% (n=7)	0.3% (n=26)
Atypical Femoral Shaft Fxs	0 (n=0)	0.1% (n=10)
ONJ	0 (n=0)	0 (n=0)
Morphea-like skin lesions	<0.1% (n=3)	0.2% (n=13)

#1099: O'Donaghue et al. The Long-Term Odanacatib Fracture Trial (LOFT): Cardiovascular Safety Results

Background: Initial data from LOFT suggested an imbalance in some cardiovascular endpoints although preclinical data suggested that cathepsin K inhibition might reduce atherosclerosis progression and promote plaque stability

Question: Are MACE (major adverse cardiovascular events) different: PLB v Odanacatib from LOFT?

Design: Complete independent adjudication from the TIMI Study Group from Brigham and Women's Hospital

Results: NOT PROVIDED IN THE ABSTRACT!

#1096: Cosman et al. Fracture Risk Reduction with Romosozumab: Results of the Phase 3 FRAME Study

Background: Based upon mechanism, an antisclerostin antibody might be powerfully anabolic for bone

Question: Does Romosozumab reduce vertebral fractures after yr 1 (Romo) and yr 2 (Denosumab) compared with PLB (yr 1 followed in yr 2 by denosumab)?

Design: Multicenter, double-blind, PLB-controlled; PM women 55-90 (age= 71; n=7,180); T-score of TH -2.5) Romo 210 mg SC monthly x 1 yr followed by denosumab, 60 mg x 1 yr

**Press Release from Merck
September 2, 2016**

KENILWORTH, N.J.-(BUSINESS WIRE)-- Merck today announced that it is discontinuing the development of odanacatib, Merck's investigational cathepsin K inhibitor for osteoporosis, and will not seek regulatory approval for its use. Merck previously reported a numeric imbalance in adjudicated stroke events in the pivotal Phase 3 fracture outcomes study in postmenopausal women. The company has decided to discontinue the development of odanacatib based on this data and the results of the Phase 3 fracture outcomes study. The company has decided to discontinue the development of odanacatib based on this data and the results of the Phase 3 fracture outcomes study. The company has decided to discontinue the development of odanacatib based on this data and the results of the Phase 3 fracture outcomes study.

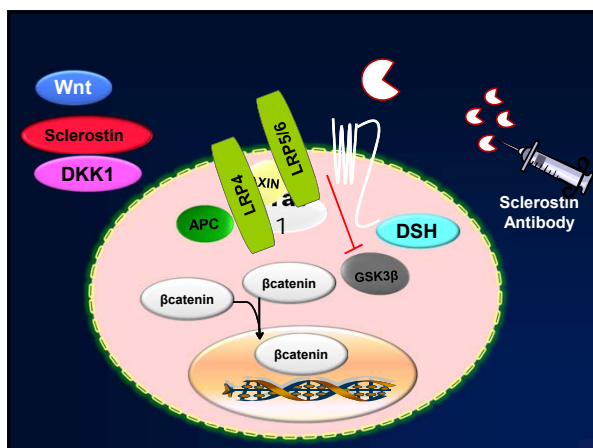
The further development of Odanacatib as a therapy for osteoporosis has been terminated

"We are very thankful to the researchers and patients who participated in the odanacatib clinical development program. We have learned that odanacatib treatment reduces the risk of osteoporotic fractures. At the same time, we believe that the increased risk of stroke in our Phase 3 trial does not support further development."

#1096: Cosman et al. Fracture Risk Reduction with Romosozumab: Results of the Phase 3 FRAME Study

Results:

Vert Fx	RR (v PLB)	Absolute RR (v PLB)
M 12:	73%	0.5% v 1.8% (p < 0.001)
M 24:	75%	0.6% v 2.5 % (p < 0.001)
Clinical Fx		
M 12:	36%	1.6% v 2.5% (p < 0.001)
NonVert Fx		
M 12:	25%	1.6% v 2.1% (p= 0.096)
M 24:	25%	(p=0.057)

