Evidence suggests that poor therapeutic adherence to osteoporosis treatments is a major issue which inevitably increases the risk of fracture and shifts the burden of disease towards the patient and society. Bone is a living tissue that renews and changes through remodelling: bone resorption (breakdown or removal) by special osteoclast cells is followed by osteoblast bone formation. High bone turnover, when the rate of bone resorption exceeds the rate of bone formation, can cause a progressive deterioration in bone structure, skeletal fragility, and eventually osteoporosis.

Most osteoporosis drug treatments, with the exception of parathyroid hormone treatment, reduce the rate of bone resorption, thereby slowing loss of bone mass. In the United Kingdom, the indication for osteoporosis treatment is high fracture risk, determined by bone mass measurement and assessment of the major risk factors that act as predictors for osteoporosis and fractures. Technology appraisals and guidelines have been produced for use of such treatments.

**Drug regimens**

A number of drug therapies to reduce fracture risk are available; research data shows that this reduction is most pronounced for spinal compression fracture, although treatment with alendronate (Fosamax), risedronate (Actonel), zoledronate (Aclasta), strontium ranelate (Protelos) and denosumab (Prolia) also protects against hip fracture. Current drug treatment options include:

- oral and intravenous (IV) bisphosphonates
- selective oestrogen receptor modulators (SERMs)
- human parathyroid hormone (PTH) preparations
- strontium ranelate
- denosumab - an inhibitor of RANKL (Receptor Activator of Nuclear Factor B Ligand)

**Bisphosphonates**

World-wide, the (amino-) bisphosphonate group of drugs, such as alendronate, risedronate, ibandronate, and zoledronate, remains the most widely prescribed for post-menopausal osteoporosis. These inhibit bone resorption by osteoclasts and reduce fracture risk. Dosage varies depending on their strength and formulation; oral bisphosphonates are administered as a weekly or monthly tablet, intravenous preparations either 3 monthly or annually. However, to be effective they must be taken consistently and correctly.

**Adverse effects**

Severe adverse effects are rare and the benefits of taking bisphosphonates for the majority of osteoporotic patients far outweigh any risks. The most common adverse effect is gastro-intestinal irritation, which can be exacerbated if medication is taken incorrectly (not taking with sufficient water, not in the upright position). More recently, bisphosphonate treatments have been associated with osteonecrosis of the jaw (ONJ); the true incidence is unknown, but is estimated as between 1 in 10,000 to 1 in 100,000 patients per year. For those cancer patients taking higher dose, more frequent intravenous bisphosphonates, incidence rises to 1 in 10 to 1 in 100 patients per year. Despite the low incidence, this adverse effect causes concern to many individuals who gain information through the media. As an example, in Australia some months after a television show highlighting the adverse effect of ONJ, prescription rates for bisphosphonates reduced by 29,000. This represented 70 hip fractures, 60 other fractures and 14 deaths that might have been prevented.

Clinical trial extensions of up to ten years with oral alendronate and 7 years with oral risedronate have shown that efficacy is maintained during long-term treatment. However, concerns have been raised about the potential risk of over-suppression of the bone turnover with long-term use; post-licensing reports of

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- Concordance

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‘unusual’ or ‘atypical’ femoral fractures which occurred after little or no force have emerged. The incidence rate appears very low23 and there may be a link between the duration of treatment and a higher risk, although it seems some people are more at risk20–23.

Research has also shown a continued effect on fracture prevention even when treatment has been discontinued27, suggesting a potential break in treatment for those who have remained stable on their medication. Current UK Medicines Health Care products Regulatory Agency (MHRA) guidance suggests clinicians review treatment after 5 years with a view to discussing the risks and benefits of staying on the treatment21. A treatment break of two to three years for alendronate and zoledronate with a shorter break for risedronate or ibandronate may be considered, but there is no consensus on the ideal time to discontinue therapy; guidance on their discontinuation needs to be drug and patient response specific29. Recommendations about monitoring after discontinuation and reinitiating anti-fracture treatments await further consensus. If a patient remains at high risk of fracture, particularly after recent or multiple fractures, treatment continuation, either with the same bisphosphonate or another osteoporosis treatment would be important.

Concordance

It isn’t surprising that with the continuing uncertainty about these treatments, adherence to osteoporosis medications, especially oral bisphosphonates, is not as good as it could be24–26. Within 12 months of starting drug therapy, approximately 75 per cent of women no longer take it as prescribed and almost 50 per cent have discontinued it completely27. This can have serious consequences; low adherence increases risk of fracture by 17 per cent and risk of hospitalisation by 37 per cent27. Common reasons for non-adherence include27:

- adverse effects, either real or perceived28
- complicated dosing regimens
- lack of knowledge surrounding osteoporosis and the importance of fracture prevention

Concordance may be difficult for patients with dementia with no resident carer, or those with diabetes who may find the strict administration instructions for oral treatments contrary to their usual regimen. Changes in bisphosphonate drug formulation from branded to the generic forms can also affect adherence29. Without treatment, a person with osteoporosis is likely to have a significantly higher rate of fractures (compared to adherent patients) and an associated reduced quality of life23–24. Fractures increase the risk of hospitalisation24, and the incidence of associated secondary complications, such as pain, hospital acquired infections, and pulmonary thromboembolism all lead to higher healthcare costs25.

