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ABSTRACT

The implementation of a pharmaceutical care tool to guide community pharmacy interventions in osteoporosis

Introduction Osteoporosis is a systematic skeletal disease characterized by low bone density resulting in enhanced risk for fractures. Osteoporosis often remains undiagnosed.

*Objective*To test an audit tool for use in evaluation of level of adherence to osteoporosis guidelines in three practicesused for application to a database of patient records. To validate a potential community pharmacy based service for osteoporosis detection and management.

*Setting*Patient records from a general medical practitioner database (GPASS®) in three general medical practices; A (n=154), B (n=62) and C (n=103) sampling .

Method Retrospective survey with the application of a tool specifically designed for medication assessment in this field (19 criteria, each representing a separate guideline recommendation).

Key findings The testing of the application of the medication assessment tool (MAT) by two independent raters showed 99.1% agreement (Total agreement 15/21 criteria; range (%) 89.6-100) for applicability, 99.6% agreement (Total agreement 18/21 criteria; range (%) 99.6-100) for yes-results, 100% agreement (Total agreement 21/21 criteria; range (%) 100-100) for justified non-adherence, 99.9% agreement (Total agreement 19/21 criteria; range (%) 98.5-100) for unjustified non-adherence. Overall adherence was 60.4% (95% CI 58.1, 62.7; n=3234 criteria applied in 154 patients) for researcher 1 and 60.7% (95% CI 58.0, 63.4; n=3234 applied criteriain 154 patients) for researcher 2 in practice A and 47.1% (95% CI 43.8, 51.2; n=1302 criteriaapplied in 62 patients) in practice B. Comparison showed adherence was 56.3% (95% CI 53.4, 58) in practice A (n= 4536 applied criteriain 216 patients) for researcher 1 and 53.9% (95% CI 51.5, 56.3) in practice A (n= 4536 applied criteriain 216 patients) for researcher 2. The tool identified 13/21 (61.9%) of criteria where adherence was <70% in both settings and. The tool identified 6/21 (28.6%) criteria where adherence was different between practices.

Conclusion The tool offers a systematic and reliable audit method using a database search facility to enable large scale audit of medication use in osteoporosis. The identification of a mean of 16.7% for non-adherences per criterion to clinical guidelines represents a first stage in addressing pharmaceutical care issues prior to informed discussion between pharmacist prescribing advisor and general medical practitioners. A potential community pharmacy based service for detection and management of osteoporosis is considered as useful and feasible.

LIST OF ABBREVIATIONS

BMD	Bone Mineral Density
BNF	British National Formulary
CRF	Clinical Risk Factor
DEXA	Dual energy X-ray absorptiometry
GP	General practitioner
GPASS	General Practice Administration System for Scotland
HRT	Hormone replacement therapy
IDQ	Insufficient data on the qualifier
IDS	Insufficient data on the standard
IV	Intravenous
NA	Not applicable
NICE	National Institute for Clinical Excellence and Health
NHS	National Health Service
NOS	National Osteoporosis Society
No(J)	No, justified
No(U)	No, unjustified
PTH	Parathyroid hormone
RANK	Receptor activator of Nuclear factor κB
RANKL	Receptor activator of Nuclear factor κB ligand
RCT	Randomised controlled trial
SIGN	Scottish Intercollegiate Guidelines Network

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1- INTRODUCTION

1.1. Osteoporosis

1.1.1. Definiton and classification

1.1.1.1. Definition

Osteoporosis is the most common bone disease in both men and women (Mauck and Clarke 2006). The World Health Organisation (WHO) defines osteoporosis as a 'disease characterized by low bone mass and structural deterioration of bone tissue, leading to bone fragility and an increased susceptibility to fractures'. Osteoporotic fractures especially occur at the hip, spine and wrist (WHO 2003). Osteoporosis is a systematic skeletal disease; hence fractures can occur at any site of the skeleton (SIGN 2003).

Before 1994, Osteoporosis was diagnosed on the basis of low-impact or fragility fractures. In 1994, the WHO established definitions for osteoporosis and osteopenia, which represents the pre-stage of osteoporosis(Mauck and Clarke 2006). These definitions and categorizations allow an early diagnosis of the disease as well as a prediction of fracture risk. Osteoporosis is defined as bone mineral density (BMD) more than 2.5 standard deviations below the young normal mean (T-score <-2.5). The T-score represents the number of standard deviations by which the patient's BMD differs from the mean peak BMD for young normal subjects of the same gender (SIGN 2003). BMD is usually measured via dual-energy X-ray absorptiometry (DXA) (Copeland and Worsley 2009).

The following table shows the categorisation of bone mineral density and related conditions set up by the World Health organization (Copeland and Worsley 2009):

Table 1 WHO bone mineral density scale

Category	Description	T- Score
Normal	A value of BMD within 1 standard deviation of the young adult reference mean	≥ -1
Low bone mass (osteopenia)	A value of BMD more than 1 standard deviation below the young adult mean, but less than 2.5 standard deviations below this value	< -1 and > -2.5
Osteoporosis	A value of BMD 2.5 standard deviations or more below the young adult mean	≤ - 2.5
Severe osteoporosis	A value of BMD 2.5 standard deviations or more below the young adult mean in the presence of one or more fragility fractures	≤ - 2.5 (+ fragility fracture)

1.1.1.2. Classification

In young human beings the rate of bone formation is bigger than the rate of bone resorption (NICE 2008). Peak bone mass is reached between 30 and 40 years of age (Copeland and Worsley 2009). By the third decade of life there is a gradual loss of bone mass(NICE 2008) since bone remodelling continues, but cannot outweigh the damages done to the skeleton by everyday life's activities (Copeland and Worsley 2009). Osteoporosis therefore usually represents a disease related with age (NICE 2008) but can also occur in younger individuals due to impaired development of peak bone mass (e.g. due to delayed puberty or undernutrition) or excessive bone loss during adulthood (e.g. due to oestrogen deficiency in women, undernutrition, or corticosteriod use)(Copeland and Worsley 2009). Osteoporosis cantherefore be classified as either primary or secondary osteoporosis (Mauck and Clarke 2006).

1.1.1.2.1. Primary osteoporosis

95% of osteoporotic patients, mainly women, are suffering from primary osteoporosis, also termed idiopathic, postmenopausal or pre-senile osteoporosis (Siegenthaler et al. 1992). The main reason in female patients with primary osteoporosis is deficiency in production of oestrogens. Oestrogens reduce the effect of parathyroid hormone on

mobilization of calcium from the skeleton (Hettenkofer 1998). Primary osteoporosis occurs as a normal result of bone loss during the aging process in both sexes (Mauck and Clarke 2006). Deficiency in sex hormones represents the principal cause for primary osteoporosis in both men and women (Copeland and Worsley 2009).

1.1.1.2.2. Secondary Osteoporosis

In secondary osteoporosis bone loss is associated with several chronic medical conditions, medications and nutritional deficiencies(Mauck and Clarke 2006).These conditions and medications represent the actual cause for the development of the disease. Decreased calcium and vitamin D levels caused by poor diet and/or insufficient exposure to sunlight contribute to the development of osteoporosis (Copeland and Worsley 2009; Hettenkofer 1998; Schettler and Greten 1998). Endocrine disorders such as hyperthyroidism,diabetes mellitus, Cushing's syndrome, hyperparathyroidism and hypogonadism can attribute to the development of secondary osteoporosis (Siegenthaler et al. 1992).Furthermore anorexia nervosa, chronic liver disease, renal disease, rheumatoid arthritis, inflammatory bowel disease and certain types of cancerrepresent conditions associated with secondary osteoporosis (Copeland and Worsley 2009; Schettler and Greten 1998; Siegenthaler et al. 1992; SIGN 2003). Some medications such as oral glucocorticoids is a main reason for secondary osteoporosis (Schettler and Greten 1998). Oral administration of 7.5 mg prednisolone or equivalents for 3 months and more should be accompanied by certain measures for prevention of osteoporosis (SIGN 2003). Drugs like phenobarbitone or phenytoin induce the production of certain enzymes activating the production of metabolites of vitamin D other than the active one (25-OH-vitamin D3) (Schettler and Greten 1998). Furthermore immobilization can cause secondary osteoporosis. 4 to 6 weeks of bed rest have been shown to induce demineralisation of bone of up to 18% (Siegenthaler et al. 1992).

