



COPN: Proudly Celebrating our 10th Anniversary **Drug Holidays: Weighing the Benefits and Risks of** **Bisphosphonate Drugs**

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Fracture Fact:

When taken as directed to treat osteoporosis, bisphosphonates significantly reduce the risk of all types of fractures, over and above the very small risk of developing ONJ or atypical femur fractures.

Should I go on a drug holiday? This is one of the questions we hear most often from individuals who are taking osteoporosis medications. Sometimes the question is prompted by a concern about potential side effects. Others wonder whether medication is still needed even when they have been fracture-free for many years. Of course the answers are complicated, but by explaining the potential benefits and risks of bisphosphonates, possibly the most common of the medications used to treat osteoporosis, this article will help you understand the factors that need to be considered before deciding to make any changes to your medication or going on a drug holiday.

A Summary of Benefits, Harms and Drug Holidays**

Introduction

Osteoporosis is a disease of bones in which there is rapid loss of bone mineral and deterioration of bone quality. This leads to an increase in the risk of osteoporotic fragility fractures (broken bones). Osteoporotic fractures decrease one's mobility, personal independence and quality of life. They also increase the risk of death. Therefore, the prevention of osteoporotic fractures is very important.

Bisphosphonates are a class of drugs that includes alendronate (Fosamax®), risedronate (Actonel®), zoledronic acid (Aclasta®), and etidronate (Didronel® or Didrocal®). These drugs have been shown to work very well in preventing fragile osteoporotic bones from breaking. As a result, they are often used as first-line therapy for the prevention of fractures (broken bones) in osteoporotic individuals who are at high fracture risk. (Etidronate is not as effective as the other three bisphosphonates and is not considered first line.)

Bisphosphonates work by binding to bone where they prevent osteoclasts from removing old bone. Bisphosphonates can remain bound to bone for many years. Consequently, even after bisphosphonates are discontinued, they continue to work by suppressing the activity of the osteoclasts.

This is in contrast to other non-bisphosphonate osteoporosis drugs that stop working soon after they are discontinued. Such drugs include denosumab (Prolia®), estrogen, raloxifene (Evista®) and injectable calcitonin (sometimes used for pain management). Of these, only denosumab has been shown to be similar to bisphosphonates in terms of how well they prevent fractures (broken bones) at the hip, spine and other bones of the skeleton.

Although clinical research has shown that bisphosphonates work very well and are considered safe, there have been concerns that prolonged use of these drugs might increase the risk of rare, but serious, adverse events (side effects). These concerns come from post-marketing reports that are based on long-term use of bisphosphonates (more than five years) and millions of person-years* of use. There are suggestions that there may be an association between taking bisphosphonates and developing rare side effects: osteonecrosis of the jaw (ONJ), atypical femur fractures (AFF), atrial fibrillation (AF) and cancer of the esophagus.

Osteonecrosis of the jaw

Osteonecrosis of the jaw (ONJ) is defined as the presence of exposed bone in the jaw region that does not heal within eight weeks after being identified by a doctor or dentist, in the absence of radiation therapy.

Osteonecrosis of the jaw is not just “jaw pain” and is easily identified visually. At the present time, how bisphosphonate therapy leads to ONJ is poorly understood.

However, what is known is that bisphosphonate-associated ONJ is very rare when the bisphosphonate is taken in **usual** doses for the treatment of osteoporosis. For such individuals the absolute risk of developing ONJ is approximately 1 case per 100,000 person-years.*

Current scientific evidence suggests that the higher the dose of bisphosphonate taken, the greater the risk of developing ONJ. In some studies, ONJ has been seen to occur in about 2.0% of cancer patients receiving **high** doses of either intravenous bisphosphonates or denosumab. In a recent survey of Canadian physicians, the overall incidence of ONJ in cancer patients was 0.4% but was only 0.001% (1 in 100,000) in osteoporosis patients taking **usual** doses. Similar statistics have been reported in the US and Scotland. ONJ is more likely to occur in cancer patients on **high** doses of bisphosphonates or denosumab, particularly if they have poor oral hygiene.

Recommendations for Patients:

- 1) Individuals who are planning to undergo any invasive dental procedures, such as dental implants or extractions, and who need to start a bisphosphonate drug for their osteoporosis **may** wish to consider completing their dental procedure(s) *before* starting their bisphosphonate drug. This will further reduce the already very low risk of developing ONJ.
- 2) Individuals already taking **usual** doses of bisphosphonates should not delay any emergency dental procedures or implants because the risk of developing ONJ is extremely low. These individuals should care for their teeth as usual: brush and floss daily and see their dentist every six months.
- 3) **High** fracture risk patients should **continue** taking their bisphosphonate drug even if undergoing invasive dental procedures.
- 4) **Low** fracture risk patients who are on a bisphosphonate drug may consider discontinuing their medication.

