From T-score to fracture risk
New BMD recommendations address diagnostic challenges

questions & answers
The scoop on vitamin D
Recognizing spinal fractures in older patients

case study
Breast cancer therapies can diminish bone-friendly estrogens
In its 1996 osteoporosis care guidelines, Osteoporosis Canada (OC) introduced the concept of using bone mineral density (BMD) results to assign an individual to one of three World Health Organization (WHO) categories: normal, osteopenia or osteoporosis. It was proposed that an individual’s WHO classification would serve as an indicator of fracture risk and could be used to determine treatment. Similar paradigms subsequently came into use in other parts of the world, and OC continued with this model in its 2002 guidelines. This approach has served its purpose over the last decade, giving physicians an organizational framework within which to manage their patients.

So, is there room for improvement? The answer, of course, is yes. There are two important limitations to relying on WHO categories to determine fracture risk. First, the fracture risk associated with a given category can vary substantially at different ages. For example, while an 80-year-old woman with osteopenia might have a higher fracture risk than a 50-year-old woman with osteoporosis, use of WHO categories would imply that it is the younger one who should be on medication. Second, DXA explains only a portion of fracture probability; other clinical factors need to be directly considered in order to improve fracture risk prediction.

To better identify those people who will benefit the most from osteoporosis treatment, OC has released a new set of BMD reporting recommendations, which are summarized on page 6. The most important aspect of the new approach is a change in the way fracture risk is determined: instead of relying on WHO categories, a method is given to establish 10-year absolute fracture probability (classed as low, moderate or high). BMD continues to be an important component of that risk determination, but sex, age, fracture history and glucocorticoid history will also be incorporated into the picture. These guidelines have been developed along with the Canadian Association of Radiologists. The intent is to integrate these items of a person’s medical record at the BMD facility, with the issued report explicitly stating the 10-year fracture risk category.

The new BMD guidelines are intended to induce a shift in the way we think about fracture risk. It will take some effort by each of us to adapt to the new approach. But we’d better get used to it. Osteoporosis Canada plans to add more risk factors to the classification system over the next few years as long-term data become available. Stay tuned.
Breast cancer and bone health: managing the risks

Mrs. Tremblay is a 64-year-old librarian who was diagnosed with Stage 1 cancer of the left breast in 2000. She underwent lumpectomy and radiation therapy and was treated with tamoxifen for three years. Subsequent to a hysterectomy for recurrent uterine bleeding two years ago, tamoxifen was discontinued and an aromatase inhibitor, letrozole, was initiated. Her oncologist recently told her that she is in remission. She has no other medical conditions, does not smoke, drinks a glass of wine a day at dinner and takes a multivitamin with breakfast. Her oncologist recommends that she consider increasing her calcium intake because of the potential side effects of letrozole; she would like to discuss this with you.

Mrs. Tremblay is fairly active; she walks to the library three days a week and is involved in volunteer work accompanying elderly patients to the local Day Centre twice a week.

She took hormone replacement therapy for six years around the age of 50 to control hot flashes. Her family history is negative for cancer or fractures; her father died of an acute myocardial infarction at the age of 62. She has not had any fractures and claims her height and weight have been stable for years. She has never undergone a bone mineral density (BMD) measurement.

Dr. Suzanne Morin comments: Breast cancer is the most common female cancer in North America. Since estrogens and progestins are thought to play a major role in the development and progression of the disease, antiestrogenic agents are an integral part of therapy. It is also well known that estrogens have a positive impact on bones throughout the female life cycle. Estrogen levels diminish at the time of menopause, followed by a rapid decrease in BMD and subsequent rise in the risk of fractures (mainly of the wrist, vertebrae and hip).

Tamoxifen, a selective estrogen receptor modulator (SERM) that has both estrogenic and antiestrogenic properties, is the traditional adjuvant therapy used to prevent cancer relapse in estrogen receptor-positive patients. In a large prospective trial, this agent has been shown to have a protective effect on bones in postmenopausal women; when compared to placebo, there was a trend towards reduced fracture risk in the treated group.