1.1.2. Epidemiology

The prevalence of osteoporosis increases with age (SIGN 2003). One in three women and one in twelve men over the age of 50 are affected by osteoporosis (NHS 2006). The disease is particularly common in postmenopausal, white women(NICE 2008; SIGN 2003). After the menopause, the prevalence of osteoporosis increases massively with age, from approximately 2% at 50 years to more than 25% at 80 years. In women aged over 50 years, the lifetime risk to sustain a vertebral fracture is estimated to be one in three, and that of hip fracture one in five which is higher than the one in nine risk of developing breast cancer (Cummings and Melton 2002; NICE 2008).Patients, who

have already sustained a fracture, are at greater risk of subsequent fractures (NICE 2008).

In Scotland one in three women over the age of 50 will suffer an osteoporotic fracture. Despite the significantly high prevalence in women, osteoporosis also affects men. One in twelve men over 50 will suffer an osteoporotic fracture.This makes around 200,000 women and 40,000 men affected. Approximately 20,000 osteoporotic fractures occur annually in Scotland (SIGN 2003). Presumably 70% of all fractures in persons aged 45 or over occur as a result of osteoporosis (Cummings and Melton 2002).

Since the proportion of elderly people among populations worldwide is greatly expanding, the number of patients suffering from osteoporosis and/or sustaining osteoporotic fractures is predicted to increase (Mauck and Clarke 2006). The sedentary lifestyle followed by more and more people nowadays, also contributes to the increase in osteoporotic fractures (SIGN 2003).

Barrett-Connor et al. reported in 2005 that the prevalence of osteoporosis varies between different ethnic groups. Studies showed that Afro-American women have greater bone mass than white women and are less affected by osteoporosis. On the other hand bone mass among Hispanics is more similar to whites. Still the fracture risk among whites is higher than among women with Hispanic origins, so the bone mineral density does not necessarily correlate with the fracture risk. Furthermore studies were conducted showing that fracture risk among Asian women is smaller than among white women (Barrett-Connor et al. 2005).

Besides variation between different ethnic groups, there is also variation among each individual ethnic group. Among European countries rates vary more than seven fold with an especially high rate in Scandinavia. Similar variations have been shown for the USA and Asia. Studies revealed that rates of hip fractures are higher in urban areas than in rural areas of the same country, which is mainly attributed to a decrease in physical activity (Cummings and Melton 2002).

1.1.3. Socioeconomic impact

Osteoporosis represents a major health issue and has enormous societal and economical implications(Faulkner 2005).Osteoporosis and osteoporotic fractures are associated with high mortality, morbidity and high cost of medical care (Mauck and Clarke 2006). Fractures tremendously diminish the quality of living of sufferers (Faulkner 2005) since they are associated with chronic pain, reduced mobility, disability and increasing degree of dependence (NICE 2008). 10% to 20% of patients who have

sustained a hip fracture die within the subsequent six months. 50% of these patients will not be able to walk without assistance and 25% will loose the ability to live independently (NICE 2008). In Scotland, patients who have sustained a hip fracture take up more than 20% of orthopaedic bed days. In the UK, osteoporotic fractures cause a cost of 1.7 billion British Pounds annually (SIGN 2003).

Although there is effective treatment available, osteoporosis still often remains undiagnosed until fractures occur. In addition, patients representing osteoporotic fractures are often not identified as being osteoporotic and might sustain a subsequent fracture (Mauck and Clarke 2006).Mortality, morbidity as well as costs could be reduced via identification and appropriate treatment of people who are at high risk of osteoporosis (Reginster 2007).

1.1.4. Bone metabolism

The human skeleton is capable of repairing the damages caused by daily use on basis of the interplay of bone formation and resorption. This balance between formation and resorption of bone is termed 'remodelling' (Copeland and Worsley 2009). Three types of cells are to be found in bone, osteoblasts, osteoclasts and osteocytes (Compston 2001). Osteoblasts are responsible for the formation and mineralisation of bone, osteoclasts for the resorption (Copeland and Worsley 2009). Osteocytes are believed to play an important role in the response to mechanical stimuli, initiating the appropriate action, formation or resorption (Compston 2001). Osteoblasts are derived from pluripotent mesenchymal stem cells, which can also differentiate into e.g. adipocytes. The osteoblast phenotype is achieved by the osteoblast stimulating factor 2 (Osf 2).

Osteoblast differentiation requires further components such as fibroblastic growth factors (FGFs), bone morphogenetic factors (BMPs), glucocorticoids and vitamin D. Osteoblasts produce type I collagen, alkaline phosphatase, osteopontin and osteocalcin (Aktories et al. 2005). Osteoclasts are derived from haematopoietic precursors of monocytes respectively macrophages. Osteoclastic differentiation and activation is stimulated via binding of receptor activator of NFκB ligand (RANKL), a member of the tumor necrosis factor (TNF) ligand family, to its transmembrane receptor RANK expressed by osteocytes (Compston 2001). Osteoprotegerin (OPG), a member of the TNF receptor family, represents a soluble receptor for RANKL and prevents its binding to and activation of osteoclasts (Aktories et al. 2005). Bone modelling takes place during growth, as response to mechanical stimuli or during

fracture healing, but the capacity decreases with increasing age. Bone modelling consists of both bone formation and resorption, while formation clearly exceeds resorption. In bone remodelling on the other hand, amounts of formed and resorbed bone are similar and the two processes are coupled, a removal of bone via osteoclast activity is followed by subsequent formation via osteoblasts. Remodelling allows maintenance of stability of the human skeleton and calcium and phosphate release from the latter. Bone remodelling is regulated via several factors including mechanical stresses, systemic hormones like sex steroids, parathyroid hormone (PTH), thyroid hormones, growth hormone and glucocorticoids.

Locally produced factors like cytokines and growth factors play an important role in bone remodelling, Interleukin (IL)-1α and -1β are stimulators of resorption, as well as IL-6. Furthermore TNFs, Epidermal growth factor (EGF), Platelet-derived growth factor (PDGF), Fibroblast growth factors (FGFs), Macrophage-colony stimulating factor (M-CSF) and Granulocyte/macrophage-colony stimulating factor (GM-CSF) are stimulators of bone resorption. Among stimulators of bone formation are Insulin-like growth factors (IGFs), Transforming growth factor β (TGF-β), Fibroblast growth factors (FGFs) and bone morphogenetic proteins (BMPs). Interleukin 4 and Interferon γ represent inhibitors of bone resorption (Aktories et al. 2005; Compston 2001). In osteoporosis, an increase in activation of remodelling units is resulting in an increased resorption rate. This is called ‘high bone turnover’ (Compston 2001; Hettenkofer 1998). The second possible mechanism underlying osteoporosis is that the amount of bone formed is less than the amount resorbed. In many cases both mechanisms coexist in osteoporosis, high burn turnover and remodelling imbalance, resulting in bone loss, changes in bone architecture and subsequent decrease in bone strength (Compston 2001).