Intravenous (quarterly injection or annual infusion) of bisphosphonates may improve adherence compared with oral treatments as they limit the adverse gastro-intestinal effects associated with oral bisphosphonates. One study concluded that both intravenous ibandronate taken monthly and intravenous zoledronic acid taken yearly are associated with improved adherence. Non-bisphosphonate treatments provide useful alternatives if bisphosphonates are not tolerated29.

Other treatments

Strontium ranelate (Protelos) - is thought to work by increasing the activity of the osteoblasts whilst decreasing the osteoclast activity linked to bone breakdown. It is associated with a rare allergic reaction, including skin rash and an increase in incidence of venous thromboembolism (VTE) or blood clot. The drug is not advised for patients with a current VTE or a history of VTE, or for patients who are temporarily or permanently immobilised. Those patients aged 80 years or over should only continue treatment after re-evaluation. Oestrogen - is now not generally used as a long term treatment for osteoporosis. However, in post-menopausal women under the age of 60 this may be considered provided that the benefit outweighs any adverse risks for that individual. Not suitable for women who have risk factors for breast cancer, heart disease, stroke or blood clots28

Raloxifene (Evista) – is a selective oestrogen receptor modulator (SERM) which acts by mimicking the action of oestrogen on bone tissue without risks to the breast and endometrium. It may increase the risk of venous thromboembolic events.

Denosumab - an injectable human monoclonal antibody which reduces bone breakdown; given subcutaneously every 6 months

Teriparatide (Forsteo) - a self-administered injection of human parathyroid hormone, an anabolic agent that stimulates bone formation and increases bone tissue quantity and strength. This high cost treatment is usually reserved for patients for whom other treatments are ineffective, contraindicated, or those at very high risk (particularly of vertebral fracture), who meet strict national or local prescribing criteria. In the UK it is administered as a once only course.

Recent licence changes and emerging drug treatments

Male osteoporosis remains under diagnosed and may be only one-third as likely to be treated as osteoporosis in women26. Treatments such as risedronate, strontium ranelate (not available in Scotland), zoledronic acid and denosumab now include men in their licensing.

A number of emerging treatments remain in late clinical stage development. These include more potent treatments and convenient formulations of existing therapies (e.g. liquid / effervescent alendronate). Calcitonin (Micalcin) has been withdrawn due to a cancer risk following a European review40. New approaches, which increase the possibility of individually targeted treatments have emerged as knowledge of bone biology increases. These include:

- odanacatib (Cathepsin K inhibitor) which slows down bone loss whilst preserving bone formation
- a sclerostin inhibitor (a monoclonal antibody) which allows increased bone formation without increased bone loss
- ZT-031, a parathyroid analogue, may be made available in an inhaled form

Prescribing practice and the role of allied health professionals

In April 2012 osteoporosis was included in the Quality and Outcomes Framework (QOF). This inclusion offers General Practitioner (GP) practices financial incentives for identifying, diagnosing and treating osteoporosis in their patients. To help equip GPs, practice nurses and other members of the practice team with relevant information, a website called ‘Osteoporosis Resources for Primary Care’ (ORPC)41, and an Allied Health Professional Network and a Journal of Community Nursing - March/April 2013, volume 27, issue 2
sharing of information and best practice with forum discussions on issues including treatments and side effects. The National Institute for Health and Clinical Excellence (NICE) recently published the new Short Clinical Guideline CG146 - assessing the risk of fragility fracture. This guideline embraces all those at risk of fragility fractures, including men and women of varying ages. In addition, NICE has announced a review of the Technology Appraisals for osteoporosis treatments. It is hoped these will provide a more complete package of care for people at high risk of fracture and help to prevent some of the costly 300,000 fragility fractures that occur annually in the UK.

Role of the community nurse
Nurses have an important role to play in influencing public health and helping to promote bone health and fracture prevention. They are in a unique position to be able to influence a patient’s holistic understanding of their care, especially helping individuals cope with the uncertainties that exist around health and disease including how to take their medications. Iverson et al demonstrated that many patients do not understand why they were taking a certain osteoporosis medication, nor were they adequately instructed about the medications.

Community nurses can help individuals to be better self-managers of their medications. They can:
- explain that the osteoporosis drug reduces risk of bone fracture, but is not an analgesic
- ensure potential adverse effects are understood - if one drug is discontinued because of side effects, individuals can be encouraged to try an alternative
- work with patients to identify barriers that might prevent the medicines being taken and help to identify solutions
- encourage individuals taking weekly bisphosphonate to take their medicine on a predetermined and consistent day of the week
- explain to individuals the potential consequences of not taking their medications, emphasising how medication can reduce their risk of breaking a bone and improve long-term outcomes - as with other chronic diseases, osteoporosis patients are potential poor treatment compliers who may be liable to discontinue treatment even after a long period.

Conclusion
The general public has a right to reliable information about the effects and risks of drug treatments. In a world of increasing medical knowledge, capabilities and expectation, a level of uncertainty naturally remains inherent within most health care decision making which includes the realm of osteoporosis drug treatments. True evidence based medicine can help provide ways to quantify and communicate uncertainty into more tangible risks and benefits. Sometimes a consensus about drug treatments can be elusive, but honest and caring communication can help an individual to better understand the issues involved and find a way forward.

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