- 5) A drug holiday from bisphosphonates **may** be considered in select individuals at **moderate** risk of fracture who no longer need drug therapy for osteoporosis.
- 6) All individuals taking bisphosphonates should **discuss** their bone health and their fracture risk with their doctor no more than every 5 years in order to determine whether or not they need to continue taking their bisphosphonate therapy.

Atypical femur fractures

Atypical femur fractures (AFF) are those that occur just below the hip or anywhere in the shaft of the femur (thigh bone) with minimal or no trauma. Atypical femur fractures are often bilateral. In other words, two-thirds of cases occur on both legs, although not necessarily at the same time. An individual may experience pain or discomfort in the thigh area for weeks or months prior to fracturing. Most atypical femur fractures occur after more than three years of bisphosphonate use, averaging approximately 3.2 to 50 cases per 100,000 person-years.*

How bisphosphonate therapy leads to atypical femur fractures is poorly understood at the present time. Up to half of atypical femur fractures occur in people not taking bisphosphonates. In one study, the risk of developing atypical femur fractures increased with more prolonged use of bisphosphonates and decreased by 70% for each year after the bisphosphonate was discontinued.

For individuals at high and moderate fracture risk, the risk of an AFF is greatly overshadowed by the anti-fracture benefit gained from taking a bisphosphonate drug. In one study, it was estimated that “for every 100 typical hip fractures prevented, there was an increase of one atypical femur fracture.” In Canada, one in three women will experience an osteoporotic fracture after the age of 50 and one in eight Canadian women will experience a hip fracture. However, treatment with bisphosphonates reduces this risk by 20% to 50% over three years of therapy. In addition to significantly reducing the risk of hip fracture in high risk individuals, bisphosphonates also prevent thousands of spine fractures and other types of fractures per 100,000 person-years* of treatment.

Although there is an increased risk of AFF with bisphosphonate use, it is still extremely small. The benefits of using bisphosphonate drugs to prevent fractures associated with osteoporosis in high risk patients far outweigh the risk of an atypical femur fracture.

Recommendations for Patients:

- 1) Individuals who experience thigh pain while taking bisphosphonates should see their physician for an X-ray of the full length of **both** femurs. Additional testing (bone scan, CT scan or MRI) may also be required.
- 2) **High** fracture risk patients should **continue** taking their bisphosphonate.
- 3) **Low** fracture risk patients may consider discontinuing their bisphosphonate.
- 4) A drug holiday from bisphosphonates **may** be considered in select individuals at **moderate** risk of fracture who no longer need drug therapy for osteoporosis.
- 5) All individuals taking bisphosphonates should **discuss** their bone health and their fracture risk with their doctor no more than every 5 years in order to determine whether or not they need to continue taking their bisphosphonate therapy.

Atrial fibrillation

Atrial fibrillation is a heart arrhythmia (irregular heart beat) that increases the risk of stroke. In recent large database analyses and a meta-analysis, no association has been shown between the use of bisphosphonates and the incidence of atrial fibrillation, with one study even suggesting a protective effect. Therefore, at this time, the weight of the evidence suggests that there is no association between bisphosphonate use and atrial fibrillation.

Esophageal cancer

Because the esophagus is exposed to bisphosphonates that are taken by mouth, it has been suggested that bisphosphonates may increase the risk for the development of esophageal cancer. The results of research studies in this regard have been conflicting. At this time, there is no consistent data to indicate that oral bisphosphonates increase the risk of esophageal cancer, but more studies are needed.

Bisphosphonates taken orally (by mouth) can irritate the esophagus. To reduce this risk, all oral bisphosphonates (with the exception of Actonel DR™) should be taken with one full glass of water first thing in the morning upon awakening, in an upright position (seated or standing). Actonel DR™ should be taken with one full glass of water once daily with a meal. After taking any oral bisphosphonate (including Actonel DR™), the individual should NOT bend over/lie down/eat/drink other liquids/take other medications for at least the next 30 minutes.

Renal function and bisphosphonates

Bisphosphonates should not be taken by individuals who have kidney failure or very low kidney (renal) function. Individuals starting on bisphosphonate therapy should first have their kidney function checked by a healthcare professional. It is important to be well hydrated when taking any type of bisphosphonate.

