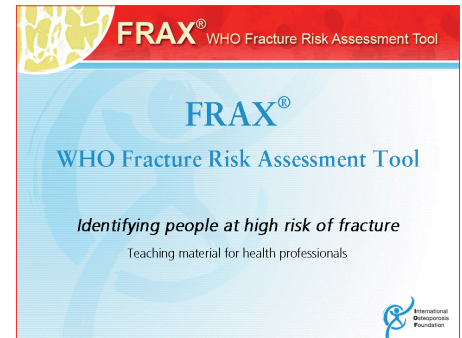


Slide Kit

Title page

Annotations

- Osteoporosis should be recognised as important public health concern because of the fractures that arise.
- For the year 2000, there were an estimated 9 million new osteoporotic fractures, of which 1.6 million were at the hip, 1.7 million were at the forearm and 1.4 million were clinical vertebral fractures. Europe and the Americas accounted for 51% of all these fractures, while most of the remainder occurred in the Western Pacific region and Southeast Asia.
- The WHO fracture risk assessment tool (FRAX[®]) identifies those people at highest risk of fracture and its application can be used in clinical settings for informed intervention decisions.



References

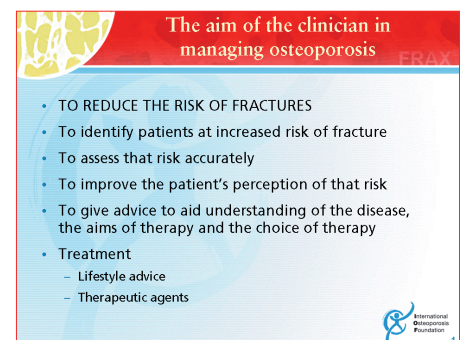
Johnell O and Kanis JA (2006) *Osteoporosis International* **17**:1726

Slide 1

The aim of the clinician in managing osteoporosis

Annotations

- An IOF survey, conducted in 11 countries, showed denial of personal risk by postmenopausal women, lack of dialogue about osteoporosis with their doctor, and restricted access to diagnosis and treatment before the first fracture result in underdiagnosis and undertreatment of the disease.
- The Global Longitudinal study of Osteoporosis in Women (GLOW) indicated that over the age of 55 years, 55% of women with osteoporosis and 75% of women with osteopenia perceived themselves to have the same or a lower fracture risk than an age-matched healthy woman.



References

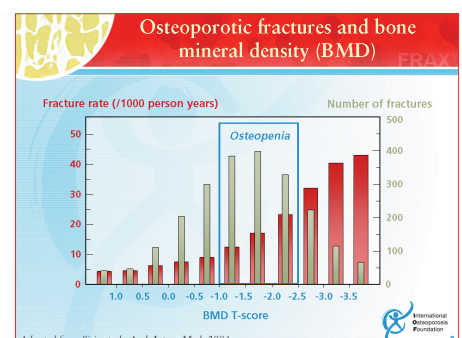
Japanese Osteoporosis Foundation and the International Osteoporosis Foundation (2000) How fragile is her future? Survey Report < <http://www.iofbonehealth.org/policy-advocacy/survey-reports.html> > Cooper C, Siris E, Adachi J, et al. (2009) *Osteoporosis International* **20** (Suppl.1): S5-S22

Slide 2

Predicting fractures with bone mineral density (BMD)

Annotations

- BMD is a strong predictor of fracture risk.
- Women with osteoporosis (BMD T-score ≤ -2.5) are at high risk of fracture, but there are relatively few such women in the population.
- The majority of fractures occur in women with BMD above the osteoporosis threshold (osteopenia).
- Additional risk factors need to be taken into account.