1.1.5. Symptoms and diagnosis of osteoporosis

Preclinical osteoporosis is painless and unaccompanied by any symptoms, whereas clinically manifest osteoporosis, which is associated with occurrence of fractures results in severe pain, mainly of the back. This backache, which is very common in osteoporotic patients results from deformations and fractures of vertebral bodies (Siegenthaler et al. 1992). Osteoporotic deformations of the vertebra very often result in hyperkyphosis, also known as ‘dowager’s hump’, relating to the curvature of the thoracic region of the spine (NOS 2009; Schettler and Greten 1998). Another very common symptom in patients suffering from osteoporosis is hyperlordosis (inward curvature of the spine) leading to the characteristic loss of height in osteoporotic

patients of up to 20cm (Bitsch 1997; Hettenkofer 1998; Siegenthaler et al. 1992). Deformation and fractures of vertebral bodies are associated with acute pain, resulting from bleeding, decompensation of statics of the vertebra or compression of nerves. Furthermore occurrence of chronic pain is very common in osteoporosis, resulting from impaired statics of the vertebra leading to muscle fatigue of the trunk, especially in the afternoon and after a period of walking or standing upright (Hettenkofer 1998; Siegenthaler et al. 1992).

Osteoporosis is usually diagnosed via dual- energy X-ray absorptiometry (DXA) which represents the goldstandard for the assessment of bone mineral density since it provides very accurate and reliable results (Copeland and Worsley 2009). The dose of radiation the patient is exposed to is relatively small - approximately 30 micro Sievert (micro Sv) which is comparable to the radiation dose of a single transatlantic flight.Although the purchase of a scan is high, the costs for the scans are low (SIGN 2003). As mentioned before, the result given by DXA scan is the T-score. The calculation of the T- score is defined as the difference between a measured bone density (BMD) and the expected young normal value (YN) divided by the population standard deviation (SD):

T- score = (BMD – YN) / SD (Reginster 2007).

There is no unit for the T- score since it is a ratio of two numbers with the same units(Faulkner 2005).Another value of BMD is the Z-score, which represents the number of standard deviations by which the patient's BMD differs from the mean BMD for subjects of the same age(SIGN 2003).

However, there are several other techniques available which serve the purpose of measuring BMD. Among these are radiography, quantitative ultrasound (QUS), quantitative computed tomography (QCT) and peripheral methods (SIGN 2003).

Radiography

Assessment via radiography might be of interest since it is simple to use and available. The disadvantage of radiographic images is that the three- dimensional micro- architecture of bone is not visible in a two- dimensional image (Kazakia and Majumdar 2006). Stillosteoporosis can often be diagnosed via radiographs, although with low sensitivity(Kanis 2002). Only massive bone loss can be detected by the radiograph (Faulkner 2005). Furthermore interpretation of radiographic is

likely to depend on the individual observer(SIGN 2003).Treatment might be started unnecessarily while patients who indeed suffer from osteoporosis might be missed. Therefore radiography should not be implemented in the assessment o bone mineral density(Cummings and Melton 2002).A possible advantage of radiographic images is that vertebral deformities that might have remained undiagnosed might be discovered on a radiograph(NICE 2008).

Quantitative ultrasound (QUS)

Most ultrasound systems measure speed of sound (SOS) and broad- band ultrasound attenuation (BUA) of the calcaneus. Different systems produce different values and are therefore not comparable (Cummings and Melton 2002).Hence QUS is not an appropriate technique for diagnosis of osteoporosis(NICE 2008).However QUS of the heel can predict the risk of spine and hip fracture(Cummings and Melton 2002), so it might be used for the assessment of fracture risk in elderly women(NICE 2008).

Quantitative computed tomography (QCT)

QCT has been widely used to measure BMD, especially in the spine (Cummings and Melton 2002). X- rays pass through the object determined for examination towards a detector (Faulkner 2005). Source and detector rotate about the object and attenuation of X-rays is measured. The important advantage of QCT over DEXA and QUS is that it provides three- dimensional spatial resolution (Faulkner 2005), which allows assessment of true volumetric density (NICE 2008) as well as of macro- architecture(Faulkner 2005). This might help to understand the individual underlying pathology as well as to monitor the effect of drug therapy (Faulkner 2005).DXA on the other hand only provides area- adjusted results(NICE 2008). Another advantage of QCT is its capability to measure cortical and trabecular bone separately(Cummings and Melton 2002). Trabecular bone is crucial for the stability of the vertebra due to its active metabolism and a separate assessment without interference caused by cortical bone is valuable in the detection of vertebral loss (Faulkner 2005). Furthermore QCT can differentiate between degenerative disease of the spine and osteoporosis, via DEXA scan this differentiation is not possible(NICE 2008). Disadvantages of QCT in comparison to DEXA are the higher

radiation dose, higher costs and the limited availability of equipment(Faulkner 2005).

Peripheral Methods

Peripheral methods are: peripheral quantitative computed tomography (pQCT), peripheral DEXA, single- energy x- ray absorptiometry (SXA) and radiographic absorptiometry (RA). Advantages of these methods compared to DEXA are the lower costs and the portability of the equipment. They are often used as screening methods for patients requiring a DEXA scan. (Cummings and Melton 2002)

1.1.6. Risk factors for osteoporosis

There are several risk factors that are significantly related to the prevalence of osteoporosis (Snelling et al. 2001). Risk factors for the development of osteoporosis can be subdivided into modifiable and non- modifiable factors(SIGN 2003). Among non-modifiable risk factors are advanced age, female sex, heredity and ethnicity. Weight, smoking, alcohol consumption, physical activity and diet represent modifiable risk factors whose avoidance could have a positive impact o bone health (Snelling et al. 2001).

1.1.6.1. Non- modifiable risk factors

1.1.6.1.1. Age

Since bone mineral density decreases with age, the prevalence of osteoporosis increases with advancing age (SIGN 2003). The NHANES III study indicated a two fold higher risk for women of the age 60 to 69 and a four fold higher risk for women aged 70 years or older relative to women in their fifth decade of life (Hirschhorn and Gennari 2008). 90% of hip fractures occur in women over the age of 50 years suggesting that age is a very strong predictor for the prevalence of osteoporosis (Hirschhorn and Gennari 2008).

1.1.6.1.2. Gender

Women are at higher risk of osteoporosis than men since they have smaller bones and therefore a lower total bone mass (SIGN 2003). Furthermore the larger bone size in men represents a biomechanical advantage, which results in a lower rate of fragility fractures (Compston 2001). In addition, the rapid decrease in oestrogen levels after the onset of the menopause further contributes to this increased risk (SIGN 2003). The Framingham Osteoporosis Study revealed that the rate of bone loss in women is bigger

than in men with an annual rate of 0.86% to 1.21% in women versus 0.04% to 0.96% in men (SIGN 2003). Secondary osteoporosis is more common in men with a proportion of up to 40% of the cases (SIGN 2003).

1.1.6.1.3. Heredity and genetics

A family history of osteoporosis represents an important risk factor for osteoporosis (Hirschhorn and Gennari 2008). In patients presenting a family history of osteoporosis, kyphosis and low impact fractures, bone mass has been proven to be lower, depending on how many family members are affected by osteoporosis (SIGN 2003). Contrarily a study conducted by Snelling et al indicated that women whose mothers never suffered from osteoporosis are at lower risk to develop osteoporosis. It revealed 40% reduction in risk in offspring of mothers who have never been osteoporotic (Snelling et al. 2001).