Aromatase inhibitors

The aromatase inhibitors (AIs) include anastrozole, letrozole and exemestane. They prevent enzymatic conversion of adrenal androgens to estrogens in postmenopausal women, effectively suppressing estrogen production by up to 98%.

Anastrozole has been used as the initial adjuvant therapy (instead of tamoxifen) since the Arimidex®, Tamoxifen, Alone or in Combination (ATAC) trial demonstrated its superiority for multiple endpoints. After a median of 68 months of therapy, however, the risk of fractures was higher in the anastrozole vs the tamoxifen group (11% vs 7.7% respectively; OR 1.49, 95% CI 1.25–1.77, p < 0.0001). BMD, measured in a subset of patients, declined in women receiving anastrozole, while those on tamoxifen experienced a small increment.

Letrozole has been shown to produce similar effects on BMD. A large trial (MA-17) randomized women to either letrozole or placebo after five years of tamoxifen. Study results showed benefits for letrozole on breast cancer endpoints and reiterated its negative influence on BMD (fracture rates between the groups did not differ significantly).

Exemestane has a similar effect on BMD as letrozole; there is no conclusive data on fractures.

All these studies suffer from short follow-up periods and a lack of rigorous skeletal endpoints. The impact of these new molecules on long-term bone health remains to be defined.

Osteoporosis risk management

Canadian and American breast cancer guidelines now recommend that:

• Postmenopausal women with risk factors for osteoporosis or who are taking aromatase inhibitors undergo BMD testing;
• Patients be counselled on exercise and adequate intake of calcium (1500 mg/day) and vitamin D (800 IU/day);
• If osteoporosis is present or if there is a prevalent fragility fracture, treatment with a bisphosphonate should be initiated;
• Otherwise, the overall risk should be evaluated and bisphosphonate therapy* should be considered.
• Raloxifene and hormone replacement therapy should not be used in this patient group. Calcitonin remains useful mainly for analgesia with vertebral fractures†.

There are no data to support the use of teriparatide in this setting.

Editor’s note: *Osteoporosis Canada guidelines recommend alendronate and risedronate as first-line therapies, while etidronate is a second choice. †OC also recommends calcitonin as a second-line drug for osteoporosis treatment.

References are available upon request from: mackinnon@parkpub.com
To treat or not to treat
New BMD reporting recommendations will facilitate decision-making

Osteoporosis Canada (OC) and the Canadian Association of Radiologists invited a multidisciplinary group to develop a practical new tool for the clinician. The recently published Recommendations for Bone Mineral Density (BMD) Reporting in Canada¹ address two main challenges in the diagnosis of osteoporosis.

BMD reports often do not incorporate all the information necessary for complete interpretation of results, and it is difficult to translate the reported scores into an individual’s fracture risk on which to base a decision for treatment or nontreatment. This new set of recommendations provides:

• The elements of a complete BMD report for adults. A BMD report format, a checklist and a patient questionnaire are included as practical tools to help ensure optimal reporting.
• A method for determining an individual’s 10-year absolute fracture risk based on age, sex, BMD, fracture history and glucocorticoid history.

BMD reports that follow this approach will provide clinicians with both a BMD diagnostic category and a useful tool to assess an individual’s risk of osteoporotic fracture. The full document is available on the following websites: www.osteoporosis.ca/local/files/health_professionals/pdfs/CARJ-June05 and www.car.ca/about_car/publications/journal/index.html.

Here, we provide a brief summary of the key points outlined in the document.

10-year absolute fracture risk
Previous OC guidelines advised intervention based on an individual’s WHO category as a marker of fracture risk. The weakness of that system is that absolute fracture risk can vary substantially within any WHO category due to other factors such as age and sex.

OC now proposes that an individual’s 10-year absolute fracture risk, rather than BMD alone, be used for fracture risk categorization. Consequently, age, sex, BMD, fracture history and glucocorticoid use are the basis for this new approach.