References

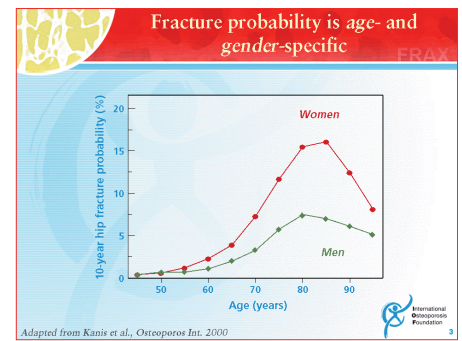
Siris E, Chen Y-T, Abbott TA, et al. (2004) *Archives of Internal Medicine* **164**:1108

Slide 3

Fracture probability is age- and gender-specific

Annotations

- Age is an important independent risk factor.
- The probability of fracture increases steadily up to 80-85 years, and thereafter decreases since the increase in mortality risk with age exceeds the increase in hip fracture risk.



References

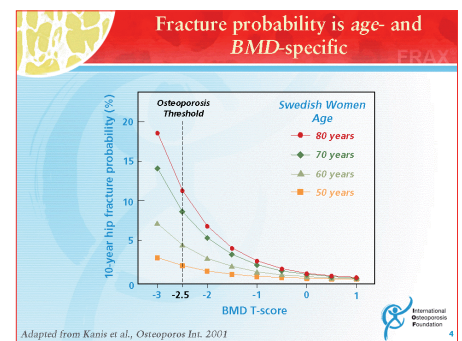
Kanis JA, Johnell O, Oden A et al. (2000) *Osteoporosis International* 11:669

Slide 4

Fracture probability is age- and BMD-specific

Annotations

- The combination of age and BMD improves the estimation of fracture probabilities.
- An 80 year old with the same T-score as a 50 year old has a much higher 10-year probability of fracture.
- Note that a 50-year old woman with osteoporosis has a lower 10-year hip fracture probability compared to a 70-year old with osteopenia.



References

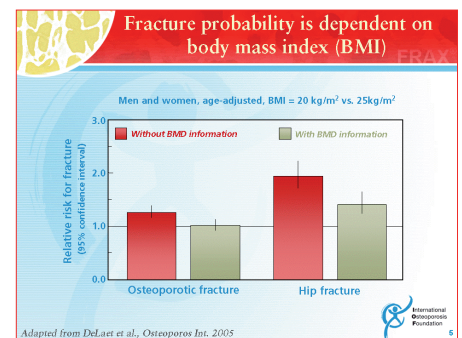
Kanis JA, Johnell O, Oden A, et al. (2001) *Osteoporosis International* 12:989

Slide 5

Fracture probability is dependent on body mass index (BMI)

Annotations

- A low BMI is a significant risk factor for osteoporotic fractures, particularly hip fractures.
- The impact of BMI on osteoporosis fracture risk is largely mediated through its effect on BMD.
- For hip fractures, low BMI remains a significant BMD-independent risk factor.



References

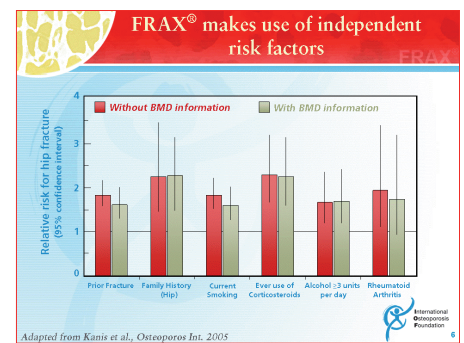
De Laet C, Kanis JA, Oden A, et al. (2005) *Osteoporosis International* 16:1330

Slide 6

FRAX® makes use of independent risk factors

Annotations

- The risk factors listed in the graph, used by FRAX®, are significant contributors to osteoporotic fracture risk, over and above that provided by BMD and age.
- The different contribution of these clinical risk factors is taken into account in calculating the 10-year fracture probabilities in FRAX®.



