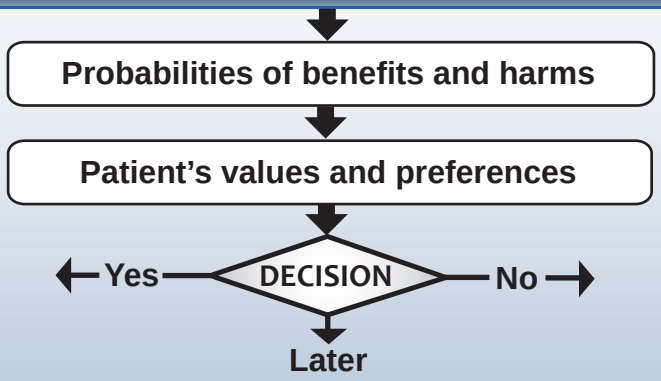
Bisphosphonates to prevent osteoporotic fractures in postmenopausal women



This document prepares the clinician to discuss scientific data with the patient so they can make an informed decision together.

Presenting bisphosphonates to patients

What are bisphosphonates for?

- **Bisphosphonates (alendronate, risedronate and etidronate)** are taken daily, weekly or monthly **to reduce the risk of osteoporotic fractures** occurring most commonly in the spine, hip and wrist. This medication slows down the cells that remove old bone tissue.

Among postmenopausal women, who might consider using bisphosphonates?

- Women diagnosed with l**ow bone mineral density** or **with a recent fracture** in the bones of their spine.
- Women **over the age of 50 at moderate to high risk** of having an osteoporotic fracture in the next 10 years. Risk level is evaluated using a risk calculator such as the FRAX*, or the CAROC**.

- **high risk:** more than 20% probability
- **moderate risk**: 10-20% probability
- **low risk:** less than 10% probability

Why do patient preferences matter when making this decision?

- **There are pros and cons to taking this medication:**

PROS: **5 to 6%** of women taking bisphosphonates for 1 to 4 years will be **protected from vertebral fractures** and as many as **2% will be protected from non-vertebral fractures**.[1-3]

CONS: This medication can cause **reversible side effects**.

- **There is a lack of evidence:**
  1- on the **long-term effects** of bisphosphonates
  2- lower quality evidence suggests an association between oral bisphosphonate use and **atypical fractures**[4, 5] and **osteonecrosis of the jaw.** [6]

- Osteoporotic fractures can also be **prevented** by taking calcium and vitamin D, smoking cessation, decreasing alcohol consumption, regular exercise, and/or by taking other medications (hormonal therapy, denosumab, teriparatide).

- **Both taking the medication and not taking the medication are acceptable options**, so we propose that**:**
  1. The decision takes into account the **patient's values and preferences**
  2. The clinician **shares this decision** with the patient

*__FRAX:__ http://www.sheffield.ac.uk/FRAX/tool.jsp?country=19 **__CAROC__: http://www.osteoporosis.ca/multimedia/pdf/CAROC.pdf

Questions to identify the patient's decision making needs:

- Do you have any question on the benefits and harms of each option?
- Which benefits and harms matter most to you?
- Do you feel sure about the best choice for you?
- Who will support and advise you in making a choice?

© Université Laval, 2012 all rights reserved

See page 2 for the current state of knowledge

State of knowledge - November 2011

Selection of the best available studies

Benefits of medication

❶ Prevents fractures

Proportion of women who will experience a fracture
(among women diagnosed with low bone mineral density or with a recent fracture in the bones of their spine)

Risedronate[3]

	Vertebral*	Non-vertebral†
Not treated	14%	10%
Treated for 2-3 years	9%	8%
Number protected by risedronate	**5%**	**2%**

Alendronate[2]

	Vertebral*	Non-vertebral†
Not treated	12%	9%
Treated for 1-4 years	6%	7%
Number protected by alendronate	**6%**	**2%**

Etidronate[1]

	Vertebral*	Non-vertebral†
Not treated	11%	13%
Treated for 2-4 years	6%	14%
Number protected by etidronate	**5%**	**-1% (not significant)**

Harms of medication

❶ Gastrointestinal (GI) side effects

GI side effects (reflux, oesophagitis and oesophageal ulcers) are the most common concern.

- Weekly and monthly preparations of bisphosphonates address these side effects.[8]
- No GI side effects were found in women treated with bisphosphonates compared to untreated women.[1-3]

❷ Intolerable side effects

No intolerable side effects were found in women treated with bisphosphonate compared to untreated women.[1-3]

❸ Serious adverse events

There is a relationship between treatment with bisphosphonates and

- osteonecrosis of the jaw.[6]
- subtrochanteric and femoral shaft fractures in women treated for more than 5 years.[4 5]

* Numbers for vertebral fractures are based on x-ray evidence: 70 to 80% of women with an x-ray diagnosis of fracture are unaware they have a fracture.[7]

† Studies varied in their definition of non-vertebral fracture. Some studies included all non-vertebral fractures and other studies included only those fractures of the hip, clavicle, humerus, wrist, pelvis or leg.

How much confidence can we have in these results?

	Vertebral fracture	Non-Vertebral fracture	Intolerable side effects	Osteonecrosis	Atypical fractures
Alendronate	Moderate	Moderate	Low	Very low	Very low
Residronate	Low	Very low	Moderate	Very low	Very low
Etidronate	Low	Low	Low	N/A	Very low

Study descriptions and references:

1. **Wells et al.** Cochrane Database Syst Rev. 2008, CD003376 (etidronate). **Design:** Systematic review of 11 randomized controlled trials. **Participants:** 1,248 postmenopausal women.
2. **Wells et al.** Cochrane Database Syst Rev. 2008, CD001155 (alendronate). **Design:** Systematic review of 11 randomized controlled trials. **Participants:** 12,068 postmenopausal women
3. **Wells et al.** Cochrane Database Syst Rev. 2008, CD004523 (residronate). **Design:** Systematic review of 7 randomized controlled trials. **Participants:** 14,049 postmenopausal women
4. **Lenart et al.** Osteoporos Int. 2009, 20, 353–1362. **Study Design:** retrospective case–control study. Participants: postmenopausal women presenting with low-energy femoral fractures. **Cases:** subtrochanteric and femoral shaft fracture cases matched by age, race, and body mass index to one intertrochanteric and femoral neck fracture.
5. **Park-Wyllie et al.** JAMA 2011, 305(8), 783-89. **Study Design:** population-based, nested case-control study. **Participants:** women aged 68 years or older from Ontario who initiated therapy with an oral bisphosphonate between 2002 and 2008. **Cases:** women hospitalized with subtrochanteric or femoral shaft fractures matched to up to 5 controls with no such fracture.
6. **Woo et al.** Ann Intern Med. 2006, 144, 753-61. **Study Design:** Systematic review of case reports and case series of women and men with bisphosphonate-associated osteonecrosis of the jaws.
7. **Vogt et al.** Mayo Clin Proc. 2000, 75, 888-96.
8. **Lopez J.** Drug and Therapeutics Bulletin of Navarre. Spain 2009, 17(5), 65-84.

© Université Laval, 2012 all rights reserved