How to determine an individual’s 10-year absolute fracture risk
1. Begin with the table appropriate for the patient’s sex (Tables 1, 2).
2. Identify the row closest to the patient’s age.
3. Determine the individual’s fracture risk category by using the lowest T-score from the recommended skeletal sites.
4. Evaluate clinical factors that may move the patient into an even higher fracture risk category, including:
   • Fragility fractures after age 40 (especially vertebral compression fractures)
   • Systemic glucocorticoid therapy > three months duration

The presence of either of these factors substantially elevates fracture risk. Such factors effectively increase risk categorization to the next level (from low to moderate risk, or from moderate to high risk). When both factors

Table 1
10-year fracture risk for women

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Low risk</th>
<th>Moderate risk</th>
<th>High risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>&gt; –2.3</td>
<td>–2.3 to –3.9</td>
<td>&lt; –3.9</td>
</tr>
<tr>
<td>55</td>
<td>&gt; –1.9</td>
<td>–1.9 to –3.4</td>
<td>&lt; –3.4</td>
</tr>
<tr>
<td>60</td>
<td>&gt; –1.4</td>
<td>–1.4 to –3.0</td>
<td>&lt; –3.0</td>
</tr>
<tr>
<td>65</td>
<td>&gt; –1.0</td>
<td>–1.0 to –2.6</td>
<td>&lt; –2.6</td>
</tr>
<tr>
<td>70</td>
<td>&gt; –0.8</td>
<td>–0.8 to –2.2</td>
<td>&lt; –2.2</td>
</tr>
<tr>
<td>75</td>
<td>&gt; –0.7</td>
<td>–0.7 to –2.1</td>
<td>&lt; –2.1</td>
</tr>
<tr>
<td>80</td>
<td>&gt; –0.6</td>
<td>–0.6 to –2.0</td>
<td>&lt; –2.0</td>
</tr>
<tr>
<td>85</td>
<td>&gt; –0.7</td>
<td>–0.7 to –2.2</td>
<td>&lt; –2.2</td>
</tr>
</tbody>
</table>

Table 2
10-year fracture risk for men

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Low risk</th>
<th>Moderate risk</th>
<th>High risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>&gt; –3.4</td>
<td>≤ –3.4</td>
<td>—</td>
</tr>
<tr>
<td>55</td>
<td>&gt; –3.1</td>
<td>≤ –3.1</td>
<td>—</td>
</tr>
<tr>
<td>60</td>
<td>&gt; –3.0</td>
<td>≤ –3.0</td>
<td>—</td>
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<tr>
<td>65</td>
<td>&gt; –2.7</td>
<td>≤ –2.7</td>
<td>—</td>
</tr>
<tr>
<td>70</td>
<td>&gt; –2.1</td>
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<td>&gt; –1.3</td>
<td>–1.3 to –3.3</td>
<td>&lt; –3.3</td>
</tr>
</tbody>
</table>
Interpreting the results

The estimate of absolute fracture risk is intended to provide guidance to the referring physician as to whether fracture risk is sufficiently high to warrant therapy in an untreated patient. The fracture risk predicted for an individual by this system applies only for a finite period of time (10 years). Risk will change with advancing age or with the development of new clinical risk factors. Repeat assessment is appropriate in five to 10 years in those with low risk and in one to five years in those with moderate risk.

