

Position Development Paper

FRAX[®] Clinical Task Force of the 2010 Joint International Society for Clinical Densitometry & International Osteoporosis Foundation Position Development Conference

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on behalf of the FRAX[®] Position Development Conference Members^a*

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Abstract

The World Health Organization fracture risk assessment tool, FRAX[®], is an advance in clinical care that can assist in clinical decision-making. However, with increasing clinical utilization, numerous questions have arisen regarding how to best estimate fracture risk in an individual patient. Recognizing the need to assist clinicians in optimal use of FRAX[®], the International Osteoporosis Foundation (IOF) in conjunction with the International Society for Clinical Densitometry (ISCD) assembled an international panel of experts that ultimately developed joint Official Positions of the ISCD and IOF advising clinicians regarding FRAX[®] usage.

As part of the process, the charge of the FRAX[®] Clinical Task Force was to review and synthesize data surrounding a number of recognized clinical risk factors including rheumatoid arthritis, smoking, alcohol, prior fracture, falls, bone turnover markers and glucocorticoid use. This synthesis was presented to the expert panel and constitutes the data on which the subsequent Official Positions are predicated. A summary of the Clinical Task Force composition and charge is presented here.

Key Words: FRAX; fracture risk; osteoporosis; ISCD; official positions.

Background

The World Health Organization fracture risk assessment tool, FRAX[®] utilizes large, population-based datasets to estimate 10-year fracture probability utilizing easily obtainable clinical fracture risk factors. These factors include age, weight, sex and personal history of fracture among

others. Input of these clinical factors into FRAX, with or without femoral neck BMD, provides a 10-year estimate of major osteoporosis related fracture (hip, spine, humerus and forearm) and hip independently. These fracture probabilities can be used to advise selection of treatment guidelines or facilitate clinical decision-making in the individual patient.

Straightforward recommendations for entering clinical data are provided on the FRAX website. However, with the increasing clinical use of FRAX, questions have been posed regarding optimal clinical usage of this tool. For example, as FRAX requires dichotomous entry (yes/no) but some risk factors may have variable effects (e.g., dose of glucocorticoid therapy) it is possible that the existing FRAX model leads to under- or over-estimation of fracture risk in a given patient. Similarly, some factors recognized to increase fracture risk, e.g., falls, are not included in the current FRAX model. Recognizing that a need existed to assist clinicians with optimal

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use of FRAX, the International Osteoporosis Foundation (IOF) in conjunction with the International Society for Clinical Densitometry (ISCD) assembled an international panel of experts for a two-day collaborative conference entitled “Interpretation and use of FRAX in Clinical Practice” in Bucharest, Romania on November 14, 2010. The day following this meeting, joint Official Positions of the ISCD and IOF were developed at a Position Development Conference. To facilitate this process, the conference steering committee identified three Task Forces (FRAX Clinical, FRAX BMD and FRAX International) and provided questions for these groups to address. Subgroups of each Task Force were developed with their charge being to critically review and summarise available evidence to develop draft Official Positions relevant to the question(s) posed to their group. Detailed description of the methodology utilized in the development of these ISCD/IOF Official Positions is presented elsewhere in this edition of the Journal of Clinical Densitometry. The following is an overview of the FRAX Clinical Task Force, which was divided into the following subgroups: Rheumatoid Arthritis, Alcohol, Smoking, Falls, Prior Fractures, Bone Turnover Markers and Glucocorticoids.

Rheumatoid Arthritis Subgroup

Subgroup Leader: Susan B. Broy

Subgroup Members: S. Bobo Tanner, Marc-Antoine Krieg

Rheumatoid arthritis is currently the only secondary cause of osteoporosis that is considered independently of BMD in the current FRAX model. This subgroup evaluated whether consideration of specific rheumatoid arthritis parameters such as disease activity or severity or the use of non-glucocorticoid medication could be included in FRAX to enhance fracture risk estimation.

