The Osteoporosis Society of Canada recently released the 2010 Clinical Practice Guidelines for the Diagnosis and Management of Osteoporosis in Canada. The revised guidelines represent a paradigm shift in the way this potentially devastating disease is prevented and treated. The new standard of care will move the focus from treating low bone mineral density (BMD) to preventing fragility fractures and their negative consequences.

“We know that many patients who have had fractures are not appropriately assessed or treated,” says Dr. Alexandra Papaioannou, Professor of Medicine at McMaster University, in Hamilton, Ontario, and lead author of the 2010 Guidelines. “The new guidelines aim to address this ‘care gap’ for high-risk patients.”

What is osteoporosis?

Osteoporosis is a common disease and a growing public health concern in this country. Approximately one in four women and one in eight men over the age of 50 have osteoporosis; it affects an estimated 1.8 million women in Canada. These numbers are expected to increase as the Canadian population ages.

Osteoporosis is a disease characterized by low bone mass and deterioration of bone tissue. This leads to increased bone fragility and risk of fracture, particularly of the hip, spine (vertebral) and wrist.

High costs, human & financial

“All key osteoporosis-related fractures, including those occurring at the hip, spine and wrist, can profoundly impair quality of life and productivity. Fractures are invariably associated with chronic pain, reduced mobility, increased functional disability, and an increasing degree of dependence. Many people with fractures do not regain their pre-fracture level of function, hence impacting their quality of life and the ability to return to their previous work.”

Hip fractures carry a significantly high risk of mortality and morbidity, resulting in death in up to 20% of cases, and disability in 50% of those who survive.

In women still in the workplace, vertebral fractures are more of a concern than hip fractures. Vertebral fractures, which are associated with back pain, limited spinal mobility, height loss, deformity and disability, are more likely than hip fractures to afflict younger people, even around the age of 50 or younger.

“In the working population, a vertebral fracture can be devastating, especially for people with jobs that require a lot of sitting — like working at a computer — or that involve manual labour,” says Dr. Kvern. For these individuals, a fracture may involve indirect costs associated with sick leave, loss of job days, unemployment payments, loss of productivity, and community expenses, as well as psychological distress.

When workers are also caregivers, osteoporosis-related fractures can place an added burden on “the sandwich generation.” As Dr. Papaioannou observes, “The impact of a fracture is not only on the individual, but also family members who may have to take time off work to care for them.”

The economic burden to the workplace is also substantial. According to a report from the International Osteoporosis Foundation, the annual medical care and medication costs of treating osteoporotic fractures of people in the workplace (i.e., individuals 50 years and older who are economically active) are estimated to be approximately $1.9 billion in Canada. These costs are expected to rise as the Canadian population ages. Additionally, in patients who are still in the workplace, there are other work-related costs associated with osteoporotic fractures, including sick leave, loss of job days, chronic pain, unemployment payments, loss of productivity, and community expenses, as well as psychological distress. The employer will likely bear an economic burden associated with loss of efficiency and productivity, payment of workmen’s compensation and health claims, and the
The cost of replacing the employee. These costs to employers are anticipated to rise as people stay in the workforce longer.

Early identification, early intervention

The 2010 Osteoporosis Guidelines recommend that women and men over age 50 should be assessed for risk factors for osteoporosis and fracture to identify those at high risk for fractures. Individuals over the age of 50 who have experienced a fragility fracture (i.e., a broken bone caused by minor impact) are considered high risk.

“Fracture predicts fracture,” says Dr. Kvern, explaining that individuals who have had a fragility fracture are at significant risk of subsequent fracture. “Younger people over the age of 40 especially need to recognize that if they’ve had an osteoporosis-related fracture, they need to be vigilant about preventing another,” he says.

Dr. Papaioannou agrees: “The first year after a fracture is a particularly high-risk period for patients. They need to take steps to reduce their risk of another fracture.”

The 2010 Guidelines recommend that patients at risk for fracture incorporate changes into their lifestyle to prevent bones from breaking. These changes include regular physical exercise (including weight-bearing activities) along with adequate intake of calcium (1200 mg/day) and vitamin D (800 – 2000 IU for individuals 50 years and older). Medication to prevent fractures is also recommended for high-risk individuals.

As outlined in the 2010 Guidelines, a growing number of therapeutic options, with a range of dosing frequencies and routes of administration, are available in Canada. These include, among other therapies, bisphosphonates, selective estrogen receptor modulators (SERMs), parathyroid hormones, a RANK ligand inhibitor, hormone replacement therapy and a bone-forming agent (teriparatide).