This document complements the standards developed by the Canadian Panel of the International Society for Clinical Densitometry (ISCD) establishing the minimum requirements for acceptable performance of BMD testing in Canada.2,3

The recommendations were endorsed by the following organizations:

Canadian Association of Nuclear Medicine
Canadian Association of Radiologists
Canadian Orthopaedic Association
Canadian Panel of the International Society for Clinical Densitometry
Canadian Rheumatology Association
Canadian Society of Endocrinology and Metabolism
College of Family Physicians of Canada
Society of Obstetricians and Gynaecologists of Canada

Elements of the report

A complete BMD report should include:

• Patient identifiers
• DXA scanner identifier
• BMD results expressed in absolute values (g/cm²; three decimal places) and T-score (one decimal place) for:
  * lumbar spine
  * proximal femur (total hip, femoral neck and trochanter)
  * alternate site (preferably forearm BMD: one-third radius, 33% radius or proximal radius) if either hip or spine is not valid.
• Statement about any limitations due to artefacts, if present
• The fracture risk category (low, moderate, high) as determined by using Tables 1 and 2 and including major clinical factors that modify absolute fracture risk probability (with an indication of the corresponding absolute 10-year fracture risk of < 10%, 10%–20% or > 20%)
• For serial measurements, a statement as to whether the change is statistically significant or not. The BMD centre’s least significant change for each skeletal site (in g/cm²) should be included.

Figures 1 and 2 illustrate the stratification into three risk zones for women and men. There are three categories for absolute risk: low (less than 10%), moderate (10% to 20%) and high (over 20%). Similar categories have been used for cardiovascular risk assessment.

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References
Is vitamin D deficiency widespread and how does it impact on bone health? What should be done to reduce the prevalence?

**Dr. David Hanley replies:** Vitamin D is important for normal calcium absorption, bone mineralization and muscle function, and there is evidence that vitamin D inadequacy is associated with an increased risk of cancers (breast, prostate, colon) and immune disorders such as rheumatoid arthritis, multiple sclerosis and type I diabetes. Severe deficiency leads to rickets in children and osteomalacia in adults. Less severe deficiency (often termed insufficiency or inadequacy) is associated with decreased bone and muscle strength, resulting in higher risk of falls and fracture. In selected groups, vitamin D supplementation has been shown to reduce the incidence of falls and even hip fracture.

Most of our vitamin D is synthesized during ultraviolet light (UVB) skin exposure, with only limited contribution from diet. It is well documented that living in northern latitudes (no UVB during winter) as well as reduced skin response to UVB with aging diminish our ability to make this vitamin.

Vitamin D inadequacy is very common in Canada. Vitamin D nutrition is best assessed by a serum 25-hydroxy-vitamin D (25OHD). While it is not clear what defines the lowest acceptable level of 25OHD, a recent study indicated that approximately one-third of a random sample of the population of Calgary fell below the most conservative definition of “inadequacy” (40 nmol/L) in at least one of the four seasons. Recent evidence suggests that 25OHD below approximately 65–80 nmol/L is associated with increased parathyroid hormone levels, greater bone turnover and decreased dietary calcium absorption, all of which would worsen bone loss in people over age 50.

Commercially available assays of 25OHD can identify an individual with frank deficiency of vitamin D at high risk for osteomalacia or rickets (< 20–25 nmol/L). Even the most cautious vitamin D expert would now suggest that normal levels should be above 50 nmol/L. If your patient is not responding to a normally effective osteoporosis therapy, or you suspect a malabsorption syndrome, you should obtain a serum 25OHD.

Current Osteoporosis Canada recommendations for vitamin D intake are 400 IU/day for all adults, increasing to 800 IU/day after age 50. This contrasts with the official positions of Health Canada and the Institute of Medicine (US): 200 IU/day for adults under age 50, 400 IU/day for adults over 50 and 600 IU/day for those over age 70. While Health Canada currently follows the unsubstantiated recommendation that 2000 IU/day is the upper limit of a safe dose, recent evidence suggests the dose associated with toxicity is probably more like 40,000 IU/day. Official government agency vitamin D recommendations are currently being reevaluated, and we anticipate that they will be revised upward. I advise all my patients with osteoporosis to take 800–1000 IU per day.

In my older patients, would it be advisable to look for vertebral fractures at the same time as they are undergoing routine chest x-rays?

**Dr. Brian Lentle answers:** Thank you for your very timely question. There is currently great interest in improving spinal fracture recognition on images in which the spine is seen incidentally, including lateral chest radiographs.

