Steps to prevention
Help patients avoid falls to reduce fractures

questions & answers
Genome studies for osteoporosis explained
BMD changes over time
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resources & announcements page 10
Focus on falls: fracture risk prediction goes beyond BMD

Increasingly, bone mineral density (BMD) is being recognized as only one determinant in assessing fracture risk and deciding on treatment. A recent publication analyzing data from the Canadian Multicentre Osteoporosis Study (Camos) by Langsetmo et al. (Bone 2008 July 1 [Epub ahead of print]) showed that low BMD did not correlate strongly with reported fracture rates, whereas an approach also accounting for age, falls, vertebral deformity and prior fracture history was a good predictor of fractures. Further, the study identified falls as an important independent risk factor for fractures.

In addition to osteoporosis therapies aimed at increasing BMD and preventing fractures, more attention is being paid to fall avoidance in reducing fragility fracture risk. The Report on Seniors’ Falls in Canada (Public Health Agency of Canada, 2005) cites falls as the cause of about 62% of injury-related hospitalizations among elderly people, and more than 90% of hip fractures. Of seniors who sustain a hip fracture, 20% die within one year. This issue of Osteoporosis Update discusses medical, behavioural, environmental and socioeconomic risk factors for falling that clinicians should be aware of. It also looks at strategies — including exercise programs, home hazard assessment and modification, medication review, and vitamin D supplementation — that have been found effective in reducing risk. While more research is needed into how such interventions can translate into clinical gains in lowering fracture risk, even a brief risk assessment by primary care physicians to identify individuals at high risk for falls who would benefit from more thorough evaluation and follow-up is an important first step.

Also in this issue, the focus is on recent Canadian research as experts bring you up to date on the genetics of osteoporosis, recommended frequency of BMD measurement, and indicators for appropriate BMD testing in perimenopausal women (questions and answers, pages 6-7). Finally, on pages 8-9, we present the winner of the 2008 Lindy Fraser Memorial Award and the recipient of a new fellowship award, as well as a unique health management program designed to improve osteoporosis care for high-risk Quebec women.

The Scientific Advisory Council (SAC) welcomes your comments on these topics, as well as others you would like to see addressed. Your feedback will help us provide relevant material to support practitioners across the country in dealing with the day-to-day management of osteoporosis — a significant and growing health concern for Canadian women and men. If you have questions arising from your clinical practice, the SAC will be pleased to answer your concerns. Please send correspondence to osteo@parkpub.com.
Fragility fractures are the major clinical outcome of osteoporosis, and lead to considerable morbidity, disability, mortality and financial costs. Fragility or low-trauma fractures may be defined as those resulting from minimal or no trauma, such as falling from standing height or less.  

Current fracture prevention strategies focus largely on identifying patients at risk of osteoporosis and measuring bone mineral density (BMD) to help detect who is at a higher risk of fracture. Once an individual is found to be at increased fracture risk, first-line therapies include bisphosphonates, raloxifene (a selective estrogen receptor modulator) and teriparatide (an anabolic agent recommended for severe osteoporosis). Although BMD is a strong predictor of fracture risk in individuals who have not yet had a fragility fracture, 82% of postmenopausal women sustaining fractures have T-scores above –2.5.

Falls and fracture risk
While preventing and treating osteoporosis is crucial to prevent fractures in high-risk individuals, the role of fall prevention in reducing fracture risk is being increasingly recognized and advocated. Falls are a key cause of injuries (including fractures), hospitalizations and deaths among seniors. In Canada, an average of 48 per 1,000 people aged 65 and over report a fall-related injury in the past year that was serious enough to limit normal activities. Over one-third (37%) of these injuries are to the lower limbs (hip, thigh, knee, lower leg, ankle or foot). The rates of injurious falls also rise with age and are consistently higher in women than men. Among fall injuries requiring hospitalization, most (47%) occur at home, while 21% of cases take place in residential institutions, though only 7.4% of seniors live in these settings. In addition, accidental falls are the leading cause of major injury in Canadians 65 and older, accounting for 67% of injury-related hospitalizations. Falls are the direct cause of death of over 1,400 people age 65 and up each year.