Osteoporosis has a strong genetic component (Hirschhorn and Gennari 2008). Genetic variations in genes associated with bone mineral density result in different bone phenotypes (Styrkarsdottir et al. 2008). Single nucleotide polymorphisms (SNPs) have been identified on 5 different loci. For these loci there is strong evidence that they are associated with BMD (Styrkarsdottir et al. 2008). Three of them are close to or within genes which have previously been shown to play an important role in bone homeostasis: the estrogen receptor 1 gene (ESR 1), OPG and the receptor activator of nuclear factor κB ligand gene RANKL. ESR 1, OPG and RANKL are crucial regulators in bone metabolism (Styrkarsdottir et al. 2008). RANKL, its receptor RANK and OPG represent major regulators of osteoclast activity and bone resorption. Consequently abnormalities within this system lead to subsequent bone abnormalities. Furthermore a decreased oestrogen sensitivity, which might be due to a defect oestrogen receptor, can result in disorder in bone homeostasis (Hirschhorn and Gennari 2008). See also chapter ‘Bone metabolism’ for OPG and RANKL.

Styrkarsdottir et al discovered 2 other sites that are strongly associated with bone mineral density, on 1p36 close to the zinc finger and BTB domain and on 6p21 near to the major histocompatibiltity complex (MHC). It is not possible to predict fracture risk via these variations, but knowledge about them provides insight into biochemical pathways that result in the development of osteoporosis (Styrkarsdottir et al. 2008). Furthermore they represent possible drug targets for the development of treatment and prevention strategies (Hirschhorn and Gennari 2008).

1.1.6.1.4.Ethnicity

Ethnic origins serve as a predictor of fracture risk, at least as concerns the comparison of white and black (Snelling et al. 2001). White Caucasian women are at highest risk of osteoporosis, similarly to white women of Hispanic or Asian origins. Afro- American women on the other hand are at a significantly lower risk of developing osteoporosis which is most likely to the fact that bone mass is higher among them (Barrett-Connor et al. 2005). In Afro- American women skeletal calcium and potassium contents are higher and they have been shown to have a higher muscle mass which probably further contributes (Snelling et al. 2001). In comparison to white women Afro-American women are at a 2.5 fold lower risk of osteoporosis (SIGN 2003).

1.1.6.2.Modifiable risk factors

Whereas there can be nothing done about non- modifiable risk factors, engagement in behavioural towards modifiable risk factors can have a significant impact on reducing the risk of developing osteoporosis or delay the onset of the disease (Snelling et al. 2001).

1.1.6.2.1. Weight

There is strong evidence that low body weight, mainly expressed as low body mass index (BMI), is a major risk factor for osteoporosis (SIGN 2003). Excess body weight on the other hand apparently represents a protecting factor due to increased skeletal loading, which enhances bone maintenance. Furthermore an increase in body fat mass induces a subsequently higher oestrogen production. Contrarily low body weight significantly increases the risk of developing osteoporosis, which might be due to lower calcium levels resulting from dieting as well as to decreased skeletal load. It has to be mentioned, that overweight represents a major risk factor for coronary heart disease, cancer, diabetes and other chronic conditions and the disadvantages definitely outweigh the advantages (Snelling et al. 2001).

1.1.6.2.2. Smoking

Smoking represents a further risk factor for osteoporosis since it is associated with a greater rate of bone loss. Bone loss due to smoking especially occurs in the hip (Kenneth and Klesges 2001). Studies revealed that smoking increases the lifetime risk to sustain a hip fracture by about half from estimated 12% to 19% in women aged up to 85 years and from 22% to 37% to 90 years of age. Of all hip fractures, 1 in eight is attributable to smoking (Law and Hackshaw 1997). In vitro tests showed the toxicity of nicotine and other components of cigarette smoke on bone cells. Smoking causes a

decrease in intestinal calcium absorption and either increases the metabolism of oestrogen or decreases production of the latter (Hoidrup et al. 2000). Levels of cortisol are raised in smokers, which has been proven to reduce bone mineral density (Law and Hackshaw 1997). The prevalence of falls is higher among smokers due to poorer balance and physical performance resulting from deleterious effects of smoking on the neurovascular and peripheral vascular system (Hoidrup et al. 2000). However, there has been no significant effect of tobacco consumption on bone detected in individuals younger than 40 years (Kenneth and Klesges 2001).

The deleterious effect of smoking on bone health increases cumulative with age. It has been shown that in postmenopausal women who are smoking there is an additional bone loss of 0.2% of the average annual bone loss per year. By the age of 80 the accumulated additional bone loss will result in a 71% higher risk of sustaining a hip fracture. Contrarily to previous beliefs, there appears to be no gender-related differences, so male smokers are most likely at the same risk of suffering additional bone loss due to smoking as women, and not at higher risk (Law and Hackshaw 1997).

1.1.6.2.3. Alcohol

The chronic consumption of alcohol is associated with an increased incidence in fractures from falls and delays in fracture healing. The so-called 'Alcohol induced bone disease' results from a dose-dependent toxic effect of alcohol on osteoblasts since it represses osteoblastic differentiation of bone marrow cells. Furthermore alcohol leads to impaired fracture healing resulting from an inhibition of cell proliferation in repair tissue (Chakkalakal 2005).

1.1.6.1.4. Physical activity

Studies have indicated that people who participate regularly in weight bearing exercise have a higher bone mass than inactive individuals (Snelling et al. 2001). Weight bearing exercise has been shown to effectively slow down or even stop bone loss (Korpelainen et al. 2006). Unfortunately this effect might be site- specific, with an impact mainly on the hip (Snelling et al. 2001). There is evidence that the incidence of fractures related with falls is smaller among people who exercise regularly (Korpelainen et al. 2006). Weight bearing exercise represents an effective and appropriate non-pharmacological approach to maintaining bone health (Snelling et al. 2001).

1.1.6.1.5. Diet

Decreased calcium and vitamin D levels caused by poor diet or and/or insufficient exposure to sunlight contribute to the development of osteoporosis (Copeland and Worsley 2009).

1.1.6.1.6. Reproductive factors

Reproductive factors play a central role in bone health in both men and women. Sex steroids are crucial for bone growth, attainment of peak bone mass and maintenance of bone mass. Late menarche and premenopausal amenorrhea resulting from anorexia nervosa are associated with low bone mass (Compston 2001; Siegenthaler et al. 1992). Consequently an early onset of menopause represents a major disadvantage in the bone health whereas a late menopause is associated with a higher bone mass (Compston 2001; SIGN 2003). Similarly in male individuals, androgen deficiency due to hypogonadotropic hypogonadism results in low bone mass (Schettler and Greten 1998).

1.1.6.1.7. Diseases and conditions associated with secondary osteoporosis

Endocrine disorders such as hyperthyroidism,hyperparathyroidism, diabetes mellitus or Cushing's syndromeare associated with secondary osteoporosis (Copeland and Worsley 2009; Siegenthaler et al. 1992).As mentioned in the section before, amenorrhoea resulting from anorexia nervosa and (mainly male) hypogonadism are a main risk factor for secondary osteoporosis (Schettler and Greten 1998; Siegenthaler et al. 1992). Furthermore chronic liver disease, renal disease, rheumatoid arthritis, inflammatory bowel disease, and certain tumours are associated with secondary osteoporosis (Siegenthaler et al. 1992).

Hyperthyroidism

Both bone resorption and formation are stimulated by thyroid hormone, but osteoclasts are more sensitive to the latter then osteoblasts. Consequently the higher stimulation of rate of bone resorption outweighs the stimulation of bone formation (Hettenkofer 1998; Siegenthaler et al. 1992).