Conclusion

While most bisphosphonates are first-line therapy for patients at high risk of osteoporotic fragility fracture, there are some rare, but serious, adverse events that have been associated with their use, most notably osteonecrosis of the jaw (ONJ) and atypical femur fractures (AFF). When bisphosphonates are prescribed for patients at high risk of future fragility fractures, the anti-fracture benefits provided by bisphosphonates far outweigh their potential for harm.

It is reasonable for individuals who have taken a bisphosphonate continuously for three to five years to be reassessed by their physician to determine if they need to continue on therapy. For those who remain at high risk of fracture, ongoing therapy is recommended. For those who are at moderate or low risk of fracture with therapy, a drug holiday may be considered, recognizing that the optimal duration of the drug holiday is unclear and that the appropriate drug with which to re-initiate therapy is also uncertain. More research is needed in this area.

In summary

Our readers should take away these 10 key messages about bisphosphonates:

- 1) **Osteoporosis** is a disease of bones that causes bones to become fragile and break easily.
- 2) **Broken bones** reduce quality of life and increase pain and risk of death.
- 3) Clinical research has shown that **bisphosphonates** are very effective at strengthening osteoporotic bones and protecting them from breaking.
- 4) However, prolonged use of bisphosphonate drugs has shown a possible connection with **osteonecrosis of the jaw (ONJ)** and **atypical femur fractures (AFF)**.
- 5) Despite this, ONJ and AFF are **very rare**. They usually occur in individuals who have additional serious illness(es) and/or who take additional medications; but they may even occur in individuals who do not take bisphosphonates.
- 6) In **high fracture risk** individuals, the anti-fracture benefits of bisphosphonates significantly outweigh the risks of serious side effects such as ONJ and AFF.
- 7) Therefore, **high** fracture risk patients should **not** take a drug holiday from bisphosphonates.
- 8) Drug holidays from bisphosphonates should be considered in **low** fracture risk individuals.
- 9) Drug holidays from bisphosphonates **may** be considered in select individuals at **moderate** risk of fracture who no longer need drug therapy for osteoporosis.
- 10) Individuals taking bisphosphonates continuously for three to five years should **discuss** their bone health and their fracture risk with their doctor in order to determine whether or not they need to continue taking their bisphosphonate therapy.

*The incidence rate is the number of new cases per population at risk in a given time period. For example, an incidence rate of 5 per 100,000 person-years means that 5 new cases are expected to develop for 100,000 persons observed over a period of 1 year or 50,000 persons over 2 years or 25,000 persons over 4 years or 10,000 persons over 10 years.

****Adapted from the article published in *Canadian Family Physician, Volume 6, April 2014, written by members of Osteoporosis Canada's Scientific Advisory Council (SAC):* J. P. Brown MD, S. Morin MD MSc, W. Leslie MD, A. Papaioannou MD, A. M. Cheung MD PhD, K. S. Davison PhD, D. Goltzman MD, D. A. Hanley MD, A. Hodsman MD, R. Josse MD, A. Jovaisas MD, A. Jubay MD, S. Kaiser MD, A. Karaplis MD, D. Kendler MD, A. Khan MD, D. Ngui MD, W. Olszynski MD PhD, L-G. Ste-Marie MD, J. Adachi MD**

Memories of Eleanor Mills and the Boney Express – 1993 and 1994

Eleanor is the woman who, at 79 and bent over her walker (to quote her “like an inverted L”), walked in more than 130 communities in Canada during the summers of 1993 and 1994. She walked with companions, also suffering from osteoporosis, to spread the word that osteoporosis could be diagnosed and treated and that an active life was possible after diagnosis.