Risk factors for falls
Many risk factors for falls have been identified, and an individual’s risk of falling and being injured rises as the number of risk factors increases. Falls typically result from a complex interplay of these risk factors, rather than a single cause. Muscle weakness is considered the foremost biologic factor, leading to a 4.4-fold higher risk of falling. Other important biologic risk factors include poor balance, unsteady gait and decreased visual acuity; physical disabilities; chronic illness, particularly arthritis; cognitive impairment; depression; and age over 80 years. Among behavioural risk factors, a history of previous falls is one of the strongest predictors of future falls, with a 3-fold higher risk. Psychotropic agents, particularly benzodiazepines, antidepressants and antipsychotics, increase the risk of falls, whereas antiepileptics and blood pressure-lowering drugs are only weakly associated with falls. Polypharmacy, defined as taking ≥ 4 medications,

Table 1. Primary care fall risk assessment

- Detailed history of past and present falls, including:
  - Falls in past 12 months
  - Indoor falls
  - Inability to get up after a fall
- Review of medical risk factors, especially:
  - Medications, particularly psychotropics (e.g. benzodiazepines, antidepressants)
  - Visual impairment
  - Cognitive function
- Watch patient walk and move to assess muscle strength, balance and gait
- Assess time taken to stand from sitting

Patients deemed to be at high risk of falling should be referred for more comprehensive evaluation.
has been implicated as an important risk factor for falls, but a new study suggests that the correlation only holds when at least one known fall-increasing drug is part of the regimen.14 Other behavioural risk factors include excessive alcohol consumption, inappropriate footwear or clothing, carrying objects, risk-taking behaviour, inactivity and poor diet. Ironically, fear of falling may raise the risk of falls if it causes patients to avoid activities, lose confidence, or “stiffen” in an attempt to maintain balance.4

Environmental risk factors are hazards in and about the home that can increase the risk of falling. These factors include stairs, especially without handrails, poor lighting, obstacles, slippery surfaces and lack of proper assistive devices.7 Among fall-related major injuries/trauma in Canadians 65 years and over, the most common specified cause (29%) is falls on the same level due to slipping, tripping or stumbling.9

The role of socioeconomic risk factors, such as income, education, housing and social relationships, in falls is uncertain, although these variables are known to relate strongly to health, disability and longevity.9 An Australian study found that being married, living in the same home for at least 5 years, having private health insurance, using proactive coping strategies, greater life satisfaction, and engaging in social activities all had a significant independent protective effect against fall-related hip fractures.15

**Patient assessment**
The first step for primary care practitioners should be a brief risk assessment to identify high-risk seniors needing referral for more comprehensive fall evaluation (Table 1).4 In routine care, all older patients should be asked once a year about falls; those reporting recurrent falls and/or showing gait or balance abnormalities require a thorough fall assessment. As well, any seniors presenting for medical attention due to a fall should automatically undergo a complete fall evaluation, most likely by a suitably experienced clinician. This examination would include a history of the fall and its circumstances, medication review, assessment of vision, gait and balance, basic neurologic examination, and basic cardiovascular status evaluation.12

The 2002 Canadian osteoporosis clinical practice guidelines recommend that older people at risk of falling, or who have already fallen, undergo individual assessment to set up tailored exercise programs, multidisciplinary if needed, to improve their strength and balance. Further, they have identified propensity for falling as one of the major risk factors that should prompt an assessment for osteoporosis. The rationale is that, while osteoporosis is not a risk factor for falls in itself, it greatly increases the risk of fractures if a fall occurs.1

**Effective fall prevention strategies**
A 2003 Cochrane Review of fall prevention interventions concluded that several are likely to be beneficial in reducing falls. Single interventions found to be effective included:

- muscle strengthening and balance retraining such as that gained by programs like Tai Chi
- home hazard assessment and modification
- withdrawal of psychotropic medication
- cardiac pacing for fallers with syncope due to cardio-inhibitory carotid sinus hypersensitivity
- Multifactorial assessment and intervention programs, which target an individual’s modifiable risk factors