Hyperparathyroidism

High levels of parathyroid hormone activate the mobilization of calcium from the bone, which represents the pathological impact of PTH on bone (Schettler and Greten 1998).

Diabetes mellitus

Diabetes mellitus and subsequent development of secondary osteoporosis are very common in younger patients treated with insulin (Siegenthaler et al. 1992).

Cushing's Syndrome

Cushing's syndrome is characterized by high blood levels of cortisole and therefore correlates with glucocorticoid-induced osteoporosis (Siegenthaler et al. 1992).

Chronic liver disease

Diseases of the parenchyma of the liver can result in impaired 25- hydroxylation of vitamin D3, which represents the active metabolite of vitamin D (Schettler and Greten 1998).

Chronic kidney disease

Chronic kidney disease can induce secondary osteoporosis due to impaired renal production of 1,25-OH-vitamin D3 and decreased intestinal resorption of calcium and subsequent 'renal hyperparathyroidism' induced by hypocalcaemia (Schettler and Greten 1998).

Rheumatoid arthritis

Impaired physical activity, inflammatory processes and intake of steroids represent the connection between rheumatoid arthritis and secondary osteoporosis (Hettenkofer 1998).

Inflammatory bowel disease

Crohn's disease is highly associated with malabsorption, especially of calcium (Siegenthaler et al. 1992).

1.1.6.1.8. Glucocorticoids

Glucocorticoids are important drugs but unfortunately produce severe adverse effects (Tamura et al. 2004). Long-term oral use of these drugs represents the most common cause for secondary osteoporosis (Migliaccio et al. 2009). Fractures occur in 30% of people taking glucocorticoids on a long- term basis (Reid 2008). A daily oral intake of more than 5 mg prednisolone or equivalent increases the fracture risk within the first three to six months of treatment (Tamura et al. 2004). Glucocortiocoids cause a decrease in bone formation due to apoptosis of osteoblasts and an increase in bone

resorption resulting from prolonged lifespan of osteoclasts (Migliaccio et al. 2009). Furthermore reductions in intestinal calcium absorption and calcium absorption from the renal tubule contribute to bone loss resulting from the destabilised balance between bone formation and resorption (Reid 2008). Long- term oral steroid use result can in hypogonadism, mainly in men, which further explains the deleterious effects on bone health (Reid 2008). High dose inhaled glucocorticoids may also increase the risk of developing secondary osteoporosis (Tamura et al. 2004). Therefore patients receiving long- term oral and probably also inhaled glucocorticoid therapy should be prescribed preventive treatment (Tamura et al. 2004).

1.1.6.2. Risk assesment

Osteoporosis remains often undiagnosed until fractures occur (WHO 2003). Studies revealed that one in two women is at risk of osteoporosis, but only one in five receives assessment of bone mineral density (Law and Shapiro 2005). Information about bone mineral density is not sufficient for the estimation of fracture risk. Many patients suffering from osteoporosis do not meet the definition respectively criteria for being osteoporotic set up in 1994 by the WHO. Therefore it is necessary to include other factors in addition to information about BMD. These factors are termed 'clinical risk factors' and their integration enables the calculation of a 10- year absolute risk or probability of fracture. The implementation of clinical risk factors allowed to move away from an intervention threshold based BMD to a threshold based on absolute risk of fracture (Silverman 2009).

FRAX®- fracture risk assessment tool

FRAX® is a WHO tool to predict fracture risk in men and women (Kanis et al. 2008a). It represents algorithms to predict age-specific 10-year probability of fracture one the basis of clinical risk factors (CRF) with or without measurement of BMD at the femur (Kanis et al. 2008b). FRAX® was published in 2008 and is accessible free of charge on the Internet (www.shef.ac.uk/FRAX) (Roux and Thomas 2008). The algorithms are based on a series of meta- analyses using the primary data from population-based cohorts that have identified several CRFs for fracture (Kanis et al. 2008b). As mentioned before, low bone mineral density does not explain all fractures, even if it is strongly related with many of them. About 40% of women with fractures have normal BMD values. In some cases, the reason might be poor sensitivity of BMD measurements, but there are other factors, CRFs, contributing to the decrease in bone strength (Roux and Thomas 2008). These clinical risk factors are more or less independent from BMD (Kanis et al. 2008a). Clinical risk factors are

- Body mass index (BMI)
- A prior history of fracture
- A parental history of hip fracture
- Use of oral glucocorticoids
- Rheumatoid arthritis and other secondary causes of osteoporosis
- Current smoking
- Alcohol intake 3 or more units daily (Kanis et al. 2008a)

Nowadays the combined use of BMD and CRFs is strongly recommended in the evaluation of fracture risk. The FRAX® tool is very easy to use. BMD at the femur is indicated as e.g. '- 2.5'. As mentioned before, the probability of fracture can also be obtained without BMD, on the basis of exclusively CRFs. The FRAX® algorithms give the 10-year probability of hip fracture and the 10-year probability of a major osteoporotic fracture, such as hip, shoulder, forearm or clinically manifest spine fracture. FRAX® can only be implemented in countries that have provided epidemiological data in order to identify the risk profile. Seven European countries did not provide this data. Risk profiles differ among countries (Roux and Thomas 2008).

The FRAX® tool has two major limitations. First, several risk factors can only be indicated as being present or absent, hence there can only be a 'no'- or 'yes'- answer given. For glucocorticoid use or presence of vertebral fracture, a 'yes'- or 'no'- answer might not provide sufficient information to assess fracture probability. In glucocorticoid therapy, dose and duration significantly influence the fracture risk. In vertebral fractures, number, severity and site strongly affect the risk of subsequent fractures. Second, only femoral BMD is taken into account by the FRAX® tool. The reason for this is, that only BMD in this site was available in all study cohorts that were assessed in order to establish the tool (Roux and Thomas 2008).

However, FRAX® represents a useful tool in the finding of decisions in osteoporosis management, if used optimally in the awareness of these limitations mentioned before. So far, decisions whether to initiate osteoporosis therapy or not were based on the presence or absence of fractures and on a T-Score of ≤ -2.5 SD. As mentioned before, 40% of women with fractures have normal BMD; so fractures might have been avoided by initiating pharmacological osteoporosis treatment, which would not have been possible previously to the occurrence of fractures since the prevalence of osteoporosis

would not have been identified in the absence of fractures. It can also be used for patient education to highlight how additional risk factors can increase the initial risk. In women of the age between 50 and 60 decisions regarding whether to start treatment or not is particularly difficult and studies indicated that the fracture probability estimated by FRAX® might be lower than the observed fracture risk. In this group, the FRAX® might solely be used in patients with low fracture probability in order to convince them that treatment is unnecessary. Nevertheless the goal of prediction of fracture probability is to enable the decision making whether to start treatment or not. For this purpose, studies were conducted in order to establish fracture risk cut-offs or intervention thresholds.

The studies have suggested that treatment is cost-effective in patients at any age presenting a 10-year risk of major osteoporotic fracture higher than 7%(Roux and Thomas 2008). The intervention threshold or cut-off is dependent on age. The intervention threshold at the age of 50 is suggested to be a 10-year probability of major osteoporotic fracture of 7.5%, rising up to 30% at the age of 80 (see table) (Kanis et al. 2008b). Besides intervention thresholds, assessment thresholds were established. There are two different assessment thresholds, the lower and the higher assessment threshold. The lower assessment threshold represents the fracture probability below which neither BMD assessment nor treatment is recommended. Above the higher assessment threshold treatment could be initiated without a previous assessment of bone mineral density. The range between the upper and the lower threshold includes cases in which measurement of BMD is indicated (Kanis et al. 2008b).

