Osteoporosis: Secondary Fracture Prevention Programme in Hospital Authority

Dr. KH Mak
Depart. Of Orthopaedics and Traumatolgy
Kwong Wah Hospital

Conclusion from our own study : FU of 2 years

Mobility after Hip fracture:

Walking Ability:

Only 50% of geriatric hip fractures can recover their walking ability, most of them however needed some form of walking aid.
Another 15% wheelchair dependent.

Institutional Care:

1/3 of the patients who used to stay with their family required long term institutional care.

Mortality in Hip Fractures:

First month: 17/673 (2.5%)
For those who have surgical fixation:
First 6 month : 47/613 (7.7%)
First 12 Months: 84/374 (22.5%)

Primay Osteoporosis Prevention

- Lifestyle modification:
  - Exercise: regular weight bearing, fall prevention
  - Sunshine
  - Smoking/ alcohol
- Dietary supplement: Calcium & Vit D
- Pharmacological treatment

Calcium

1000 gm /day

Vitamin D

- Critical in promoting absorption of Calcium
- Def. in vit D: ↑ risk of fall in the elderly:
  - 72% reduction with 800 iu when given with Calcium
  - Severe Vit. D is associated with persistent, non-specific musculoskeletal pain
  - Vit. D receptors in cells of brain, heart gut , skin pancreas & immune system.
- Getting Old:
  - Loss of lipid content in the elderly , results in 75% ↓ of Vit. D synthesis in skin
- Prevalence of Vit. D deficiency is greater in individuals in nursing homes than those living in community.

Fall Prevention & Hip Protector

Identify the High Risk

- Body build: short and thin, under weight
- Familial
- Hobbies
- Diseases: thyrotoxicosis, rheumatoid
- Medications
- Previous fracture

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Frax

WHO fracture risk assessment tool :
John A. Kanis (2009)

The probabilities of hip fracture in women :

The tables give the 10-year probability (%) of hip fracture according :

- body mass index (BMI kg/m2),
- the number of clinical risk factors (CRF)
- and age.

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Clinical Risk Factors (I)

Age	The model accepts ages between 40 and 90 years. If ages below or above are entered, the programme will compute probabilities at 40 and 90 year, respectively.
Sex	Male or female. Enter as appropriate.
Weight	This should be entered in kg.
Height	This should be entered in cm.
Previous fracture	A previous fracture denotes more accurately a previous fracture in adult life occurring spontaneously, or a fracture arising from trauma which, in a healthy individual, would not have resulted in a fracture. Enter yes or no (see also notes on risk factors).
Parent fractured hip	This enquires for a history of hip fracture in the patient's mother or father. Enter yes or no.
Current smoking	Enter yes or no depending on whether the patient currently smokes tobacco (see also notes on risk factors).
Glucocorticoids	Enter yes if the patient is exposed to oral glucocorticoids or has been exposed to oral glucocorticoids for more than 3 months at a dose of prednisolone of 5mg daily or more (or equivalent dose of other glucocorticoids) (see also notes on risk factors).

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Clinical Risk Factors (II)

Rheumatoid arthritis	Enter yes where the patient has a confirmed diagnosis of rheumatoid arthritis. Otherwise enter no (see also notes on risk factors).
Secondary osteoporosis	Enter yes if the patient has a disorder strongly associated with osteoporosis. These include type I (insulin dependent) diabetes, osteogenesis imperfecta in adults, untreated long-standing hyperthyroidism, hypogonadism or premature menopause (<45 years), chronic malnutrition, or malabsorption and chronic liver disease.
Alcohol 3 or more units/day	Enter yes if the patient takes 3 or more units of alcohol daily. A unit of alcohol varies slightly in different countries from 8-10g of alcohol. This is equivalent to a standard glass of beer (285ml), a single measure of spirits (30ml), a medium-sized glass of wine (120ml), or 1 measure of an aperitif (60ml) (see also notes on risk factors).
Bone mineral density (BMD)	(BMD) Please select the make of DXA scanning equipment used and then enter the actual femoral neck BMD (in g/cm^2). In patients without a BMD test, the field should be left blank (see also notes on risk factors) (provided by Oregon Osteoporosis Center).

Bone mineral density (BMD)
The site and reference technology is DXA at the femoral neck. T-scores are based on the NHANES reference values for women aged 20-29 years. The same absolute values are used in men. Although the model is constructed for BMD at the femoral neck, the total hip site is thought to predict fracture equ[illegible]ently in women.

