

postmenopausal health Overview

University Health Network (UHN) Osteoporosis & Postmenopausal Research Centre | www.uhn.ca/osteoporosis

Clinical trials 101

The MAP.3 study was a *placebo-controlled, randomized, double-blind, phase III* clinical trial to determine if exemestane could prevent breast cancer in postmenopausal women at high risk for the illness.

Placebo-controlled refers to the design of a study where the experimental drug, exemestane in this case, is given to one group of participants while the other group of participants receives a placebo or a blank pill. Results from the two groups are compared.

Randomized refers to the method by which participants are assigned either to the exemestane group or the placebo group. Which group a patient ends up in is determined entirely by chance.

Double-blind means neither the participants nor the researchers know who is receiving placebo and who is receiving exemestane. Double-blind trials provide more objective results since the expectations and biases of the researchers or the participants do not affect the study results.

Phase III is the stage of clinical trials where the study drug or treatment is given to large groups of people (1,000-3,000) to confirm its effectiveness, monitor side effects, compare it to commonly used treatments (or placebo), and collect information that will allow the drug or treatment to be used safely.

Source: clinicaltrials.gov

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Research studies

Interested in health research? We are recruiting for the studies below:

Spine fracture study: You may be eligible to participate in a research study looking at the use of a new bone medication if you:

- had a spine (backbone) fracture in the past
- are female
- are 60 years of age or older
- are **not** presently taking prescription medications for bones
- are **not** presently taking hormone replacement therapy

If you are interested in participating or would like more information, please contact: **Alice Demaras** at **416-340-4800 ex.5505** or alice.demaras@uhn.ca.*

Muscle & bone health study: We are looking for volunteers to participate in a study examining how our muscle changes with age and how this affects our mobility, quality of life, physical function and bone health.

As a study participant you can expect to come to the Toronto General Hospital for 2-2.5 hours and complete questionnaires, perform a few physical function tests, and have some muscle and bone imaging scans done (all procedures are painless). For more information or to volunteer, please contact: **Marta Erlandson** at **416-340-4800 ex.6276** or marta.erlandson@uhnresearch.ca.*

**Please note that the security of e-mail messages is not guaranteed. Please do not use e-mail to discuss information you think is sensitive.*

Enjoying your calcium

Osteoporosis guidelines recommend that all adults over the age of 50 should consume at least 1200mg of calcium daily (diet plus supplements). Try this **Fettuccine with mushroom sauce** recipe for some added calcium punch to your daily eating:

Makes 4 servings | Calcium: 323mg per serving

Ingredients

- 1 tbsp olive oil
- ½ lb mushrooms, sliced
- 1 leek, sliced
- 1 clove garlic, minced
- 1 tbsp all-purpose flour
- 1 can(385ml) 2% evaporated milk
- ½ tsp dried thyme
- ¼ tsp pepper
- 1 pkg (375g) fettuccine
- ¼ cup chopped fresh parsley

Directions

1. In a saucepan, heat oil over medium heat. Add mushrooms,

- leek and garlic; cook for 5 minutes or until mushrooms release liquid.
2. Stir in flour; cook, stirring, for one minute.
3. Gradually add milk, whisking constantly. Add thyme and pepper; continue to cook, whisking, for 5 minutes or until thickened.
4. In a large pot of boiling salted water, cook pasta for 8 to 10 minutes or until al dente. Drain.
5. Toss pasta with mushroom sauce. Garnish with parsley.

from *Bone Vivant!* by Jan Main in co-operation with The Osteoporosis Society of Canada ©1997

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Osteoporosis guidelines updated in Canada

New guidelines reframe the narrative on osteoporosis by highlighting the role of bone health in fragility fractures.

Facts on fractures

The numbers are startling – 1 in 4 women and 1 in 8 men in Canada suffer from osteoporosis, a disease of bone loss and compromised bone strength, resulting in weaker bones that are more amenable to breaking. **When osteoporosis-related fractures occur, they are mostly fragility fractures**, so-called because even a slight minimal trauma, such as falling from standing height, is sufficient to cause a break in the affected bone(s). With 2 million Canadians living with osteoporosis, it is no surprise that the prevalence of these fractures is also quite high – in people over the age of 60, at least 80% of fractures are linked to osteoporosis.