Table 2 Intervention threshold

Age (years)	Major fracture	Hip fracture
50	7.5	1.0
55	10	1.5
60	12.5	2.4
65	15	3.6
70	20	5.6
75	25	8.4

80	30	12

1.1.7. Treatment and prevention of osteoporosis

1.1.7.1. Non- pharmacological measures to maintain bone health

1.1.7.1.1. Falls prevention

Falls, fractures and osteoporosis are closely linked since falls often result in fractures, especially in osteoporotic patients (Lowrie 2008). It is estimated that a third to one half of people of the age over 65 who live in the community fall every year. In Glasgow this results in 45 000 to 68 000 people falling each year. Many people fall more than once and the prevalence of falls increases with age. It is estimated that 12 000 falls occur annually among inhabitants of care homes (NHS 2006). The National Institute for Clinical Excellence (NICE) has issued a guideline for the assessment and the prevention of falls in elderly people. Elderly people who are in contact with healthcare professionals should be asked routinely whether they have fallen in the past year as well as about frequency, context and characteristics of the fall. Elderly people who report a fall or are considered to be at risk of falling should be observed for balance and gait deficits and considered to participate in interventions to improve strength and balance(NICE 2004). For patients identified as being at risk of falling, multifactorial falls risk assessment should be conducted, including

- assessment of gait, balance, mobility and muscle weakness
- assessment of osteoporosis risk
- assessment of the older person's perceived functional ability and fear relating to falling
- assessment of visual impairment
- assessment of cognitive impairment and neurological examination
- assessment of urinary incontinence
- assessment of home hazards and
- cardiovascular examination and medication review (NICE 2004)

Certain medications can increase the risk of falling, especially if a patient takes four or more at the same time (polypharmacy) (Lowrie 2008). The drug group mainly

associated with an increase in risk of falling are drugs acting on the central nervous system like psychotropics such as benzodiazepines, antidepressants and antipsychotics (Hartikainen et al. 2007). Antiepileptics and drugs that lower blood pressure are also, but only weakly associated with an increase in falls (Hartikainen et al. 2007). An increase in risk of falling resulting from certain drugs who are known to increase risk of falls and/or polypharmacy might be avoided by the conduction of a clinical medication review via e.g. a GP or a pharmacist. Drugs that increase risk of falling might be withdrawn or doses reduced (Lowrie 2008).

1.1.7.1.2. Calcium and vitamin D

Calcium is a crucial component of the skeleton since the inorganic phase of bone is mainly composed of calcium hydroxyapatite (Compston 2001). Vitamin D improves the absorption of calcium from the gastrointestinal tract (Copeland and Worsley 2009). It can be found in the literature that calcium and vitamin D are regarded as drugs capable of reducing bone resorption, so called 'antiresorptive' drugs (Reid 2008). However, there is no evidence that the supplementation of calcium and vitamin D alone represents an efficient preventive measure; therefore they are mentioned apart from antiresorptive treatment in this context.

Supplementation of calcium and vitamin D is recommended in all patients receiving 'bone treatment' (Copeland and Worsley 2009). The daily calcium intake should be 1000mg, which represents the calcium contained in two slices of cheese and a glass of milk. In case of balanced nutritional uptake, supplementation of calcium does not appear to be necessary. Supplementation should not exceed a daily dose of 1500 mg. Vitamin D deficiency decreases the intestinal calcium intakes as well as muscular balance. A daily exposure to sunlight of the face and arms for 30 minutes on a daily basis provides a sufficient vitamin D production. Since this might be difficult to be achieved in central respectively northern European countries, vitamin D substitution might be necessary, especially in people living in nursing homes or housebound patients. The daily dosage of vitamin D supplementation should comprise 800 to 2000 I.U. vitamin D3 (Jehle and Pfeilschifter 2009).

1.1.7.2. Pharmacological managment of osteoporosis

Pharmacological treatment of osteoporosis is indicated if a patient's 10 year- fracture probability is exceeding 30% (Jehle and Pfeilschifter 2009).

1.1.7.2.1. Antiresorptive treatment

Antiresorptive agents inhibit bone resorption by osteoclasts (Reid 2008). Potential antiresorptive drugs such as bisphosphonates can reduce the risk of vertebral fracture by approximately 50% and the risk of non-vertebral fractures by 25% (Li et al. 2009b). Although mechanisms of action differ among different antiresorptive drugs, the effect on increasing bone strength and decreasing risk of fragility fractures represents a result from an increase in bone mineral content and reduction in bone turnover (Miller 2008). Antiresorptive drugs are bisphosphonates, estrogen whose supplementation in terms of hormone replacement therapy (HRT) has to be mentioned very critically because of the risks the latter, selective estrogen receptor modulators (SERMs) like raloxifene and calcitonin (Reid 2008). Strontium ranelate as well represents a potential antiresorptive drug but will be mentioned separately due to its additional, dual mechanism of action (Jehle and Pfeilschifter 2009).

1.1.7.2.1.1. Bisphosphonates

Bisphosphonates are first line treatment for both primary and secondary prevention of osteoporosis (Copeland and Worsley 2009). Bisphosphonates that are most common in use for the management of osteoporosis are alendronate, risedronate, etidronate, ibandronate and zoledronic acid (Jehle and Pfeilschifter 2009). It has to be mentioned that the bisphosphonates ibandronate and zoledronic acid, which have to be administered intravenously, are not explicitly recommended by current guidelines, but since they are licensed for the treatment of osteoporosis and recommended by the British National Formulary (BNF), they are mentioned in this context (BNF 2009). The decision whether to prescribe alendronate, risedronate, etidronate, ibandronate or zoledronic acid should be taken according to the guideline-recommended order of choice: 1. Alendronate, 2. alternatively risedronate or 3. etidronate (SIGN 2003). The ‘i.v. bisphospohantes’ ibandronate or zoledronic acid should be considered for use in patients who are unable to comply with the instructions for administration for bisphosphonates or have severe gastrointestinal side effects which are very common in bisphosphonate use and can be avoided by intravenous administration (Li et al. 2009b; Reid 2008). Furthermore the dosing intervals (once every three months in ibandronate and once a year in zoledronic acid) may represent a major advantage for patients who are unable to comply with daily or weekly uptake of medication like e.g. patients with cognitive impairment (Jehle and Pfeilschifter 2009).

Alendronate, risedronate and etidronate are the only drugs that have a license for both primary and secondary prevention of glucocorticoid- induced osteoporosis (BNF 2009; NICE 2008; SIGN 2003).

Table 3 Bisphosphonates in the management of osteoporosis, brand names and dosages

Agent	Brand names	Dosages
Alendronate	Fosamax®, Fosavance® (+5600 I.E. vitamin D)	10 mg daily or 70 mg weekly
Risedronate	Actonel®, Actonel plus® (+calcium and vitamin D)	5 mg daily or 35 mg weekly
Etidronate	Didronel®	Administered in a 90 day cycle, each cycle consisting of 400 mg etidronate daily for 14 days followed by 1.25 mg calcium-carbonate daily for the remaining 76 days
Ibandronate	Bonviva®	150 mg p.o. monthly or 3 mg i.v. every 3 months
Zoledronic acid	Aclasta®	5 mg i.v. every 12 months

1.1.7.2.1.1.1. Alendronate

Alendronate is recommended by guidelines for the primary prevention of fragility fractures in

- Women at or over the age of 70 who are diagnosed with osteoporosis and have an independent clinical risk factor for fracture (see) or an indicator of low BMD (see). In women over the age of 75 who present two or more independent clinical risk factors or indicators of low BMD, a DXA scan may not be required if it is considered to be infeasible or inappropriate by the clinician.
- Women at the age of 65 to 69 who are diagnosed with osteoporosis and presenting an independent clinical risk factor
- Postmenopausal women diagnosed with osteoporosis who are younger than 65 and presenting an independent clinical risk factor and at least one indicator of low BMD

as well as for the secondary prevention of osteoporosis (NICE 2008).