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Anti-resorptive Agents

- Calcitonin
- Hormone replacement therapy:
- Selective Estrogen Receptor Modulators
- Bisphosphonates:
  - Alendronate
  - Risedronate
  - Ibandronate
  - Zoledronic acid

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Oestrogen

- Oestrogen: ↓ hip, clinical vertebral and total osteoporotic fractures: 30-39%
- Oestrogen + progestin:
  - ↓ hip and clinical vertebral fractures by 34%
    ↓ total osteoporotic fractures by 24%
- Risks: ↑ stroke & DVT; breast cancer, dementia and gall bladder disease

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Selective Estrogen Receptor Modulators

- Raloxifene:
  - ↑ bone mineral density in lumbar spine and femoral neck by 2-3 % &
  - ↓ level of bone turnover markers by 30 -40 %
  - ↓ risk of vertebral fracture
  - 62% ↓ of breast cancer
  - Risks: ↑ venous thromboembolic events & ↑ risk of fatal stroke

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Anabolic agents

Parathyroid hormone: teriparatid

- Enhancement of bone turnover, ↑ in trabecular number & thickness
- Daily subcutaneous teriparatide most effective for restoring bone quality
- ↑ bone mass up to 13% over 2 years of therapy
- Risk of vertebral fracture and non-vertebral fracture ↓ by 65% & 53% respectively

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Bisphosphonates: Alendronate

- The mean effect on hip BMD in the placebo group vs the alendronate group was :
  - Placebo: ↓ 0.004 g/cm2 per year (P < .001) vs
  - Alendronate: ↑ 0.0085 g/cm2 per year (P < .001)
- Alendronate treatment for 3 years
  - led to increased hip BMD by 0.030 g/cm2
  - 0.13 g/cm2 plus 0.0085 g/cm2 per year for 2 more years.
- Alendronate treatment results in at least a 0.019-g/cm2 increase in hip bone density in 97.5% of patients

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Alendronate

- ↓ fracture risk by 50%
- 3 yrs treatment :Women with low bone mass and a history of vertebral # : 47% vertebral #.
- Risk of hip fracture ↓ by 45%.
- Efficacious in men for osteoporosis.

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Combination Therapy

- Synergistic effect of teriparatide & bisphosphonate not seen
- Bisphosponate may blunt (↓)the bone building effect of teriparatide
- Raloxifene bone forming (↑)effect of teriparatide

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Sequential therapy

- Bisphosphonate then PTH:
  - ↓ initial response to PTH
  - Drug holiday before PTH
- PTH then followed by a bisphosphonate:
  - Soon after discontinuation of teriparatide, gains in bone mineral density begin to regress rapidly, as early as eighteen months after the last dose of teriparatide
  - Subsequent treatment with bisphosphonates facilitates mineralisation of the osteoid laid down during the previous period of increased metabolic activities

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NICE : Sheffield:Primary prevention of osteoporotic fragility fractures

- Alendronate is recommended as a treatment option for the Women aged >70 years
  - who have an independent clinical risk factor (CRF) for fracture or
  - an indicator of low BMD and who are confirmed to have osteoporosis (that is, a T-score of – 2.5 SD or below).
- In women aged > 75 years
  - who have two or more independent clinical risk factors (CRF) for fracture or indicators of low BMD
- a DEXA scan may not be required if the responsible clinician considers it to be clinically inappropriate or unfeasible.

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NICE : Sheffield:Primary prevention of osteoporotic fragility fractures

Women aged 65–69 years
who have an independent CRF risk factor for fracture and
who are confirmed to have osteoporosis (that is, a T-score of – 2.5 SD or below).

Postmenopausal women <65 years
who have an independent CRF for fracture and
at least one additional indicator of low BMD (see section 6) and
who are confirmed to have osteoporosis (that is, a T-score of – 2.5 SD or below).

When the decision has been made to initiate treatment with Alendronate:
the preparation prescribed should be chosen on the basis of the lowest acquisition cost available.

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NICE : sheffield:primary prevention of osteoporotic fragility fractures

If a woman aged >75 years
who has two or more independent CRF for fracture or indicators of low BMD has not previously had her BMD measured,

a DXA scan may not be required if the responsible clinician considers it to be clinically inappropriate or unfeasible.

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NICE : Sheffield:primary prevention of osteoporotic fragility fractures

Risedronate (actonel) & etidronate (didronel) :

as alternative treatment options for the primary prevention of osteoporotic fragility fractures in postmenopausal women:

who are unable to comply with the special instructions for the administration of **alendronate**, or have a contraindication to or are intolerant of **alendronate.**

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Canadian Agency for drugs & technology: health technology assessment (HTA) database

Bisphosphonates for 1^0 & 2^0 prevention of osteoporotic fractures:a meta-analysis:publications@cadth.ca

Alendronate: benefit in 2^0 prevention in vertebral, nonvertebral, hip & wrist fractures, no statistical sig. in 1^0 prevention, except in vertebral fractures

Risedronate: benefit in 2^0 prevention in vertebral, nonvertebral & hip , not in wrist fractures

Etidronate: no statistical sig. Benefit in 1^0 & 2^0 prevention

Conclusions: main benefit of the three bisphosphonates in Canada is for secondary prevention.

