Journal of Clinical Densitometry: Assessment of Skeletal Health, vol. 14, no. 3, 184–189, 2011

1094-6950/14:184–189/$36.00
DOI: 10.1016/j.jocd.2011.05.012

Position Development Paper

Official Positions for FRAX® Clinical Regarding Rheumatoid Arthritis

From Joint Official Positions Development Conference of the International Society for Clinical Densitometry and International Osteoporosis Foundation on FRAX®

Susan B. Broy*[*,1] and S. Bobo Tanner[2]
on behalf of the FRAX® Position Development Conference Members[a]

[1]*Rosalind Franklin School of Medicine, Chicago Medical School, North Chicago, IL, USA; and* [2]*Division of Rheumatology & Allergy, Vanderbilt University Medical Center, Nashville, TN, USA*

Abstract

Rheumatoid arthritis is the only secondary cause of osteoporosis that is considered independent of bone density in the FRAX® algorithm. Although input for rheumatoid arthritis in FRAX® is a dichotomous variable, intuitively, one would expect that more severe or active disease would be associated with a greater risk for fracture. We reviewed the literature to determine if specific disease parameters or medication use could be used to better characterize fracture risk in individuals with rheumatoid arthritis. Although many studies document a correlation between various parameters of disease activity or severity and decreased bone density, fewer have associated these variables with fracture risk. We reviewed these studies in detail and concluded that disability measures such as HAQ (Health Assessment Questionnaire) and functional class do correlate with clinical fractures but not morphometric vertebral fractures. One large study found a strong correlation with duration of disease and fracture risk but additional studies are needed to confirm this. There was little evidence to correlate other measures of disease such as DAS (disease activity score), VAS (visual analogue scale), acute phase reactants, use of non-glucocorticoid medications and increased fracture risk. We concluded that FRAX® calculations may underestimate fracture probability in patients with impaired functional status from rheumatoid arthritis but that this could not be quantified at this time. At this time, other disease measures cannot be used for fracture prediction. However only a few, mostly small studies addressed other disease parameters and further research is needed. Additional questions for future research are suggested.

Key Words: Rheumatoid arthritis; osteoporosis; osteoporotic fracture; vertebral fracture; fracture risk; FRAX.

Introduction

Rheumatoid arthritis is a systemic inflammatory disease that is commonly associated with both local (peri-articular) and systemic osteoporosis. Multiple studies have documented decreased bone density in patients with rheumatoid arthritis *(1–6)* as well as increased hip *(1,7–10)*, clinical spine *(1)* and morphometric spine *(11–14)* fractures compared to control populations. Although there are many other causes for secondary osteoporosis, their effect can usually be explained by the effect of the disease on decreasing bone density. Rheumatoid arthritis is the only secondary cause of osteoporosis that is considered independent of bone density in the FRAX® algorithm *(15)*.

Etiology of systemic osteoporosis and fragility fracture in rheumatoid arthritis is multifactorial and includes use of

Received 05/21/11; Accepted 05/21/11.
[a]Position Conference Members: See appendix 1.
*Address correspondence to: Susan B. Broy, MD, Rosalind Franklin School of Medicine, Chicago Medical School, North Chicago, IL, USA. E-mail: broysusan@gmail.com

glucocorticoids, chronic inflammation with associated cytokine production, inactivity and increased risk of falling *(16,17)*. The relative contribution of these factors to the development of osteoporosis and osteoporotic fractures in these patients is not well understood. Although input for rheumatoid arthritis in the FRAX algorithm is a dichotomous variable,intuitively, one would expect that more severe or active disease would be associated with more severe osteoporosis. There are multiple methods to characterize disease severity/activity in rheumatoid arthritis. These can be divided into

1. Severity measures
   a. Functional measures − includes disability scores such as HAQ (health assessment questionnaire), and functional class.
   b. Structural measures − reflects amount of end-stage disease and includes number of deformed joints and erosion scores.
2. Activity measures − includes standard measures of disease activity such as VAS (visual analog scale of disease activity by both physician and patient re: pain or global activity of disease), acute phase reactants (e.g. ESR and/or CRP) and DAS (disease activity score - includes number of tender/swollen joints as well as VAS).