The authors noted, however, a general lack of data on the effectiveness of these interventions in avoiding fall-related injuries.16 A subsequent meta-analysis determined that, among single-intervention strategies, multifactorial risk assessment and management programs are the most effective approach, reducing both the risk and rate of falling, followed by exercise programs.17

A growing body of evidence indicates that vitamin D is important not only in maintaining bone density, but also in preventing falls, primarily by improving muscle function. In a recent 12-month trial of supplementation with 800 IU/day of vitamin D, the number of first falls decreased by 27% and fell even more (by 39%) by month 20, eight months after treatment stopped. As well, measures of muscle function improved significantly.18 These findings correspond with those of an earlier meta-analysis of 10 vitamin D trials, which showed a 22% reduction in the

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### Table 2.
**Best practices to prevent falls**8,16,17

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risk of falls. The authors suggest that given the high morbidity, mortality and financial costs of falls, vitamin D supplementation should be considered for the elderly.19

Table 2 (page 4) outlines various approaches to effective fall prevention. Increasing patient awareness about the importance of avoiding falls is also a key component. For a list of resources to direct patients towards, see below.

Does preventing falls prevent fractures?

While it seems intuitive that preventing falls would also reduce fractures and other injuries, results from trials are conflicting. To date, no fall prevention trials have used fractures as a primary outcome, although some studies have reported fewer fractures.20 A meta-analysis of multifactorial falls prevention trials in community and emergency care settings found no clear evidence for effectiveness in reducing either fall-related injuries or the number of fallers.20 Even in residential care and hospital settings, multifaceted interventions reduce falls but have no significant effect on the number of fallers or fractures, while using hip protectors in residential care homes reduces fractures, but not falls; other single or multifaceted interventions tested in either setting have insufficient evidence to reach any conclusion.21 Clearly, more research is needed to determine the most effective strategies.

Regardless of trial findings, the ultimate challenge is translating them to clinical practice. A novel approach to reducing fall-related injuries in the elderly was implemented and investigated in the state of Connecticut. It consisted of educating clinicians from various disciplines who were involved in care of older people on evidence-based fall prevention practices and increasing fall awareness in seniors. When the intervention and usual-care regions were compared, the rates of serious fall-related injuries and fall-related use of medical services for the intervention regions fell by 9% and 11%, respectively.22

References

What do I need to know about genome studies and osteoporosis?

Dr. Brent Richards responds: To answer this question, we can break it down into several queries dealing with different aspects:

First, why does the genetics of osteoporosis matter? Osteoporosis and osteoporotic fractures are both highly heritable conditions: osteoporosis approximately 80%, and fractures about 50%–60% heritable. Although many environmental risk factors for osteoporotic fractures have been well described, their ability to predict fractures lacks sensitivity and specificity. Identification of the genetic risk factors for osteoporotic fractures will enable the discovery of novel proteins central to bone metabolism, illuminate its pathophysiology, and help to identify populations at risk.

Next, what is a genome-wide association (GWA) study? Despite many efforts over the years, very few genes have been shown to be reproducibly associated with osteoporotic fractures; this is largely because, previously, researchers were only able to select several single nucleotide polymorphisms (SNPs) at a time to genotype. Recent advances in technology now permit the simultaneous genotyping of up to 1 million SNPs at a time. Thus, the resolution of the genetic map has improved by several orders of magnitude. The researcher asks: “Are people who have a certain disease more likely to have the same variant at a SNP as people who do not have the disease?” and simply repeats the question up to a million times. The SNPs that are most strongly associated with the disease of interest are subsequently tested in an entirely separate cohort to see if they remain associated with the disease. This replication testing is done to decrease the number of false positives.