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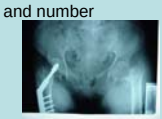
NICE : Sheffield Secondary prevention of osteoporotic fragility fractures

Strontium ranelate and raloxifene:

are recommended as alternative treatment options for the secondary prevention of osteoporotic fragility fractures in postmenopausal women:

who are unable to comply with the special instructions for the administration of **alendronate** and either **risedronate or etidronate**,
or have a contraindication to or are intolerant of **alendronate** and either **risedronate or etidronate** and

who also have a combination of T-score, age and number of independent CRF for fracture .



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Check list (I) before prescription of anti-osteoporotic drugs:

Any CRF that can be reversed, e.g. stop smoking, stop steroid if possible, treatable medical conditions.

Routine oral examination

Dental examination for patients with a history of

concomitant risk factors for osteonecrosis of jaw: cancer, chemotherapy, poor oral hygiene, and on corticosteroids etc.

(Pregnancy)

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Check list (II) before prescription of anti-osteoporotic drugs:

- Adequate Calcium and vitamin D intake: for postmenopausal women : Ca : 1200 mg and Vit. D: 400 to 800 IU per day.
- hypocalcaemia
- severe renal impairment
- recent history of a major GI ulceration or oesophagitis
- Body mass index: high risk if < 19.
- Patient with a reasonable quality of life.

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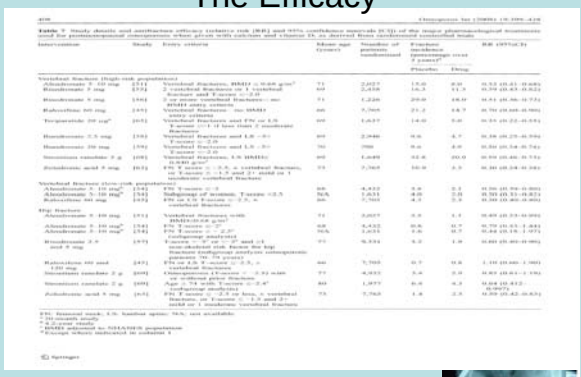
The Efficacy



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Efficacy in seconday fracture prevention

Table 6 Antifracture efficacy of the most frequently used treatments for postmenopausal osteoporosis when given with calcium and vitamin D, as derived from randomised controlled trials. (Updated from [42, 43])

	Effect on vertebral fracture risk		Effect on non-vertebral fracture risk	
	Osteoporosis	Established osteoporosis[a]	Osteoporosis	Established osteoporosis[a]
Alendronate	+	+	NA	+ (including hip)
Risedronate	+	+	NA	+ (including hip)
Ibandronate	NA	+	NA	+[b]
Zoledronic acid	+	+	NA	NA (+)[c]
HRT	+	+	+	+
Raloxifene	+	+	NA	NA
Teriparatide and PTH	NA	+	NA	+
Strontium ranelate	+	+	+(including hip)	+ (including hip)

NA: no evidence available
+: effective drug
[a] Women with a prior vertebral fracture
[b] In subsets of patients only (post-hoc analysis)
[c] Mixed group of patients with or without prevalent vertebral fractures

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HA : To prevent the second osteoporotic fracture

- Initiated with the Orthopaedic Fraternity
- Pick up high risk group and treat
- Application to include anti-osteoporosis drugs in the HA formulary
- To prevent the second fracture, especially the hip fracture

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Special drugs for Osteoporosis

Alendronate :

1. First line for secondary prevention of osteoporotic fracture in patients with reasonable Quality of Life
2. Patient with steroid induced osteoporotic fracture (NOT JUST OSTEOPOROSIS)

[Endo / Med / O&G/ O&T / Paed specialists]

Second line for patients who are GI intolerant or contraindicated to first line treatment

- **Ibandronic acid** (Bonviva)
- **Strontium ranelate** (Protos)
- **Zoledronic acid** (Aclasta)

[Endo / Med / O&G/ O&T / Paed specialists]

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SFI osteoporosis

- **Alendronate + cholecalciferol** (Fosamax Plus)
- **Risedronate** (Actonel)
- **Teriparatide** (Forteo)

[Endo / Med / O&G/ O&T / Paed specialists]

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Ibandronate

To compare Monthly Ibandronate/weekly alendronate or risedronate

- 3 months treatment
- 12 months observation:
  - Fracture rate: < 2% in of 7345 monthly ibandronate vs 56837 weekly Bisp.
  - (hip:1.06; non vertebral:0,88; any clinical #:0.82
  - Ibandronate give sig. lower risk of vertebral #.