What new research tell us

A diagnosis of osteoporosis is generally based on test results from a bone mineral density (BMD) scan. Up until a few years ago, it was thought that low bone density causes fractures and as such, results from a bone density scan were relied upon primarily to assess fracture risk. But more recent osteoporosis research has revealed that bone density is only one aspect of bone strength and there are many other

factors that contribute to overall fracture risk. Dr. Angela Cheung, Director of UHN's Osteoporosis Program, explains this phenomenon with an apt analogy: "If you think about it from an engineering point of view, a solid structure depends on many different properties, not just strong building material." In other words, it is quite possible that an individual with relatively normal BMD test results can still suffer from a fragility fracture, and in fact, physicians and osteoporosis specialists see many such cases on a regular basis.

New advances in the study of osteoporosis have led researchers to identify **factors other than BMD which can modify an individual's risk of fracture**. These include age, sex, family history of fractures, lifestyle factors such as lack of exercise and smoking, and use of certain medications that negatively affect bone health.

The new 2010 guidelines

These recent additions to our knowledge of osteoporosis and how fractures occur have led to the development of new osteoporosis guidelines for physicians and health care providers in Canada. The *2010 clinical practice guidelines for the diagnosis and management of osteoporosis in*

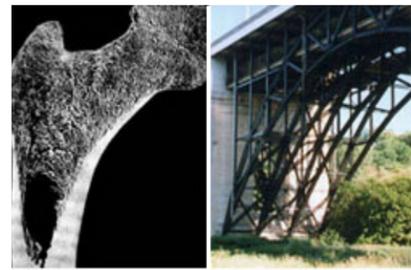


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Canada were prepared by the Scientific Advisory Council of Osteoporosis Canada, with Dr. Cheung as one of the co-authors, and published in the Canadian Medical Association Journal last fall. These new guidelines are targeted towards men and women over the age of 50 and recommend that physicians who see patients in this population group routinely assess them for osteoporosis and fracture risk.

Focus on fractures

The 2010 osteoporosis guidelines emphasize the use of fracture risk assessment tools in order to translate the new holistic understanding of bone strength into clinical practice. The fight against fractures is now at the forefront of osteoporosis prevention, treatment, and management.



Apart from strong building materials, many factors affect how strong a bridge is and if it will collapse. Similarly, when bones break, several factors other than bone density may be the culprit.

For individuals who are at moderate to high risk for fracture, lifestyle changes are emphasized in order to protect bones from breaking. These include weight-bearing aerobic exercises, exercises that focus on balance for those at risk of falls, as well as adequate intake of calcium and vitamin D. For patients at high risk of fracture, and for some patients at moderate risk as well, medication may be necessary for fracture prevention.

Some specific changes from the old guidelines include:

- **Focus on predicting fracture risk** with either the Canadian version of the Fracture Risk Assessment tool (FRAX), developed by the World Health Organization (WHO), or the updated tool of the Canadian Association of Radiologists and Osteoporosis Canada (CAROC).
- **Increase in daily vitamin D intake:** 400 – 1000 IU for adults less than 50 years of age and 800 – 2000 IU for adults more than 50 years of age.
- **Decrease in daily calcium intake** (diet plus supplements) for adults over 50 years of age: 1200 mg.
- **Updates on osteoporosis therapies** based on more recent research and evidence.

Clinical practice guidelines

Clinical practice guidelines (CPGs; guidelines for short) are documents that support clinicians in making decisions about patient care. They are meant to provide physicians and health care workers with an overview of the most current and updated methods of diagnosis, management, and treatment of specific diseases and conditions.

CPGs are usually prepared by national advocacy organizations (such as Osteoporosis Canada for osteoporosis guidelines), and also by government bodies as well as other health care and medical organizations. The development of a CPG usually involves an extensive review and evaluation of current research on prevention, diagnostic tools, as well as risks and benefits of therapies. The authors of the guidelines will then develop recommendations based on the best available evidence.

CPGs are useful not only because they describe the most appropriate care for patients, but also because they help to improve the quality and standard of care. In addition, CPGs highlight areas of care where evidence is lacking and future research is needed.