Several studies have associated various disease parameters seen in rheumatoid arthritis patients with decreased bone density including HAQ measures *(2,4,5,18)*, functional class *(6)*, disease duration *(1,2,4)*, DAS *(2,4,18)*, acute phase reactants *(2,19,20)*. Other studies have associated specific rheumatoid arthritis medications with decreased bone density. However, few studies have correlated disease parameters or medication use with fracture risk in these patients.

We reviewed the available literature to determine if specific disease parameters or medications used in rheumatoid arthritis could be used to better characterize fracture risk in patients with rheumatoid arthritis. We included all studies that evaluated either clinical fractures (nonvertebral and vertebral) or morphometric spine fractures. Although morphometric vertebral fractures were not evaluated in the FRAX cohorts that included rheumatoid arthritis, these fractures represent the majority of vertebral fractures and are clearly associated with future fractures *(21,22)*.

Methodology & Data sources

To determine the effect of various disease parameters and medication use on fracture risk in rheumatoid arthritis patients, a Medline search limited to English language publications was completed September 1, 2010. Items searched were: rheumatoid arthritis and fracture, rheumatoid arthritis and osteoporotic fracture, rheumatoid arthritis and vertebral fracture, medication and rheumatoid arthritis and fracture. Abstracts were reviewed and complete articles that correlated disease activity/severity or medication use to fracture prevalence or incidence were further evaluated. Studies looking at clinical fractures were distinct from studies looking at morphometric vertebral fractures so these were analyzed separately.

Statements

***Question*:** Can parameters of disease activity or severity be used to assess fracture risk in rheumatoid arthritis patients in a modified FRAX calculation?

***Official Position*:** Impaired functional status in patients with rheumatoid arthritis may be a risk factor for clinical fractures. FRAX may underestimate fracture probability in these patients.

***Grade*:** Good, A, W

Rationale

Clinical Fractures

We found 8 studies that examined the effect of disease activity or severity on clinical fractures *(1,10,23,24,25,26,27,28)*- see Table 1. Six of the eight studies documented a significant correlation between disability measures (HAQ, JHAQ for the Japanese studies or functional class) and fracture risk. Risk was particularly significant for clinical vertebral fractures. In the three studies where vertebral fractures were considered separately, risk ranged from a RR 2.42 *(25)*, OR 4.99 *(28)* and OR 7.74 *(26)*. One small study *(23)* found no association and the final study *(1)* did not include a disability measure.

The effect of duration of disease was mixed: three Japanese observational cohort studies showed no association *(25,26,28)*, two did not evaluate disease duration *(10,24)* and two showed a marginal association *(20,23)*. However, the largest study, the British General Practice Research Database (GPRD) of 30,262 men and women over age 40 with rheumatoid arthritis, median follow-up 7.6 years, documented a significant association of incident fractures with duration of disease *(1)*. In fact, disease duration was the strongest predictor of future fractures in this study with a RR 3.4 with disease duration >10 years.

There was little evidence to associate other disease parameters and fracture risk. Only two studies *(25,26)* looked at acute phase reactants and surprisingly found a decreased risk of nonvertebral fractures with increased CRP with a RR 0.46 (0.17−1.28) in one study *(25)* and a HR of 0.60 (0.38−0.95) in the other *(26)*. However, neither study looked at gradient of risk; risk was based on less than or greater than a CRP of 0.7. In addition, one of these studies *(25)* found an increased risk of clinical vertebral fractures with increased CRP: RR 1.31 (0.43−4.00). No association of fracture with VAS scores were seen in three studies *(24,25,26)* or DAS in one study *(23)*. Only two studies looked at structural measures of disease severity. One showed a correlation with number of deformed joints *(23)*, the other showed no association with erosion scores *(24)*.