References

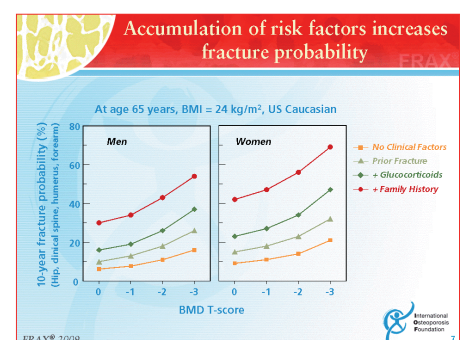
Kanis JA, Borgström F, De Laet C, et al. (2005) *Osteoporosis International* 16:581

Slide 7

Accumulation of risk factors increases fracture probability

Annotations

- As the clinical risk factors used in FRAX® act independently, the accumulation of risk factors increases fracture probability in both women and men.
- Fracture probability is dependent on the number of clinical risk factors.
- Cumulative effects are seen in both women and men, with higher fracture probabilities in women for the same BMD T-score.



References

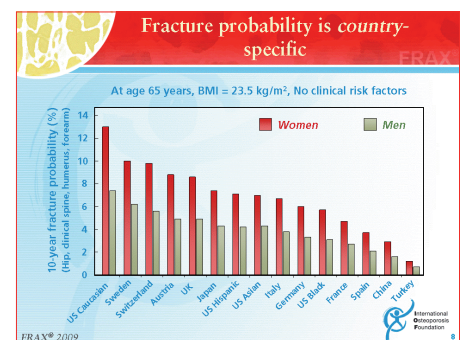
Kanis JA, Johnell O, Oden A, et al. (2008) *Osteoporosis International* 19:385

Slide 8

Fracture probability is country-specific

Annotations

- The risk of osteoporotic fractures differs by up to 10-fold from country to country.
- Mortality rates also differ significantly between countries.
- Both rates need to be known for a country-specific model to be included in FRAX®.
- Ethnicity is not taken into account, with the exception of the United States where there is sufficient epidemiological information to make the appropriate adjustments.
- FRAX® will expand to other countries as population-based epidemiologic data become available



References

Kanis JA, Johnell O, Oden A, et al. (2002) *Journal of Bone and Mineral Research* 17(7):1237
Elffors I, Allander E, Kanis JA, et al. (1994) *Osteoporosis International* 4:253

Slide 9

WHO fracture risk assessment tool (FRAX®)

Annotations

- Reasons for risk factor selection:
 - Data availability
 - Internationally validated
 - Easily ascertainable
 - Evidence that the identified risk is modifiable by subsequent treatment
 - Good intuitive value

WHO fracture risk assessment tool
FRAX®

10-year probability of fracture

Country

Bone mineral density

Age

Gender

Clinical risk factors

- Low body mass index
- Previous fragility fracture
- Parental history of hip fracture
- Glucocorticoid treatment
- Current smoking
- Alcohol intake (3 or more units per day)
- Rheumatoid arthritis
- Other secondary causes of osteoporosis

www.shef.ac.uk/FRAX

International Osteoporosis Foundation

References

<http://www.shef.ac.uk/FRAX/index.htm>

Slide 10

Limitations of FRAX®

Annotations

- FRAX® is well validated, but no model is perfect.
- Further risk factors may be incorporated in the future.
- FRAX® should not be seen as a substitute for the need to improve education about osteoporosis management.

Limitations of FRAX®

- Does not accommodate all known risk factors:
 - Falls, biochemical markers, QUS, etc.
- Lacks detail on some risk factors:
 - Dose response effects of glucocorticoids, smoking, prior fracture, etc.
- Depends on adequacy of epidemiological information
- Limited country models available
- Model relevant only for untreated patients
- Does not replace clinical judgment