Identifying such fractures is of great importance, because vertebral fractures are associated with not only an immediate increase in the risk of further fractures of the spine but also an increased risk of hip fracture (Hassirius R et al. *Osteoporos Int* 2003; 14:61–8; Lindsay R et al. *JAMA* 2001; 285:320–3; Lindsay R et al. *Osteoporos Int* 2005;16:78–85). Moreover, spinal fractures result in increased morbidity and mortality if further fractures are not prevented. The situation is compounded since it has been found that some 60% or more of spinal fractures cause no immediate symptoms that might lead to an x-ray examination — hence the importance of fracture recognition as an incidental finding. The cumulative impact of fractures, although individually they may not cause symptoms, includes kyphosis, impaired lung function and erosion of self-image, among other consequences.

While fractures correlate with a diagnosis of osteoporosis according to bone mineral density (BMD) classification, that relationship is not inviable. It is increasingly clear that low-trauma fractures result not only from low BMD but also from impaired bone “quality.” Occasionally, quality is a factor leading to fractures even in people with normal BMD. Such patients...
may have osteoporosis and the fracture history should be considered in conjunction with the BMD results when deciding on treatment.

Be aware, however, that a number of Canadian and US studies have found that radiologists tend to overlook such fractures and that other clinicians involved have ignored their implications (Gehlbach SH et al. Osteoporos Int 2000;11:577–82). Your thinking is in tune with a number of international initiatives to improve spinal fracture recognition, reporting and treatment. Because your radiological colleague may be focused on the lungs or heart in a chest image, and because it is not always easy to see the spine in an elderly person with thin bones, it may pay to look at the image yourself (either on film or a computer screen) as well as telephone or visit the radiologist involved.

If the images suggest a possible fracture and you choose to do spinal radiographs, most radiologists believe that lateral images from T4 to L4 suffice, certainly for follow-up. This limits the impact of this new awareness on our sometimes over-stretched health system.

Of interest, some modern machines for measuring BMD now have the capacity to produce low-radiation lateral spinal images (again from T4 to L4) that are often adequate to diagnose higher grade fractures. You may wish to follow that evolving story too.

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questions & answers

Dr. Alexandra Papaioannou wins 2005 Lindy Fraser Memorial Award

osteoporosis Canada was delighted to present the 2005 Lindy Fraser Memorial Award to Dr. Alexandra Papaioannou, in recognition of her valuable contributions to osteoporosis research and education. As past Chair of the Society Board and current Chair of the Guidelines and Research Committees, she has provided outstanding leadership. Her generosity and collaborative spirit have fostered growth among many colleagues and students. Dr. Papaioannou’s tireless work with the Ontario Ministry of Health contributed significantly to the creation of the Ontario Osteoporosis Strategy and subsequent funding for education, prevention, assessment and treatment.

In addition to her clinical duties, Dr. Papaioannou is a researcher in geriatric medicine and osteoporosis, and has published studies in the areas of falls prevention, the osteoporosis care gap in Canada, quality of life and pharmacology in the elderly.

Dr. Papaioannou is Associate Professor in the Department of Medicine and Acting Medical Director in the Division of Geriatric Medicine, Faculty of Health Sciences, McMaster University. She is an Associate Member of the Centre for Evaluation of Medicines, St. Joseph’s Health Care, and Co-Director of the

R. Samuel McLaughlin Centre for Research and Education in Aging and Health.

The Lindy Fraser Memorial Award, established in 1994, honours the founder of the first osteoporosis support group in the world. With her independent spirit and determination, Lindy Fraser was an inspiration for many in the osteoporosis community, and her model of self-help has been emulated across the country. In 1982, she was the key catalyst for the establishment of Osteoporosis Canada.

Please join us in congratulating Dr. Papaioannou.
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- Risk factors & fragility fractures
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- Why we do the things we do
- Alternate osteoporosis screening tools
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- Dairy Farmers of Canada
- Institute of Musculoskeletal Health and Arthritis

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