Third, have GWA studies been performed for osteoporosis-related traits? To date, two replicated GWA studies have been performed for bone mineral density (BMD), and these have identified SNPs associated with both decreased BMD and risk of fracture. In the paper by Richards et al, which assessed BMD in 8,557 women, the authors found that SNPs in the osteoprotegerin gene and LRP5 (lipoprotein-receptor-related protein) were strongly associated with decreased BMD (lumbar spine p = 6.3 x 10−12 and p = 7.6 x 10−10 for LRP5 and osteoprotegerin, respectively). Interestingly, despite controlling for BMD, the presence of risk alleles at these loci remained associated with a 1.3-fold increase in the odds of osteoporotic fracture (p = 0.006). While confirming these results, Styrkarsdottir et al described SNPs in the receptor-activator of nuclear factor K-B ligand (RANKL) gene, estrogen receptor 1 gene, and two novel regions at a gene called ZBTB40 and the major histocompatibility complex region. These SNPs were also strongly related to BMD (minimum p-value = 7.5 x 10−14), but were associated with a small risk of osteoporotic fracture (the highest risk described for osteoporotic fracture was odds ratio = 1.12, p = 5.4 x 10−4). Other studies are currently ongoing, including a large-scale meta-analysis of these results.

Finally, how might this information change my clinical practice? The identification of novel proteins and pathways in osteoporosis in humans has provided novel drug targets. In addition, although it is unlikely that the identified SNPs will immediately change clinical practice, it is possible that extended panels of several SNP markers could be used in the future, along with traditional risk factors, to improve our ability to identify populations at high risk for osteoporotic fracture. This may become a clinical reality as genotyping costs are dropping exponentially. Importantly, because these risk factors are genetic, safe and simple interventions may be instituted years prior to the development of osteoporosis. How to best deploy these advances in the clinic requires further investigation.

References

Definitions

Single Nucleotide Polymorphism (SNP): A change in a single base pair in DNA that differs from the usual base at that position.

Genome Wide Association Study (GWA): A new technique that permits the simultaneous genotyping of several hundred thousand SNPs and their correlation with a phenotype of interest.

Allele: Different versions of the same gene or SNP.
A new study suggests bone loss is greatest among women aged 50–54, then increases again after age 70; in men, the rate rises after age 65. What is the significance of this in terms of BMD testing?

Dr. David Goltzman comments: A study by the Canadian Multicentre Osteoporosis Study (CaMos) Research Group examined the rate of change of BMD over time in 9,423 individuals aged 25 to 85, stratified by sex and use of antiresorptive agents (Berger C, Langsetmo L, Joseph L et al. *CMAJ* 2008;178[13]:1660-8). BMD was measured in the lumbar spine, total hip and femoral neck at baseline and at 3-year (participants between 40–60 years only) and 5-year follow-ups. The recently published results confirm that the perimenopausal period is one of major bone loss in women; it can account for over 40% of the bone loss that a woman will sustain during her lifetime. The study also identified a second period of rapid bone loss — not previously recognized — in both older men and women, that may contribute to the development of hip fractures.

From a very practical point of view, the CaMos study found that in individuals without risk factors for osteoporosis, the rate of BMD change, even at its most rapid, was such that a repeat test would not have to be done more often than every 5 years. This is because if testing were done much more frequently than that, BMD machines could not likely detect the amount of change per year.

It is important to note that this frequency of measurement does not apply to individuals who have osteoporosis risk factors or who have been diagnosed with osteoporosis and are receiving therapy. In these patients, more frequent BMD measurements may be indicated.

What risk factors are the best indicators of when BMD testing is appropriate in perimenopausal women?

Dr. Gillian Hawker answers: There is general agreement that perimenopausal women (i.e. women around the time of menopause) who have medical conditions and/or are using medications associated with bone loss, low BMD or fracture (e.g. aromatase inhibitors, corticosteroids) should receive BMD testing and appropriate management. However, the majority of women who undergo BMD testing at this age are healthy, with no such comorbidities.

Guidelines to facilitate decision-making regarding BMD testing in these women do not currently exist. Current risk assessment for low BMD is based primarily on data from older women (≥ 65 years), which does not incorporate risk factors for low peak bone mass or accelerated perimenopausal bone loss. Additionally, risk factors for low BMD or fracture in older women may not be relevant to, or highly prevalent among, younger women. Although the absolute risk of fragility fracture is low in younger women, detection of individuals with significantly reduced BMD is useful in identifying those in need of preventive measures and/or closer surveillance.