International Osteoporosis Foundation

References

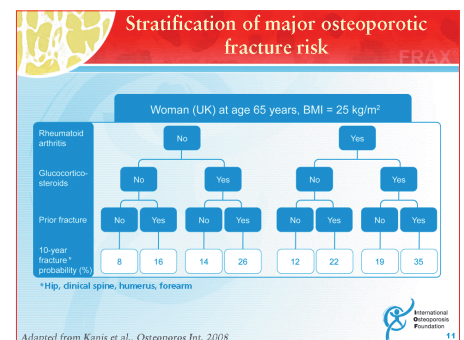
Kanis JA, Johnell O, Oden A, et al. (2008) *Osteoporosis International* **19**:385

Slide 11

Stratification of major osteoporotic fracture risk

Annotations

- The stratification of fracture risk helps understand how the FRAX® tool may apply in individual patient-based scenarios and clinical practice.
- This slide is an example of what generally happens in clinical settings to identify a patient at risk of osteoporotic fracture.
- Although the calculation of 10-year fracture probabilities does not replace clinical judgment, the clinician is provided through FRAX® with computed probabilities derived from evidence-based epidemiological data.
- In this specific UK example, a woman with rather than without rheumatoid arthritis, in the presence of a prior fracture and glucocorticoid use, had a 33% increase in fracture probability (35% instead of 26%).



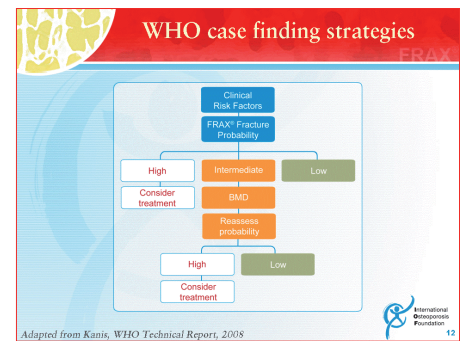
References

Kanis JA, Johnell O, Oden A, et al. (2008) *Osteoporosis International* **19**:385

WHO Case finding strategies

Annotations

- In Member States with no access to BMD testing, treatment can be allocated on the basis of fracture probability only, assessed from a patient's clinical risk factors.
- In Member States where BMD testing is recommended in segments of the population, BMD testing can be performed alongside the assessment of fracture probability using clinical risk factors.
- Member States with limited access to BMD testing lie somewhere in between and BMD testing is dependent on clinical practice, availability, affordability or health economic criteria.



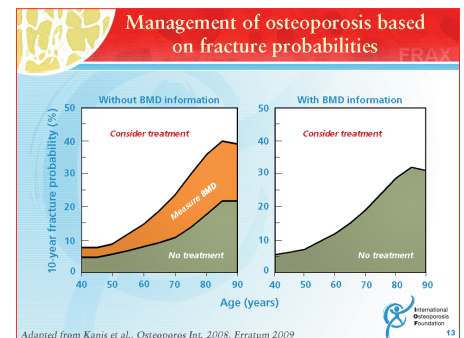
References

Kanis JA on behalf of the World Health Organization Scientific Group (2008) Assessment of osteoporosis at the primary healthcare level. Technical Report. WHO Collaborating Centre, University of Sheffield, UK.

Management of osteoporosis using fracture probabilities

Annotations

- This UK example demonstrates how fracture probabilities, computed from FRAX®, have been used in the development of national guidelines for the management of osteoporosis.
- The right hand panel shows the intervention threshold set at a fracture probability equivalent to a woman with a previous fragility fracture. BMD testing is recommended in individuals in whom fracture probabilities (assessed from clinical risk factors alone) is close to the intervention threshold (left hand panel).
- This minimises the risk of misclassifying a high risk patient as low risk and vice versa.
- This approach may not be applicable to other countries where bone mineral density testing may be more or less available, where fracture probabilities and the cost of fracture or treatment differ from the UK.
- Assessment and intervention thresholds should be set nationally to determine at which level the fracture probability is acceptably high enough to recommend BMD evaluation or pharmaceutical treatment.



References

Kanis JA, McCloskey EV, Johansson H, et al. (2009) *Osteoporosis International* 20:449; Erratum to (2008) *Osteoporosis International* 19:1395