Morphometric Vertebral Fractures

Seven studies evaluated the correlation between morphometric vertebral fractures and disease parameters *(11,12,29−33)*- see Table 2. However, these were much smaller

Table 1
Disease Parameters and Clinical Fractures

Study	Study size	f/u	Disability (HAQ or equiv)	Disease duration
(1) Britain (GPRD)	30,262 men and women	7.6 years median	NR	RR 3.4 > 10 years (3.0−3.9)
(23) Norway (county register)	249 women	NR	No assoc	OR 1.04/year (1.01−1.07)
(24) USA (CORRONA)	8,419 women	18 mos	IRR[a] 1.5	NR
(25) Japan	1,733 women	54 mos	RR 1.76 non-vert (1.07−2.89) 2.42 vert (1.42−4.14)	No association
(26) Japan	1,050 men	6−66 mos (median 49)	HR 1.33 non-vert (0.60−2.98) 7.74 vert (2.10−28.48)	No association
(27) Canada and USA (ARAMIS)	1,110 men and women	8.4 years	OR 1.28/1unit (1.05−1.57)	OR 1.01/year (0.998−1.03)
(28) Japan	209 men and women	1 year	OR 2.96/class[b] nonvert (1.60−4.50) 4.99/class[b] vert (2.03−12.24)	No association
(10) USA (MAYO clinic)	388 women	25 years	RR 4.21 hip (1.82−8.30) functional classes III and IV[b]	NR

Abbr: NR, not reported.
[a]Adjusted incidence rate ratio.
[b]Disability assessed by Steinbrocker's functional class I-IV.

studies and parameters evaluated varied widely between them. Only three looked at HAQ scores: two showed no association *(32,33)*, one suggested an association *(31)* with an MHAQ (modified HAQ score, range 1 to 3) of 1.87 in patients with an incident deformity vs. 1.53 in those without an incident deformity($p = 0.008$). Of interest, both studies that looked at erosion scores and fracture risk *(29,30)* found a positive association with a p value < 0.0001 in one study *(29)*. The other study reported that only age and Larsen erosion scores were independent determinants of vertebral deformities in multiple regression analyses. Although these studies did not look at measures of disability, it is likely that patients with greater erosion scores would have greater disability. Of interest, other studies suggest that erosion scores correlate with decreased bone density *(34,35)* with one *(34)* documenting a linear correlation between disability measured by Steinbrocker's functional stage and frequency of osteoporosis ($p = 0.0001$). This observation deserves further evaluation to determine if this translates into an increased risk of fracture. At this time, there is no evidence that disease parameters can be used to predict risk for morphometric vertebral fractures in patients with rheumatoid arthritis.

***Question*:** Does medication use in rheumatoid arthritis alter the calculated fracture risk?

***Official Position*:** There is no consistent evidence that nonglucocorticoid medications for rheumatoid arthritis alter fracture risk

Grade: Fair, B, W

Table 2
Disease Parameters and Risk for Morphometric Vertebral Fracture

Study	Study size	HAQ	Disease duration	DAS	VAS	ESR/ CRP	Erosion score	Deformed joints	Gluco-corticoids
(29) Morocco VFA	172 women		+			+	+ (Sharp Score)		+
(11) UK x-ray	191 women		No assoc						Neg assoc
(31) Norway VFA	255 women	+		No assoc				No assoc	No assoc
(32) Norway x-ray	229 women	No assoc	No assoc	No assoc	No assoc	+		No assoc	+
(33) Netherlands x-ray	98 men and women	No assoc		No assoc					No assoc
(12) Turkey x-ray	100 women		+					+	
(30) Norway, UK, Netherlands x-ray	150 women						+ (Larsen score)		

Table 3
Fracture Risk and Rheumatoid Arthritis Medications

Medication and reference	Study design	Study size	Data bank	Risk	Comments
"DMARD"[a]					
(1) UK	Case-control median 7.6 years	30,362 men and women	GPRD	RR 1.5 (1.3−1.8)	RR hip 2.0 (1.8−2.3) spine 2.4 (2.0−2.8)
Methotrexate					
(36) Denmark	Case-control 1 year	124,655 men and women	National Danish Registers[b]	none	Trend of decreased risk forearm fracture
(14) Japan	Cross-sectional	117 post-menopausal	Spine x-rays	none	Increased risk steroids only
(37) Japan	Prospective observational	795 women >50	IORRA	HR 1.88 (1.12−3.15)	Increased non-vertebral fracture risk
Cyclosporine					
(36) Denmark	Case-control 1 year	124,655 men and women	National Danish Registers[b]	none	Cases more "frail"
Azathioprine					
(36) Denmark	Case-control 1 year	124,655 men and women	National Danish Registers[b]	OR 1.17 (1.03−1.33)	Increased overall fracture risk only at low dose. No increase in hip, spine or forearm risk
Anti-TNF					
(24) USA	Linear regression models	11,429 men and women	CORRONA	IRR[c] 0.568	Decreased overall fracture risk