Conclusions: They had similar low risks of hip#, non-vertebral #, & any clinical #

- ST Harris, et al. Risk of fracture with monthyly oral ibandronate or weekly bisphosphonates.Bone 2009: 758-765

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Other anti-resorptive agent

- Denosumab :
  - A human monoclonal antibody against receptor activator of nuclear factor κ B ligand (RANKL)– a key mediator in osteoclast activation
- Cathepsin K inhibitors :
  - Inhibit cathepsin K, a powerful osteoclast protease
- Strontium:
  - only drug with dual mechanism of action: anti-resorptive and anabolic agent.
  - Shown to have decrease # risk and increase bone density

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NICE : sheffield:primary prevention of osteoporotic fragility fractures

Strontium ranelate

is recommended as an alternative treatment option for the primary prevention of osteoporotic fragility fractures in postmenopausal women:

who are unable to comply with the special instructions for the administration of :

alendronate and either risedronate or etidronate,or

have a contraindication to or are intolerant of **alendronate** and either **risedronate or etidronate**

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Prescriptions and follow up

- Start the anti-osteoporosis therapy after fixation of fracture and before discharge:
- First course of treatment suggested to be 3 to 6 months, and then every 6 or 12 months:
- Follow up of any drug intolerance, back pain, mobility and of course, any new fracture
  - adynamic femoral shaft fracture.
  - avascular necrosis of jaw:
    - exposed bone in the maxillofacial region that failed to heal within 8 wks.
    - High IV doses of zoledronic or pamidronate in patients with multiple myeloma or metastatic carcinoma (1: 10 or 1:100)
    - Oral : Incidence =1:10,000 to 1:100,000 patient treatment years

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Use of bisphosphonates in Fracture

- Bisphosphonate
  - does not impair and
  - may actually enhance fracture healing.
- Primary callus in the first 2 weeks
- Initiate or continuation after formation of primary callus, or initial fracture repair has passed

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Zoledronic acid

- Once a year
- IV infusion of 5 gm
- 70% ↓ of new spinal #
- 41% ↓ of hip #
- Horizon Recurrent Fracture Trial: New Engl J Med. 2007:
  - Zoledronate given within 90 days after a hip # repair,
  - Risk of any #: ↓ by 35% &
  - Mortality from any cause: ↓ by 28%.
  - No osteonecrosis of jaw.

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Use of teriparatide in fracture

- Acceleration of fracture healing
- Stimulation of proliferation & differentiation of chondrocytes & osteo-progenitor cells
- ↑ healing and
- ↓ of non-union for high risk fractures.

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Bisphosphonates & arthroplasty

- Aseptic loosening & Osteolysis caused by wear-debris-mediated stimulation of osteoclasts
- Improve life of prostheses:
  - by inhibiting osteoclasts and
  - ↑ endosteal bone formation.

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Assessment of response

- Fracture : a key efficacy end point
- Bone density: limited value in assessing response
- Markers for bone turnover:
  - Bone specific alkaline phosphatase
  - Osteocalcin
  - Markers of bone resorption:
    - urine N-telopeptide of collagen cross links (NTX) &
    - serum C-telopeptide of collagen cross links

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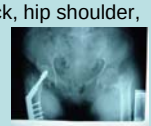
Our Mission:

Osteoporotic Clinic to be part of the service of Orthopaedics and Traumatology, under the Orthopaedic-Rehabilitation Subspecialty, apart from taking care of Orthopaedic Rehabilitation as it is, will also provide:

1. Clinical Assessment of Risk of Osteoporosis
2. Follow up of response
3. DEXA / QCT/ Ultrasound follow up when clinically indicated.
4. Medication for primary and secondary prevention.
5. Rehabilitation in osteoporotic fractures: back, hip shoulder, and elbows.



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Equilibrium in long term

- The drug budget and financial implication will probably plateau off in about 5 years.
  In 5 years, the drug budget on secondary fracture prevention will be about HK$18,000,000 to 20,000,000
- Can be saved by $18,000,000/ $3500 = 5000 bed-days.

Can be paid off by just
↓ in 100 to 120 hip fractures, (average lengthen of stay 30-40 days/ hip),not to mention the
↓ of other osteoporotic fractures and their associated morbidities and mortalities

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Osteoporosis/ Fragility Fracture Clinic

- Expect accumulation of patients over 1 to 2 years will need to run a clinic that
  - provision of additional professional and drug resources for the Orthopaedic service in HA.
  - Download to the Family Physician after stabilisation, like follow up treatment for DM and hypertension.

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