“In general, pharmacotherapy can reduce the risk of fracture by 20% to 70%, depending on the agent, site of fracture and level of adherence to therapy,” says Dr. Papaioannou.

For menopausal women requiring treatment of osteoporosis, the 2010 Osteoporosis Guidelines recommend that, among other therapies, bisphosphonates (including alendronate, risedronate, zoledronic acid) and a RANK ligand inhibitor (denosumab) can be used as first-line therapies for prevention of hip, nonvertebral (i.e. pelvic, long bone fractures) and vertebral fractures (see Table: First Line Therapies with Evidence...

First-line therapies with evidence for fracture prevention in postmenopausal women Based on Grade A evidence*1

<table>
<thead>
<tr>
<th>Type of Fracture</th>
<th>Antiresorptive Therapy</th>
<th>Bone Formation Therapy</th>
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<tr>
<td></td>
<td>Bisphosphonates</td>
<td>Denosumab</td>
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<tr>
<td>Vertebral</td>
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<td>✓</td>
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<tr>
<td>Hip</td>
<td>✓</td>
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<tr>
<td>Non-Vertebral</td>
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In clinical trials, non-vertebral fractures are a composite endpoint including hip, femur, tibia, humerus, radius, and clavicle.

*For postmenopausal women, ✓ indicates first line therapies and Grade A recommendation. For men requiring treatment, alendronate, risedronate, and zoledronic acid can be used as first-line therapies for prevention of fractures (Grade D).

**Hormone therapy (estrogen) can be used as first-line therapy in women with menopausal symptoms.
for Fracture Prevention in Postmenopausal Women). Individuals need to work with their physician to determine which medication is right for them, based on the benefits and risks of each medication and taking into account such factors as side effects, convenience, cost, and lifestyle considerations.

**First-line therapeutic choices**

**Bisphosphonates**

First-line bisphosphonates include the oral therapies alendronate, risedronate and the intravenous therapy zoledronic acid. Oral bisphosphonates are the current standard of care and by far the most commonly prescribed medications in Canada for both men and postmenopausal women. Patients must carefully follow the dosing instructions for oral bisphosphonates in order to promote absorption and reduce the risk of stomach upset and esophageal irritation. These instructions include taking the drug on an empty stomach, with a full glass of water, and not eating or drinking anything but water, or lying down within 30 minutes after a dose.

“We know that in the real world many patients stop taking their oral bisphosphonate one year out,” says Dr. Papaioannou. A claims analysis published in 2006 by the Institute for Clinical Evaluative Sciences using the Ontario Drug Benefits Program database reported that 30% of patients discontinued oral bisphosphonate treatment within the first six months, and 50% discontinued within the first year. Failure to take a medication as prescribed, known as non-compliance or non-adherence, may result in drug wastage. If only half of patients who start a medication persist with therapy beyond a year, then half the costs spent on the drugs may be wasted, as non-compliance may limit the medication’s effectiveness in reducing the risk for fracture. Some studies suggest that patients need continuous treatment with an oral bisphosphonate for at least six to 12 months and taking at least 80% of the prescribed doses in order to realize fracture risk reduction. Future bisphosphonate therapies may address these compliance issues.

**RANK Ligand Inhibitor**

Unlike oral therapies, the RANK ligand inhibitor denosumab is administered as a subcutaneous injection once every six months. A randomized open-label study found that after 12 months of therapy, patients treated with denosumab were 42% likely more adherent, 52% likely more compliant, and 46% likely more persistent than patients treated with weekly oral alendronate.

Patients have also indicated a greater preference for a subcutaneous injection every six months over a weekly oral pill, as demonstrated in two randomized controlled studies. When postmenopausal women with low bone mass were surveyed after 12 months of treatment for osteoporosis, more patients preferred, were more satisfied and less bothered with a six-month denosumab injection than weekly oral alendronate.

“How these studies translate in the real world remains to be seen, but one can hypothesize that twice yearly injections might be easier for some patients, says Dr. Papaioannou.
To the future

As the population ages and people stay in the workforce longer, employers need to be more aware of the health concerns of their aging workers. “Osteoporosis can affect lives dramatically, so we need strategies that raise awareness, improve overall health and prevent fractures,” says Dr. Kvern.

References


8 Merck Frosst Canada Ltd., Fosamax Product Monograph. 2009.