[a]Includes any of the following in the previous 6 months: sulfasalazine, gold, penicillamine, hydroxychloroquine, azathioprine, leflunomide, methotrexate, cyclosporine, etanercept, anakinra, cyclophosphamide.
[b]National hospital discharge register, psychiatric central register, Danish medicines agency.
[c]Adjusted incidence rate ratio.

Rationale

Multiple studies have documented increased fracture risk in patients on glucocorticoids. However, it has been difficult to separate the effect of the disease from the effect of glucocorticoid use. Of interest, all of the studies in Table 1 except a small Norwegian study *(23)* documented a significant association between use of glucocorticoids and clinical fracture in patients with rheumatoid arthritis. However, dose and duration were poorly characterized. In addition, effect of glucocorticoids on morphometric vertebral fractures in patients with rheumatoid arthritis is mixed with two studies showing no association *(31,33)*, two studies showing a positive association *(29,32)* and one suggesting a negative association *(11)* in Table 2. Since another task force is evaluating the dose-effect of glucocorticoid use, we limited our evaluation to nonglucocorticoid medications used in rheumatoid arthritis and fracture risk.

We found five relevant studies *(1,14,24,35,36)* evaluating the correlation between use of nonglucocorticoid medications in rheumatoid arthritis and fractures − Table 3. The large GPRD study found a significant correlation with all DMARD's and fracture, especially in the spine with a RR 2.4 (2.0−2.8), but individual medications were not evaluated separately *(1)*. Three studies looked at methotrexate: increased risk was seen only in one Japanese study *(37)*, not in another Japanese study *(14)* or a much larger Danish study *(36)*. In the same large Danish study of three registries, azathioprine was associated with an increase in overall fracture risk but the increase did not come from the traditional osteoporotic skeletal sites such as hip, spine and forearm *(36)*. In addition, the increased risk was only seen at low doses suggesting a chance finding. Interestingly, the use of anti-TNF agents were shown to be protective of fractures in the CORRONA data base *(24)*. Other classes of biologic agents have not been analyzed.

In summary

Rheumatoid arthritis is a systemic inflammatory disease that varies in severity from a mild, well controlled disease to a severe, crippling and life-threatening disease. Although it is logical to assume that more severe disease would be associated with a greater risk for fractures, evidence for this is limited.

Disability measures such as HAQ and functional class do show a correlation with clinical fracture risk in several studies and could be used to improve risk prediction for clinical fractures but not morphometric vertebral fractures. There is no current evidence that other parameters of disease activity can predict fractures. One large study found a strong correlation with duration of disease and fracture risk *(1)* but additional studies are needed to confirm this. There is not enough evidence to associate specific rheumatoid arthritis medications and fracture risk.

Additional Questions for Future Research:

1. Does FRAX overestimate fracture risk in rheumatoid arthritis because input for rheumatoid arthritis in the FRAX algorithm was based on self-report?

Of note, Pluijm et al. reviewed data from two prospective cohort studies (Rotterdam n= 4157 and Longitudinal Aging Study Amsterdam n = 762) and found that 14% of patients reported a diagnosis of rheumatoid arthritis, yet only 4% were diagnosed by a physician *(38)*.

2. Does FRAX overestimate fracture risk in patients with rheumatoid arthritis and glucocorticoids?

The effect of glucocorticoids on bone health in rheumatoid arthritis patients is complex. FRAX does not consider dose and duration of glucocorticoid use, yet many rheumatoids are on a very low maintenance dose of ≤5mg which may be protective by controlling the inflammatory process. Some studies do suggest that fracture risk is no greater in patients with rheumatoid arthritis taking glucocorticoids compared to patients with rheumatoid arthritis who are not on glucocorticoids *(8,23,31,33)*. One smallstudy (n = 191 postmenopausal women) even suggested a greater fracture risk in rheumatoid patients who were not taking glucocorticoids *(11)*. Further study is needed.