Alendronate is the only agent that is licensed for primary prevention in men (BNF 2009; NICE 2008; SIGN 2003).

1.1.7.2.1.1.2. Risedronate and etidronate

Risedronate and etidronate are recommended as alternative treatment options for patients who are unable to comply with the instructions of use for alendronate or have a contraindication to alendronate (NICE 2008).

1.1.7.2.1.1.3. Side effects and administration of bisphosphonates

Side effects associated with bisphosphonates as well as the complicated instructions for use represent major disadvantages of bisphosphonates. Common adverse drug caused by bisphosphonates are dyspepsia, abdominal pain, gastritis and oesophagitis (Peters et al. 2001). The most severe side effect resulting from bisphosphonate is osteonecrosis of the jaw (Lewiecki 2009a). Bisphosponates present a very low bioavailabilty. Hence compliance with the instructions of use is very important. These instructions include the intake with plain water on an empty stomach after an overnight fasting- period at least one hour before the intake of food, liquids or other medications. Patients must remain upright for 30 to 60 minutes after intake in order to avoid side effects within the oesophagus (Peters et al. 2001; SIGN 2003). This complexity of the oral administration of bisphosphonates explains the advantages of the intravenous administrable bisphosphonates ibandronate and zoledronic acid whose three months- respectively 12 months- dosing interval clearly are able to improve the quality of living in patients (Lewiecki 2009a).

1.1.7.2.1.1.4 Mechanism of action of bisphosphonates

All bisposphonates mentioned before are nitrogenous bisphosphonates, meaning that they contain nitrogen. They influence bone metabolism via binding and blocking the enzyme farnesyl diphosphat synthase (FPPS) in the HMG-CoA reductase pathway, which is also known as the mevalonate pathway. Disruption of the mevalonate pathway at the level of FPPS prevents the production of two metabolites, farnesol and geranylgeraniol, which are crucial for the connection of some small proteins to the cell membrane, a process termed ‘prenylation’. The inhibition of protein prenylation via bisphosponates particularly affects proteins in osteoclasts that play a central role in osteoclastogenis, cell survival and cytoskelelet dynamics (Aktories et al. 2005). This mechanism underlies the inhibition of bone resorption promoted by bisphosphonates (Reid 2008).

1.1.7.2.1.2. Selective Estrogen Receptor Modulators (SERMS): Raloxifene

Raloxifene is a selective estrogen receptor modulator (SERM) and is recommended as a treatment option for the primary and secondary prevention of osteoporosis in postmenopausal women (NICE 2008). Raloxifene has been shown to reduce the risk of vertebral fracture by 30 to 50%, but there is no evidence that it reduces the risk of hip- or other non-vertebral fractures (Lewiecki 2009a). Raloxifene provides the beneficial effects of estrogen on bone, but without the negative proliferative effects of oestrogen on breast and endometrium(Rey et al. 2009). Among these beneficial effects of estrogens are an increased DNA synthesis and proliferation of osteoblasts and bone matrix protein production. Furthermore oestrogen represses the number and activity of osteoclasts (Compston 2001). A disadvantage of raloxifene is the increased risk of thromboembolic events (Sontag et al. 2009). Hence raloxifene is not indicated in women with previous or recent thromboembolic events, in women who are at risk for stroke. Furthermore it is contraindicated in pregnant women. Common side effects are leg cramps and hot flashes. Due to the increase in thromboembolic events raloxifene represents a second line agent, which should only be prescribed in patients who are not or poorly tolerating first line therapy (Lewiecki 2009a). Recent studies have indicated that cessation of raloxifene therapy results in accelerated bone loss. Bone loss following cessation of raloxifene therapy at 96 weeks was greater than in the control group. The beneficial effect on bone metabolism of 96 weeks of raloxifene was lost 6 months after cessation of treatment(Naylor et al. 2009).

1.1.7.2.1.3. Calcitonin

Calcitonin is a naturally occurring polypeptide hormone playing a central role in the calcium and bone metabolism (Blahos 2007). Like other antiresorptive drugs it performs its effect on bone health via decreasing bone resorption resulting in an increase in bone mineral density and bone strength (Karsdal et al. 2008). Contrarily to other antiresorptive agents calcitonin shows an additional analgetic effect on bone pain (Blahos 2007). Therefore it can be used to lower pain associated with fractures (Morgan and Kitchin 2008). It appears to target the most active osteoclasts, but unlike other antiresorptive drugs it does not reduce the number of osteoclasts. Calcitonin is available for nasal and subcutaneous application (Karsdal et al. 2008). The usual dose regimen is 200 IU intranasally per day. This dose evidently reduces the incidence of vertebral fractures, but the effect seems to be independent from the dose administered: neither 100 nor 400 IU were associated with a change of incidence of fractures (SIGN 2003). The PROOF- study (Prevent Recurrent of Osteoporotic Fractures) revealed a reduction of 36% in the relative risk of sustaining a new fracture (Blahos 2007).

However, calcitonin has not been shown to reduce the incidence of non- vertebral fractures (SIGN 2003). Recently there have been attempts to find an optimal oral formulation (Karsdal et al. 2008). Calcitonin is licensed for the secondary prevention of osteoporotic fractures in both men and women (BNF 2009; NICE 2008; SIGN 2003). Reported nasal side effects of calcitonin have been found to occur only locally and to be transient and mild (Chatziavramidis et al. 2008).

1.1.7.2.1.4. Strontium ranelate

Strontium ranelate represents an exceptional position since it provides a dual effect of both reducing bone resorption and increasing bone formation (Jehle and Pfeilschifter 2009). It evidently provides efficacy in reducing vertebral, non- vertebral and hip fracture (Li et al. 2009a). Strontium ranelate is licensed for the treatment of osteoporosis in postemenopausal women to reduce the risk of vertebral and hip fracture (NICE 2008). It has a marketing authorisation for both primary and secondary prevention in women, but not for men and not for the treatment of glucocorticoid induced osteoporosis (NICE 2008; SIGN 2003). It is prescribed in patients who can not tolerate or have a contraindication to alendronate and either risedronate or etidronate (NICE 2008). The mechanism of action underlying the effects promoted by strontium ranelate consists on the synthesis of strontium-calcium-hydroxyapatite via strontium substitution on the calcium site in hydroxyapatite (Li et al. 2009a). Strontium ralenate is available as Protelos® 2g sachets which is administered as a suspension in water (NICE 2008). Common side effects are nausea and diarrhoea (Lewiecki 2009a).

1.1.7.2.2. Anabolics

1.1.7.2.2.1. Teriparatide

'Teriparatide' is the term for the polypeptide sequence 1 to 34 in human recombinant parathyroid hormone. Administered subcutaneously on a daily basis it stimulates bone formation. Teriparatide is the only agent not showing antiresorptive activity but solemnly anabolic effect on bone (Lewiecki 2009a). Therefore it represents a separate category, namely the one of 'Anabolics'. The effect wanes with continued application. However the beneficial effect on bone strength was shown for all sites of the skeleton and to continue up to 30 months. Hence there could be strategies implemented which combine the use of teriparatide followed by an antiresorptive drug (Blahos 2007). Long-term treatment with teriparatide, meaning more than two years, is not recommended since its safety has not yet been proven beyond this point (Morgan and Kitchin 2008). Teriparatide is only prescribed in very few cases due to its high costs and the special requirements that have to be met in order to justify its prescription (NICE 2008).