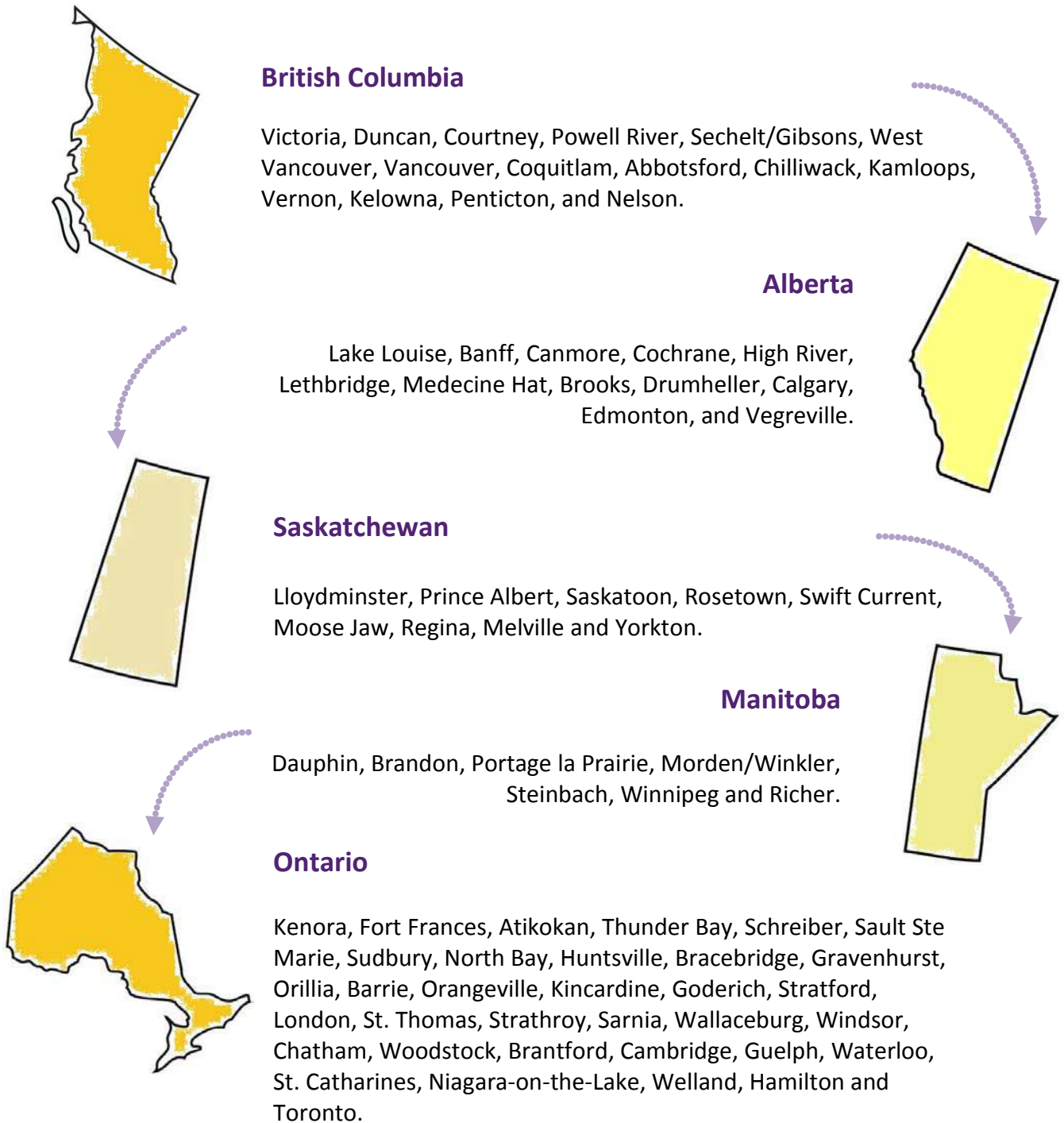
I continue to write the story of Eleanor Mills and The Boney Express. I have lots of basic facts, have talked to many wonderful people, but I hope to hear from more – any of you who remember walking with the group in your community, perhaps meeting Eleanor, Gerda, Mona and Marguerita in the summer of 1993 when they

walked from Victoria to Toronto or Eleanor and Denise Pilon when they walked from Toronto to St. John's the next summer. I would be delighted to talk to a local organizer; I have found so few of them to date.

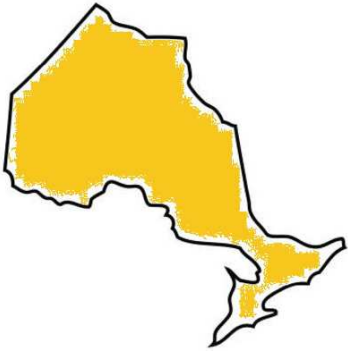
I would love to know where they walked in your community – the main street or a park? Was the day warm and sunny or cold and miserable (there were both); did the team meet with walkers, with the press, set up a panel discussion? Do you have pictures that remind you of the day? Did your local newspaper cover the event?

I know it was 20 years ago but any little bits of your memories will improve my telling of the story.