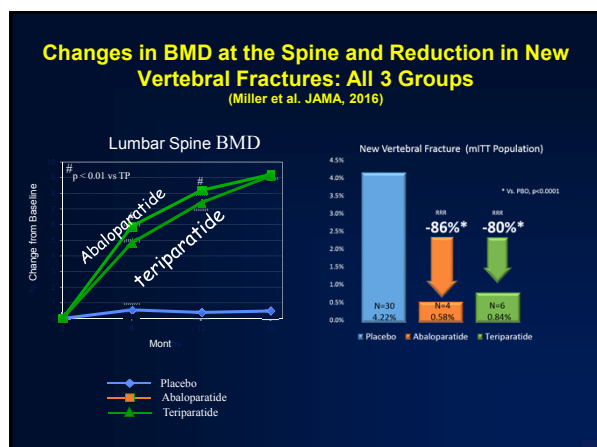
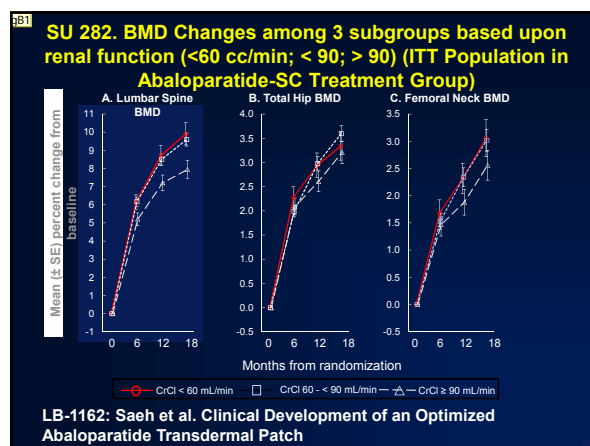
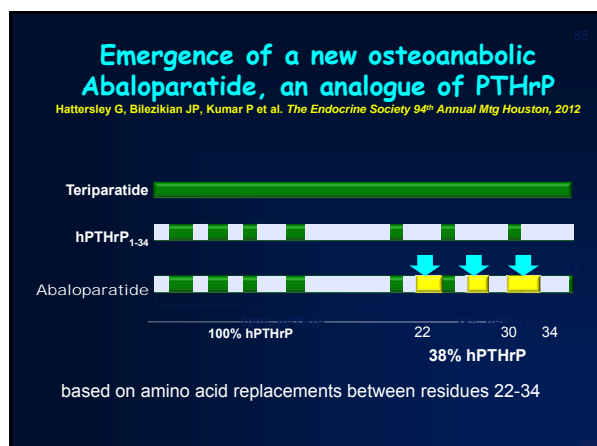


#1096: Cosman et al. Fracture Risk Reduction with Romosozumab: Results of the Phase 3 FRAME Study

Results:

Pre-planned Analysis: interaction by geography was significant at 12 mos (p=0.042)

Nonvert Fx	Latin/Central America	Rest of World
RR reduction	20% (NS)	42% (p < 0.001)
Abs incidence	1.2% (PLB)	1.5% (Romo)



DIABETES, OBESITY AND BONE		
Mon : 9/19 11:00 AM	MTP: Bone Marrow Adipose Tissue Development and Detection	M. Horowitz
Abstracts: 1001, 1070, 1075, 1126,		

#SU 282: Bilezikian et al. Abaloparatide-SC has Minimally –different- effects in subjects with mild to moderate renal impairment

Background: ACTIVE trial enrolled subjects with a spectrum of renal clearances (cc/min): 30-60; 60-90; > 90.

Question: Are there differences in BMD accrual and/or side effects based upon differences in renal function?

Results: There were minimal differences in BMD accrual and side effects when analyzed according to renal function

#1075: Leslie et al. Longer Duration of Diabetes Strongly Impacts Fracture Risk Assessment: The Manitoba BMD Cohort

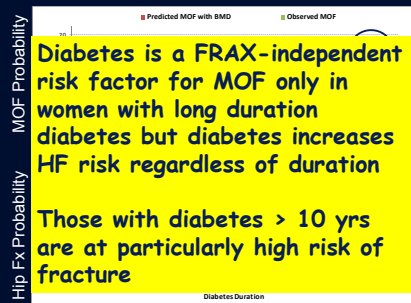
Background: T2 Diabetes Mellitus is associated with a higher risk of major osteoporotic fractures (MOF) and hip fracture (HIP); not accounted for by FRAX.

Question: Is duration of diabetes a factor in fracture risk assessment with FRAX?

Method: Manitoba cohort of 49,098 women without DM and 8840 with DM. Most (75%) had DM before first DXA measurement

Results: HF risk increase in all but gradient of risk was seen as a function of DM duration: MOF risk was evident only in those with DM > 10 yrs.