3. Does FRAX overestimate fracture risk because patients with rheumatoid arthritis have a higher mortality rate than population controls?

Management of rheumatoid arthritis has improved dramatically over the past 10 years and it was thought that mortality was also improving. However, the large British General Practice Research Database reported 17.5% 5-year mortality in rheumatoid arthritis patients compared to 11.8% in population controls *(1)*. In addition, a recent review concluded that ''patients have about a 50% increased risk of premature mortality, and their life expectancy is decreased by 3 to 10 years compared with the general population'' *(39)*. If mortality in rheumatoid arthritis patients is much greater than the mortality data used in FRAX, fracture risk would be overestimated.

References

1. van Staa TP, Geusens P, Bilsma JWJ, et al. 2006 Clinical assessment of long-term risk of fracture in patients with rheumatoid arthritis. Arthritis Rheum 54(10):3104−3112.
2. Kvien T, Haugeberg G, Uhlig T, et al. 2000 Data driven attempt to create a clinical algorithm for identification of women with rheumatoid arthritis at high risk of osteoporosis. Ann Rheum Dis 59:805−811.
3. Lane NE, Pressman AR, Star VL, et al. 1995 Rheumatoid arthritis and bone mineral density in elderly women. J Bone Miner Res 10(2):257−263.
4. Laan RF, Buijs WC, Verbeek AL, et al. 1993 Bone mineral density in patients with recent onset rheumatoid arthritis: influence of disease activity and functional capacity. Ann Rheum Dis 52: 21−26.
5. Haugeberg G, Uhlig T, Falch JA, et al. 2000 Bone mineral density and frequency of osteoporosis in female patients with rheumatoid arthritis. Arthritis Rheum 42(3):522−530.
6. SambrookPN, Eisman JA, Champion GD, et al. 1987 Determinants of axial bone loss in rheumatoid arthritis. Arthritis Rheum 30(7):721−728.
7. Kim SY, Schneeweiss S, Liu J, et al. 2010 Risk of osteoporotic fracture in a large population-based cohort of patients with rheumatoid arthritis. Arthritis Res and Ther 12:R154.
8. Cooper C, Coupland C, Mitchell M. 1995 Rheumatoid arthritis, corticosteroid therapy and hip fracture. Ann Rheum Dis 54: 49−52.
9. Huusko TM, Korpela M, Karppi P, et al. 2001 Threefold increase risk of hip fractures with rheumatoid arthritis in central Finland. Ann Rheum Dis 60:521−522.
10. Hooyman JR, Melton J, Nelson AM, et al. 1984 Fractures after rheumatoidarthritis: a population-based study. Arthritis Rheum 27(12):1353−1361.
11. Spector TD, Hall GM, McCloskey EV, et al. 1993 Risk of vertebral fracture in women with rheumatoid arthritis. BMJ 306: 506.
12. Baskan BM, Sivas F, Alemdaroglu E, et al. 2007 Association of bone mineral density and vertebral deformity patients with rheumatoid arthritis. Rheumatol Int 27(6):579−584.
13. Orsatavik RE, Haugeberg G, Mowinckel P, et al. 2004 Vertebral deformities in rheumatoid arthritis. Arch Intern Med 164: 420−425.
14. Arai K, Hanyu T, Sugitani H, et al. 2006 Risk factors for vertebral fracture in menopausal or postmenopausal Japanese women with rheumatoid arthritis: cross-sectional and longitudinal study. J Bone Miner Metab 24(2):118−124.
15. Kanis, JA, on behalf of the World Health Organization Scientific Group. 2007 Assessment of osteoporosis at the primary health-care level. Technical Report. World Health Organization Collaborating Centre for Metabolic Bone Diseases, University of Sheffield, UK: Printed by the University of Sheffield.
16. Kaz Kaz H, Johnson D, Kerry S, et al. 2004 Fall-related risk factors and osteoporosis in women with rheumatoid arthritis. Rheumatology 43:1267−1271.
17. Smulders E, Schreven C, Weerdesteyn, et al. 2009 Fall incidence and fall risk factors in people with rheumatoid arthritis. Ann Rheum Dis 68:1795−1796.
18. Haugeberg G, Uhlig T, Falch JA, et al. 2000 Reduced bone mineral density in male rheumatoid arhtritis patients. Arthritis Rheum 43(12):2776−2784.
19. Ding C, Parameswaren V, Udayan, et al. 2008 Circulating levels of inflammatory markers predict change in bone mineral density and resorption in older adults: a longitudinal study. J Clin Endocrinol Metab 93(5):1952−1958.
20. Cauley JA, Danielson ME, Boudreau, et al. 2007 Inflammatory markers and incident fracture risk in older men and women: The health aging and body composition study. J Bone Miner Res 22(7):1088−1095.