Alcohol Subgroup

Subgroup Leader: Bente Langdahl

Subgroup Members: Peter Vestergaard, Eugene V. McCloskey

High consumption of alcoholic beverages is associated with increased risk for fracture. While a dose level is partially captured within FRAX (≥ 3 units daily), the nature of this dose response was felt to require further exploration including possible differences between men and women. The charge of this subgroup was to evaluate these possibilities and, if possible, provide guidance to clinicians regarding how alcohol intake may alter fracture risk estimation in FRAX.

Smoking Subgroup

Subgroup Leader: Hans P. Dimai

Subgroup Members: Manju Chandran, Bente Langdahl, Eugene V. McCloskey

Tobacco use is associated with lower bone mineral density and elevated fragility fracture risk. This subgroup considered

whether dose and type of tobacco, duration of smoking and time from exposure would affect the FRAX reported fracture risk.

Falls and Frailty Subgroup

Subgroup Leader: Tahir Masud

Subgroup Members: Neil Binkley, Steven Boonen, Marian T. Hannan

Falls become extremely common with advancing age, likely at least in part to reduced muscle mass and function, and often lead to fracture. Currently, falls, frailty and sarcopenia are not considered in the FRAX model. This subgroup considered whether it is possible to include falls risk, number of falls and other potential markers of falls risk such as frailty/sarcopenia in fracture risk estimation.

Fractures Subgroup

Subgroup Leader: Robert D. Blank

Subgroup Members: Andrew Laster, Kris Ensrud

Fracture risk is increased with greater number of prior fractures and greater severity of vertebral fracture. However, currently prior fracture is entered as a yes or no variable in FRAX. This subgroup considered the evidence regarding the effect of number of past fractures, severity of prior vertebral fracture and site of past fracture on future fracture risk and whether these relationships differed between men and women. Additionally, FRAX currently includes only family history of hip fracture; whether family history of additional sites of fracture or fracture in other family members should be considered in the FRAX calculation was considered.

Bone Turnover Marker Subgroup

Subgroup Leader: Samuel Vasikaran

Subgroup Members: Eugene V. McCloskey, Richard Eastell, Olivier Bruyere, Joseph Foldes, Patrick Garnero, Andrea Griesmacher, Michael McClung, Howard Morris, Stuart Silverman, Tommaso Trenti, Denys A. Wahl, Cyrus Cooper, John A. Kanis

Levels of bone turnover markers are negatively correlated with bone mineral density and their measurement might facilitate estimation of fracture risk. This subgroup reviewed the association of bone turnover markers with fracture risk estimation and considered whether altering the FRAX estimated fracture risk based upon these markers, when available, is appropriate.

Glucocorticoid Subgroup

Subgroup Leaders: Edward S. Leib, Kenneth G. Saag

Subgroup Members: Jonathan D. Adachi, Piet P. Geusens

Glucocorticoid use is clearly associated with increased fracture risk. At any given BMD, the fracture risk is approximately doubled for those patients receiving glucocorticoid

therapy. This subgroup assessed the effect of glucocorticoid dose, duration (including short term and intermittent use) and provided recommendations for clinical implementation into FRAX. Additionally, the effect of non-oral glucocorticoid use on fracture risk estimation was considered.

The full reports of each task force subgroup are included in this issue of the Journal of Clinical Densitometry.

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. Bilezikian (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, Bente Langdahl, Andrew Laster, Edward S. Leib, Tahir Masud, Mike McClung, Howard Morris, Sergio Ortolani, Kenneth G. Saag, Ethel Siris, Stuart Silverman, S. Bobo Tanner, Tommaso Trenti, 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. Bilezikian (Moderator), Socrates E. Papapoulos (Co-moderator), Jonathan D. Adachi, Robert D. Blank, Roland Chapurlat, Wu (Paulo) Chih-Hsing, Edward Czerwinski, Adolfo 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.