Osteoporosis exercise guide



Exercise is an essential component of any osteoporosis prevention or treatment program. Developed by UHN's Osteoporosis Program, the *Osteoporosis Exercise Guide* is a unique exercise book designed for all adults who are interested in taking charge of their bone health. For more details, visit www.uhn.ca/osteoporosis.

Exemestane – a new answer for breast cancer prevention

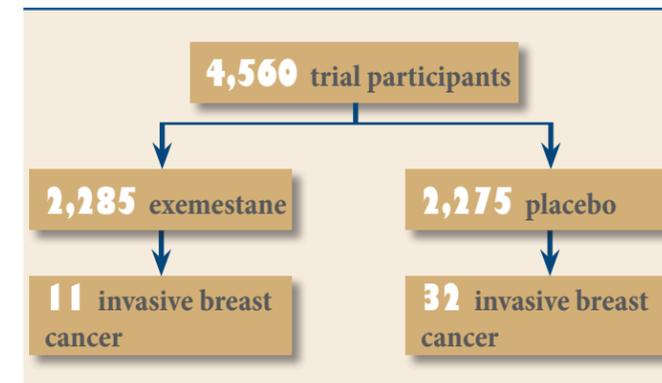
Women who are at high risk for breast cancer now have a new reason for optimism. Results from a recent clinical trial have shown that the drug exemestane can reduce breast cancer risk by more than 50%.

What does estrogen have to do with it?

Breast cancer is the most common form of cancer that affects Canadian women. It is unclear what specifically causes the disease, but we do know that **the hormone estrogen plays a major role in the development of some types of breast cancer.** One way to think about breast cancer prevention is in terms of estrogen production – if the amount of estrogen can be reduced in women who are at high risk, we may be able to stop the cancer from developing in the first place.

Exemestane on trial

Exemestane is a drug that prevents estrogen production. Since exemestane has not been used previously as a cancer prevention drug, **a clinical trial was designed to test if exemestane could prevent breast cancer in postmenopausal women** who are at a greater risk of suffering from the illness. The international study, entitled the Mammary Prevention (MAP).3 trial, began in 2004 and was led by the National Cancer Institute of Canada Clinical Trials Group (see Clinical trials 101 on page 4 for more details about the study). In all, 4,560 women from across Canada, US, Spain, and France participated in the MAP.3 trial. The UHN site was the largest participating Canadian site and the second largest site worldwide.



Participants entering the MAP.3 trial were randomly given either exemestane or placebo, a blank pill with no medicinal components, for 5 years. Results from the study showed that breast cancer occurred significantly less in the group of women taking exemestane compared

to the group taking placebo. Overall, women who were given exemestane had a **65% lower risk of developing invasive breast cancer** compared to women in the placebo group. Data from the study also confirmed that exemestane is a safe drug and does not generally cause serious side effects. (Exemestane is not currently approved for primary prevention of breast cancer.)

What about bone health?

Since low estrogen levels can increase the risk of osteoporosis and fractures, drugs like exemestane have the potential to negatively affect bone health. In order to examine whether exemestane impacts bone density and structure, our group has been running a substudy called the **MAP.3 Bone Strength Study (MAP.3BSS)**. 351 women from the main MAP.3 study participated in this substudy. Results show that taking exemestane for two years worsens age-related bone loss in postmenopausal women, despite calcium and vitamin D supplements. Key findings are included in the table below.

Change in BMD from baseline to 2 years		
BMD site	Exemestane	Placebo
Distal radius (wrist)	- 6.1%	- 1.8%
Distal tibia (ankle)	- 5.0%	- 1.3%
Lumbar (lower) spine	- 2.4%	- 0.5%
Hip	- 1.8%	- 0.6%
Change in thickness		
Cortical bone (outer shell)	- 7.9%	- 1.1%

There were also no differences in the number of fractures between the two groups and no participants in the study developed osteoporosis over the two years. In light of these results, Dr. Lianne Tile, one of the study authors at UHN advises: “For women taking [exemestane], it is a good idea to have regular bone monitoring, and adequate calcium and vitamin D.”

Our research group is continuing the MAP.3BSS study in order to see the long term effects of exemestane on bone (2-5 years, and then up to 2 years post therapy).