1993 walks



1994 Walks

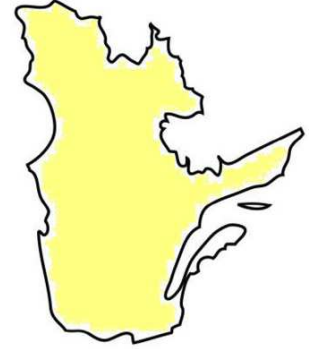


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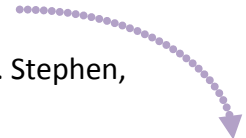


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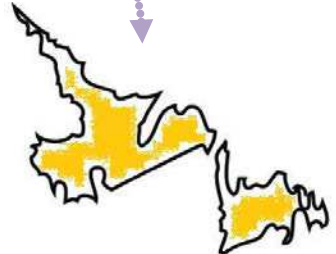
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Upcoming Presentation

Treatments of Osteoporosis: Expected Benefits, Potential Harms and Drug Holidays

FREE EVENT!

What YOU need to know about Osteoporosis

Treatments of Osteoporosis: Expected Benefits, Potential Harms and Drug Holidays

DATE: Friday, October 17, 2014
TIME: 2:00-3:00 pm EDT

PRESENTER:
Dr. Suzanne Morin, MD, MSc, FRCPC

Watch live and archive with Ask a Question feature from your computer!

HOW TO REGISTER?
Click here or call 1-800-463-6842 ext. 2224

For more information on Osteoporosis Canada and the Canadian Osteoporosis Patient Network (COPN) call 1-800-463-6842 or visit our website at www.osteoporosis.ca

Date – Friday, October 17, 2014

- Speaker – Dr. Suzanne Morin, MD, MSc, FRCPC
- Participate in the comfort of your own home!
- [REGISTER NOW](#)
- This presentation is also available in [French \(Friday, October 24, 2014\)](#). For more information click [here](#).

New Chair of the Canadian Osteoporosis Patient Network (COPN)

I am pleased to announce that Cheryl Baldwin is the new Chair of the Canadian Osteoporosis Patient Network. Cheryl brings a wealth of experience to her new role. With almost 30 years of experience as a volunteer or staff person with various non-profits she has a diverse background to draw from when it comes to the strengths and weaknesses of the non-profit sector. Cheryl has served on the OC Board of Directors for eight years in a variety of positions including Chair (2011-2013) and has just completed her term as Past Chair. She has also been involved at a local level with the Manitoba Chapter.

I am also pleased to announce that Cherylle Unryn has assumed the role of Vice-Chair of COPN. Cherylle has been a very active volunteer with OC for over 8 years. Currently, she is the Chair of the Manitoba Chapter and for the past three years she has been a member of COPN's Executive Committee.

We are indeed fortunate to have such talented and dedicated individuals assuming these leadership roles at COPN. Welcome Cheryl and Cherylle!

Although Larry Funnell has stepped down as Chair of COPN he will remain on the COPN Executive Committee where he will continue to contribute to the direction of COPN while focusing his efforts on making men more aware of the consequences of not paying attention to their bone health. Thank you Larry for your invaluable contributions to Osteoporosis Canada and COPN. Your passion, dedication, and vision have lifted COPN to a new level. Countless people are and will continue to live well with this disease because of your passion and tireless efforts to educate, empower, and advocate for all who are affected by osteoporosis.

Famida Jiwa,
President and CEO
Osteoporosis Canada

A Recipe from our Sponsor

Corn Soup - By Stefano Faita

Course: *Soups & Creams*
Preparation Time: *45 mins*
Cooking Time: *30-35 mins*
Yields: *4 to 6 servings*

1 milk product serving(s) per person



For more information about this recipe:

<http://www.dairygoodness.ca/get-enough/recipes/corn-soup>

Ingredients

1 medium onion, diced
1 fennel bulb, diced
1 carrot, diced
6 corn on the cob, shucked, or 5-6 cups (1.25-1.5 l) frozen corn
1/2 cup (125 mL) diced ham
3 sprigs thyme
6 cups (1.5 L) **milk**
Salt and pepper
1 tbsp (15 mL) finely chopped parsley
Dash of olive oil

Preparation

Sauté onion in a skillet and cook for 3 or 4 minutes. Add the other vegetables and cook for 5 to 7 minutes. Add the ham and thyme, then cook for another 2 to 3 minutes.

Lower heat, add milk and allow to simmer gently for around 20 minutes. Thicken soup with a few pulses from a hand blender. Season to taste. Garnish with finely chopped parsley and drizzle with olive oil just before serving.

This issue of COPING is sponsored by Dairy Farmers of Canada

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