To address this knowledge gap, in conjunction with the Ontario Ministry of Health and Long Term Care’s provincial Osteoporosis Strategy, an extensive literature review was conducted to identify risk factors for low BMD in healthy women aged 40–60 years (Waugh EJ, Lam MA, Hawker GA et al. *Osteoporos Int* 2008 June 4. Epub ahead of print). Few studies had focused on this age group, and those that had suffered from methodologic limitations, in particular, lack of control for potential sources of bias. There was convincing evidence for only two risk factors for low BMD: low body weight and postmenopausal status. A further study to better delineate risk factors in this group of women was therefore undertaken.

Healthy women aged 40–60 years, referred for their first BMD test at a large urban hospital, completed questionnaires to assess for possible risk factors for low BMD, including: socio-demographics, height and weight, lifestyle factors, and reproductive, menstrual, family and fracture history. BMD at the lumbar spine, femoral neck and total hip were assessed with DXA, and predictors of low BMD (T-score ≤ –2.0 at any site) were assessed statistically.

Almost 70% of the women having their first BMD test had no medical risk factors for low BMD; of the 628 study participants, fewer than 15% had low BMD, underscoring the need for better targeting of BMD testing to those most likely to have low BMD. Consistent with the systematic review noted above, the study confirmed that, compared with women with normal BMD, those with low BMD were more prone to have lower body weight and to be postmenopausal. Moreover, older age (within the 20-year span of interest), older age at menarche, physical inactivity as an adolescent (defined by a negative response to the question, “During your teens, did you regularly participate in physical activity vigorous enough to work up a sweat?”), and history of a low-trauma fracture after age 40 years were also identified as risk factors for low BMD in this population.

The best sensitivity (88.7%) and specificity (41.3%) were achieved when BMD testing was limited to healthy women with any one or more of: weight ≤ 65 kg, low-trauma fracture after age 40, age at menarche > 15 years, or physical inactivity during adolescence. Using this rule, 241 of the 628 women (38%) who had none of these risk factors would not have been tested; of those not recommended for testing, only 7 had low BMD. Thus, limiting BMD testing in healthy women at midlife to those with one or more of these four easily assessed risk factors would substantially reduce the rates of testing in this age group, without significant compromise. However, further research is warranted to evaluate the feasibility and acceptability of incorporating these recommendations into clinical practice.
Lindy Fraser Memorial Award 2008

Osteoporosis Canada is pleased to announce that Dr. William (Bill) D. Leslie has been unanimously chosen to receive this year’s Lindy Fraser Memorial Award. Established in 1994, this prestigious award is given to individuals who have made a significant contribution to research and education in the field of osteoporosis.

Dr. Leslie is Professor of Medicine and Radiology at the University of Manitoba. He obtained his specialty training from the University of Manitoba and McGill University, qualifying in Internal Medicine in 1989 and Nuclear Medicine in 1990. His research interests include osteoporosis testing and other nuclear diagnostic techniques, including PET (positron emission tomography) scanning.

Dr. Leslie joined Osteoporosis Canada’s Scientific Advisory Council (SAC) in 1997 and has contributed to many of their publications, including the 2002 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada, Recognizing and reporting vertebral fractures: reducing the risk of future osteoporotic fractures and Recommendations for bone mineral density reporting in Canada (see www.osteoporosis.ca, Health Professionals section). More recently, he has been involved in Ministry of Health and Long-Term Care (MOHLTC) projects addressing bone density testing in men, testing in women aged 40–59 years, and vitamin D recommendations.

He is currently Vice-Chair of the SAC, Chair of the Guidelines Committee for Osteoporosis Canada, Director of the Manitoba Bone Density Program, and Co-Director of the Winnipeg PET Imaging Centre. He also sits on the Board of the International Society for Clinical Densitometry.

Dr. Leslie accepted the Lindy Fraser Memorial Award during the SAC luncheon at the 30th American Society for Bone and Mineral Research Annual Meeting held in Montreal, Quebec from September 12–16, 2008.

Please join us in congratulating Dr. Leslie for his well-deserved award!