#1075: Leslie et al. FRAX Calculation



* Predicted vs Observed 10-Year probability of major osteoporotic fracture (MOF) and hip fractures with competing mortality

METABOLIC BONE DISEASES: EMPHASIS THIS YEAR ON RARE DISEASES

Abstract #	Authors	Disease
1003	Ramnitz et al	Hyperphosphatemic Tumoral Calcinosis
1004	McKee et al.	XLH
1154	Carpenter et al.	XLH
1011	Hendrickx et al	Hyperostosis Cranialis Interna
1061		Osteogenesis Imperfecta
1062		Familial Hypomagnesemia
1063	Roizen et al.	VDDR
1064	.	Feingold Syndrome
1065	Denker et al.	Hypophosphatasia
1066	Wuerzburg et al.	Hypophosphatasia
1098	Carpenter et al.	TIO
1098	Carpenter et al.	Epidermal Nevus Synd.

12 oral presentations;
10 rare Diseases;
4 Special Sessions

METABOLIC BONE DISEASES: EMPHASIS THIS YEAR ON RARE DISEASES

Fri: 9/16 6:30 AM	ASBMR Clinical Breakfast: How Discoveries Lead to Treatment of Rare Bone Diseases	M. Whyte D. Shoback K. Insogna
Fri: 9/16 7: 15 PM	Rare Bone Disease Working Group	C. Waldman
Fri: 9/16 7:30 PM	Bone Turnover Working Group	N. Guanabens
Sun: 9/18 11:00 AM	MTP: Hypophosphatasia	JL Milan M Whyte
Sun: 9/18 7:15 PM	Adult Bone and Mineral Working Group	N. Cusano

PEDIATRICS/ADOLESCENTS AND DEVELOPMENT

Sun; 9/15: All day	MTP: Skeletal Development and Mineral Metabolism in the Fetus and Newborn: Insights from Animal Models and Limited Human Data	C. Kovacs D. Krakow
Sun: 9/18 7:15 PM	Working Group: Pediatric Bone and Mineral	M. Misra

Abstracts related to pediatrics and development:
#s 1067, 1068, **1069**, 1070., 1071, **1072**

#1069: Singh et al. Microstructure of the tibia is abnormal in anorexia nervosa. (previously shown at the radius)
#1072: Arpad et al. Treated HIV-infected children have reduced bone formation markers but not increased bone resorbing cytokines

METABOLIC BONE DISEASES: EMPHASIS THIS YEAR ON RARE DISEASES

Mon: 9/19 11:00 AM	MTP: Osteogenesis Imperfecta	K Kozloff J Marini
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CLINICAL GENETICS

Thurs: 9/15: All Day	ASBMR Symposium: Bone-omics. Translating Genomic Discoveries into Clinical Applications	E. Orwoll J. McGowan C. Ackert-Bicknell P. Croucher F. Rivadeneira L. Bonewald E. Duncan D. Kiel
Fri: 9/16 10:45 AM	MTP: Genome Editing-From Patients to Mice with CRISPR/Cas	B. Williams
Sat: 9/17	Hands-on Workshop-Interpreting the Influence of Genomics on BMD	E. Duncan P. Leo

CLINICAL GENETICS

Mon: 9/19 11:00 AM	MTP: Following up GWAS Finding- From Dry Lab to the Wet Lab	M. Maurano B. Richards
Abs #: 1001, 1011, 1029, 1030, 1031, 1032, 1061, 1062, 1063, 1064, 1066, LB 1160		

Topics covered

- EFF-ASBMR Fellows' Symposium
- Vitamin D, Calcium, Nutrition, Exercise
- Epidemiology and Outcomes Research
- Muscle, Sarcopenia, Frailty, Aging
- Clinical Applications of Advanced Imaging
- Therapeutics of Osteoporosis
- Diabetes, Obesity and Bone
- Rare Metabolic Bone Diseases
- Pediatrics/Adolescents/Development
- Clinical Genetics
- Others

OTHER TOPICS

Biomechanics Sat: 9/17; 11:00 AM	MTP: Biomechanics Meets Bone Biology: The Ultimate in Multidisciplinary Translational Research	M. Bouxsein
Histomorphometry Mon: 9/19 11:00 AM	Hands-on Workshop: Histomorphometry: an Introduction to Guidelines, Applications, and protocols	D. Novack E. Scheller
Cancer and Bone Sun: 9/18 4:30 PM	Greg Mundy Symposium: New Mechanisms of Cancer and Bone	A. Gioccia P. Clezardin Z. Zhang
Bone Marrow Niche	MTP: Bone Marrow Microenvironment and Myeloma	

ENJOY THE MEETING!

OTHER TOPICS

Bone Marrow Niche Sun: 9/18 11:00 AM	MTP: Bone Marrow Microenvironment and Myeloma	C. Edward D. Roodman
Bone Strength Sun: 9/18 7:15 PM	Bone Strength Working Group	A. Cheung