21. Black DM, Arden NK, Palermo L, et al. 1999 Prevalent vertebral deformities predict hip fracture and new vertebral deformities but not wrist fracture. J Bone Miner Res 14:821−828.
22. McCloskey EV, Vasireddy S, Threlkeld J, et al. 2008 Vertebral fracture assessment (VFA) with a densitometer predicts future fractures in elderly women unselected for osteoporosis. J Bone Miner Res 23:1561−1568.
23. Orstavik RE, Haugeberg G, Uhlig T, et al. 2004 Self reported non-vertebral fractures in rheumatoid arthritis and population based controls: incidence and relationship with bone mineral density and clinical variables. Ann Rheum Dis 63:177−182.
24. Coulson KA, Reed G, Gilliam BE, et al. 2009 Factors influencing fracture risk, T score, and management of osteoporosis in patients with rheumatoid arthritis in the consortium of rheumatology researchers of North America (CORRONA) registry. J Clin Rheum 15(4):155−160.
25. Furuya T, Kotake S, Inoue E, et al. 2007 Risk factors associated with incident clinical vertebral and nonvertebral fractures in Japanese women with rheumatoid arthritis: a prospective 54-month observational study. J Rheumatol 34:303−310.
26. Furuya T, Kotake S, Inoue E, et al. 2008 Risk factors associated with incident fractures in Japanese men with rheumatoid arthritis: a prospective observational cohort study. J Bone Miner Metab 26:499−505.
27. Michel BA, Bloch DA, Wolfe F, et al. 1993 Fractures in rheumatoid arthritis: an evaluation of associated risk factors. J Rheumatol 20:1666−1669.
28. Nampei A, Hashimoto J, Koyanagi J, et al. 2008 Characteristics of fracture and related factors in patients with rheumatoid arthritis. Mod Rheumatol 18:170−176.
29. Maghraoui AE, RezQi A, Mounach A, et al. 2010 Prevalence of risk factors of vertebral fractures in women with rheumatoid arthritis using vertebral fracture assessment. Rheumatology 49: 1303−1310.
30. Lodder MC, Haugeberg G, Lems WF, et al. 2003 Radiographic damage associated with low bone mineral density and vertebral deformities in rheumatoid arthritis: the Oslo-Troro-Amsterdam (OSTRA) collaborative study. Arthritis Rheum 49(2):209−215.
31. Orstavik RE, Haugeberg G, Uhlig T, et al. 2005 Incidence of vertebral deformities in 255 female rheumatoid arthritis patients measured by morphometric x-ray absorptiometry. Osteoporos Int 16:35−42.
32. Orstavik RE, Haugeberg G, Uhlig T, et al. 2003 Vertebral deformities in 229 female patients with rheumatoid arthritis: associations with clinical variables and bone mineral density. Arthritis Rheum 49(3):355−360.
33. Ursum J, Britsemmer K, van Schaardenburg D, et al. 2009 High prevalence of vertebral deformities in elderly patients with early rheumatoid arthritis. Ann Rheum Dis 68:1512−1513.
34. Sinagaglia L, Nervetti A, Mela Q, et al. 2000 A multicenter cross-sectional study on bone mineral density in rheumatoid arthritis. Italian study group on bone mass in rheumatoid arthritis. J Rheumatol 27(11):2582−2589.
35. Sambrook P, Raj A, Hunter D, et al. 2001 Osteoporosis with low dose corticosteroids: contribution of underlying disease effects and discriminatory ability of ultrasound versus bone densitometry. J Rheumatol 28(5):1063−1067.
36. Vestergaard P, Rejnmark L, Mosekilde L. 2006 Methotrexate, azathioprine, cyclosporine and risk of fracture. Calcif Tissue Int 79(2):69−75.
37. Urano W, Furuya T, Inoue E, et al. 2009 Associations between methotrexate treatment and methylenetetrahydrofolate reductase gene polymorphisms with incident fractures in Japanese female rheumatoid arthritis patients. J Bone Miner Metab 27(5): 574−583.
38. Pluijm SK, Koes B, de Laet C, et al. 2009 A simple risk score for the assessment of absolute fracture risk in general practice based on two longitudinal studies. J Bone Miner Res 24(5):768−774.
39. Myasoedova E, Davis JM, Crowson CS, et al. 2010 Epidemiology of rheumatoid arthritis: rheumatoid arthritis and mortality. Curr Rheumatol Rep 12:379−385.