New joint venture fellowship award

In June 2008, Osteoporosis Canada, the Strategic Training Program in Skeletal Health Research (STPSHR) and the Canadian Multicentre Osteoporosis Study (CaMos) Group were proud to announce an exciting new partnership that will further the commitment of all three organizations to improving the lives of individuals with osteoporosis through better prevention and treatment. As President of the Scientific Advisory Committee, Dr. Alexandra Papaioannou presented this joint venture’s first fellowship award to George Ioannidis, a PhD candidate at McMaster University (Hamilton, ON) in the Department of Health Research Methodology.

Mr. Ioannidis’ PhD research focuses on the impact of osteoporotic fractures on mortality in Canadian men and women as well as on new methodology that will help
Results from ROCQ reveal care gap among Québec women

R
cognizing Osteoporosis and its Consequences in Québec (Reconnaître l’ostéoporose et ses conséquences au Québec) is a unique health management program that aims to improve diagnosis and treatment of women over age 50 who have suffered a fragility fracture, by implementing strategies that target patients as well as health professionals. This program is the result of collaborative efforts between Dr. Jacques Brown (Clinical Professor, Université Laval; Head of the Division of Rheumatology at the Centre hospitalier universitaire de Québec; President of the Executive Committee of ROCQ), Dr. Louis Bessette (Centre hospitalier de l’Université Laval), Dr. Louis-Georges Ste-Marie (Centre hospitalier de l’Université de Montréal – Hôpital Saint-Luc), and various partners including physicians, pharmacists, patients, women’s and seniors’ groups, and pharmaceutical companies.

Results of ROCQ, the first large Québec study of its kind, were presented in Barcelona, Spain, in May 2008 at the European Symposium on Calcified Tissues. In the first phase of the project, women 50 years of age and older were recruited from cast clinics across the province of Québec following a fragility fracture and were followed over time to assess the rate at which they were investigated for osteoporosis after this fracture event. A total of 3,288 women participated in the research, in 18 centres in Québec. The study’s findings point to a significant care gap in the management of osteoporosis: while 80% of fractures reported in women were felt to be associated with osteoporosis, 80% of these women were neither investigated nor treated for it. Further, the study reveals that physicians’ treatment decisions are often based primarily on the results of BMD tests rather than on clinical events of fragility fractures.

The implications of the ROCQ study for health professionals are important. It is crucial for physicians to be aware of and take into account their patients’ fracture history. According to Dr. Suzanne Morin, founding member of the Greater Montreal branch of Osteoporosis Canada, member of Osteoporosis Canada’s Scientific Advisory Council and Associate Professor of Medicine at McGill University, “Osteoporosis should be considered in all cases of nontraumatic bone fractures. Bone density tests are not enough; the fracture history must be analyzed, since it is an important fracture risk factor. This is an essential step in the diagnosis that is neglected more often than not.”

In the second phase of the project, a therapeutic educational intervention aimed at improving the care gap is being investigated. The results of this study may change the way osteoporosis is managed in very high-risk women.

Bone density tests are not enough
Key factors physicians should consider in assessing a patient’s bone health status should include all of the following:
• Age
• History of fragility fracture after the age of 40 years
• BMD
• Family history of osteoporotic fracture
• Height loss (over the age of 50, height loss of more than 2 cm in the past 3 years may be a sign of an undetected vertebral fracture)

Earlier diagnosis will hopefully lead to optimal treatment, reduced risk of recurrent fractures and improved quality of life for women with osteoporosis.
Osteoporosis Canada is a national, not-for-profit organization dedicated to educating, empowering and supporting individuals and communities in the risk reduction and treatment of osteoporosis. The organization, guided by its Scientific Advisory Council (SAC) made up of osteoporosis experts from across the country, works with healthcare professionals to make the latest prevention, diagnostic and treatment options available to Canadians.

www.osteoporosis.ca

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Bangkok, Thailand

The International Osteoporosis invites osteoporosis specialists and health professionals to attend the world’s largest osteoporosis conference, providing a comprehensive overview of new developments in research, diagnosis and therapy including:

Plenary lectures on hot topics by leading experts
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Special orthopedic sessions
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www.iofbonehealth.org/wco/2008/homepage.html;
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