Appendix 1. Position Conference Members

Organizers: Didier B. Hans (Chair), Cyrus Cooper (Co-chair), Sanford Baim, Bess Dawson-Hughes, John A. Kanis, William D. Leslie, Marjorie M. Luckey, Rene Rizzoli, Catalina Poiana, John P. Bilezekian (Moderator), Socrates E. Papapoulos (Co-moderator).

FRAX® Clinical: Eugene V. McCloskey (Chair), Neil Binkley (Co-chair), Jonathan D. Adachi, Sanford Baim (Program committee liaison), Robert D. Blank, Steven Boonen, Susan B. Broy, Olivier Bruyere, Manju Chandran, Cyrus Cooper, Bess Dawson-Hughes (Co-program committee liaison), Richard Eastell, Kris Ensrud, Hans P. Dimai, Joseph Foldes, Patrick Garnero, Piet P. Geusen, Andrea Griesmacher, Marian T. Hannan, John A. Kanis, Michael Kleerekoper, Marc-Antoine Krieg, BenteLangdahl, Andrew Laster, Edward S. Leib, TahirMasud, Mike McClung, Howard Morris, Sergio Ortolani, Kenneth G. Saag, Ethel Siris, Stuart Silverman, S. Bobo Tanner, TommasoTrenti, Samuel Vasikaran, Peter Vestergaard, Denys A. Wahl.

FRAX® BMD: E. Michael Lewiecki (Chair), Juliet E. Compston (Co-chair), Jonathan D. Adachi, Judith E. Adams, Robert A. Adler, Doug C. Bauer, Glen M. Blake, Patricia Clark, Adolfo Diez-Perez, Didier B. Hans, Robert G. Josse, John A. Kanis (Co-Program committee liaison), David L. Kendler, Aliya A. Khan, Marc-Antoine Krieg, William D. Leslie (Program committee liaison), Roman R. Lorenc, Alireza Moayyeri, Basel K. Masri, Paul D. Miller.

FRAX® International: Jane A. Cauley (Chair), Ghada El-Hajj Fuleihan (Co-chair), Asma Arabi, Andrew Calderon, Zhao Chen, Siok Bee Chionh, Jeffrey Curtis, Michelle E. Danielson, Saeko Fujiwara, David Hanley, Heikki Kroger, Annie Kung, Olga Lesnyak, Anne Looker, Marjorie M. Luckey (Program committee liaison), Dan Mellstrom, Jeri Nieves, Wojciech Pluskiewicz, Rola El Rassi, René Rizzoli (Co-program committee liaison), Sergio Ragi-Eis, Anne-Marie Schott-Pethelaz, Stuart Silverman.

Expert Panel: John P. Bilezekian (Moderator), Socrates E. Papapoulos (Co-moderator), Jonathan D. Adachi, Robert D. Blank, Roland Chapurlat, Wu (Paulo) Chih-Hsing, Edward Czerwinski, Aldolfo Diez Perez, Hans P. Dimai, Ghada El-Hajj Fuleihan, Saeko Fujiwara, Ruxandra M. Ionescu, John A. Kanis, Mike McClung, Sergio Ragi-Eis, Jan Stepan, Kenneth G. Saag, John T. Schousboe, Wei Yu, Cristiano Zerbini.

Supporting Person: Peter D. Brown (ISCD), Patrice McKenney (IOF), Helena Johansson, Judit Nagy, Anders Oden and Denys A. Wahl.