Teriparatide is recommended as an alternative treatment option for the secondary prevention of osteoporotic fragility fractures in those postmenopausal women who

- are unable to take alendronate and either risedronate or etidronate, or have a contraindication to or are intolerant ofalendronate and either risedronate or etidronate

- have a contraindication to, or are intolerant of strontium ranelate

- have had an unsatisfactory response to treatment with alendronate, risedronate or etidronate **and**

  are 65 years or older and have a T-score of –4.0 SD or below, **or** a T-score of –3.5 SD or below plus more than two fractures, **or** who are aged 55–64 years and have a T-score of –4 SD or below plus more than two fractures(SIGN 2003).

Furthermore teriparatide is licensed for the secondary prevention of osteoporosis in men (BNF 2009; NICE 2008; SIGN 2003).

1.1.7.2.3. Hormone replacement therapy (HRT)

Oestrogen monotherapy or combined estrogen/progesterone therapy was shown to efficiently reduce risk of hip, vertebral and other fractures in postmenopausal women (Lewiecki 2009a). Due to the risks of hormone replacement therapy, it should only be implemented very critically (NICE 2008). Oestrogen substitution increases the risk for stroke, thromboembolic events and breast cancer. The FDA recommends the use of HRT only in women at high risk of osteoporosis for whom non-oestrogen medications are considered to be inappropriate (Lewiecki 2009a).

1.2. Pharmaceutical care

Pharmaceutical care is defined as the responsible provision of drug therapy for the purpose of achieving definite outcomes that improve a patient's quality of life (Hepler and Strand 1990). These outcomes are:

- cure of a disease
- elimination or reduction of a patient's symptomatology
- arresting or slowing of a disease process
- arresting a disease or symptomatology (Hepler and Strand 1990)

Pharmaceutical care is described as a 'patient-centred practice in which the practitioner assumes responsibility for a patient's need' (Cipolle et al. 2004).

By the beginning of the 20th century, the pharmacist's role mainly consisted on preparing and selling medicinal drugs, a service that was gradually taken over by the pharmaceutical industry. The profession was reduced to the distribution of drugs. By the mid 60's, drugs of higher complexity emerged. Drug-to-drug interactions and adverse drug reactions brought up the needs for clinical pharmacists whose appropriate knowledge and skills enabled the assurance of optimally safe and efficient drug use. In 1987 the United States Food and Drug Administration (FDA) reported 12,000 deaths and 15,000 hospital admissions due to adverse reactions in prescribed drugs. This number is estimated to be only 10% of the actual number of cases (Strand et al. 1991). The need for pharmaceutical care results from multiple practitioners prescribing for one patient and a large number of drugs and related information available for the patient (Cipolle et al. 2004).

Cipolle et al define key concepts of pharmaceutical care as optimizing a patients drug therapy by using drug therapy appropriately for each medical condition, using the most effective and safest drug, reassuring that the patient is willing and able to take a medications as intended to and identifying as well as resolving drug related problems. Pharmaceutical care can be applied in all settings, community pharmacy, hospital, long term care and clinic for all kinds of patients with all kinds of diseases and all kinds of drug therapy (Cipolle et al. 2004).

Cipolle et al described the stages of a patient care process to be:

- *assessment of the patient:* patient data (demographic information, medication experience) ,disease data (current medical condition, medical history, nutritional status) as well as drug data (current medications, past medications, allergies, alerts) are assessed in order to understand a patient's medical problems to make decisions regarding therapy with him or her

- *care plan development:* to negotiate and agree upon endpoints and timeframe for pharmacotherapies, to establish goals. The appropriate therapeutic intervention has to be selected by considering alternative treatment options, selecting patient-specific drug therapy, taking into account non-drug interventions and educating the patient.

- *follow up evaluation*: To evaluate effectiveness of pharmacotherapy and safety of the latter, to determine a patient's compliance. To judge the clinical condition of a patient while being treated and to identify new drug related problems and their cause. To provide continous care.(Cipolle et al. 2004)

Nevertheless several barriers for the implementation of pharmaceutical care exist which vary between different countries and include education, skills, resources and environment. Though, different studies indicate the value of the provision of pharmaceutical care in patients with diabetes, asthma, hypertension, chronic pain, psychiatric disorders as well as in polymedicated patients (Berenguer et al. 2004).

As mentioned before, provision of patient-specific drug therapy as well as development and implementation of plans of care designed to provide the highest benefit for the patient are crucial aspects of pharmaceutical care (Strand et al. 1991). Nonetheless there are other aspects. The major link between pharmaceutical care and osteoporosis represents the need for increased screening and awareness of the risk of osteoporosis in order to prevent fractures and related mortality, morbidity and costs. Awareness programmes performed by pharmacists in the community setting can engage more people to refer themselves for a DXA scan and diagnosis. Pharmaceutical care in the field of osteoporosis consists on screening patients to identify those who are at high risk of osteoporosis and create awareness among patients. Furthermore the provision of relevant recommendations concerning lifestyle modifications and support with drug compliance are crucial aspects in the pharmaceutical care of osteoporosis (Law and Shapiro 2005). In Scotland there are strategies to prevent people from falling and sustaining fractures performed by pharmacists (Lowrie 2008). All these aspects represent pharmaceutical care.

1.2.1. A model of care for the management of osteoporosis

A model of care for osteoporosis was designed by Anton Luf in 2009 to enable a better detection and management of osteoporosis. Within this potential service the community pharmacy plays a central role. Men above the age of 50 and postmenopausal women presenting a prescription for chronic medication in a community pharmacy are invited to a screening process consisting of a questionnaire. The questionnaire includes age, weight, height, fractures resulting from mild falls, parental history of hip fracture, smoking status and alcohol intake. An entry in the patient's Pharmacy Medication Record (PMR) is made in order to document the patient has been recruited. Besides the questionnaire a questionnaire for the pharmacist exists. The pharmacist completes the questionnaire via accessing patient data from the PCR and asking the patient directly. The pharmacist questionnaire consists of questions like gender, diagnosis of osteoporosis, rheumatoid arthritis and diabetes mellitus type 1.

Patients who have a reported diagnosis of osteoporosis are recordedfor evaluation using GPASS data. For patients without a recorded diagnosis of osteoporosis the risk of osteoporosis is interpreted. 10 year fracture probability is calculated by applying patient information retrieved from both questionnaires to the FRAX® tool. The action required by the FRAX® is identified and the patient is informed during his or her next visit. Patients with a fracture probability in the amber or red zone (this means their fracture probability exceeds the assessment threshold) are referred to the GP for a DEXA scan. Patients in the green zone (which means that their fracture risk is below the assessment threshold) are verified to be at low risk. Patients with a recorded diagnosis of osteoporosis, rheumatoid arthritis or diabetes mellitus type 1 are verified as candidates for MAT-assessment via GPASS®. In patients referred for BMD measurement a DXA scan at least at two specific sites is performed. Osteoporotic and osteopenic patients are identified by using WHO T-Score thresholds. MATosteo is applied to calculate applicability and adherence to guideline recommendation. Audit findings are used to identify care issues for follow-up with the GP. Specific treatment decisions for the individual patient are made according to clinical guidance and a treatment plan is created.

Both osteoporotic/osteopenic patients as well as patients with normal bone mass are given specific advice concerning regular low impact weight bearing exercise, high intensity strength training, smoking cessation, reduction of alcohol consumption to less than 10 units/week and calcium rich diet with an aimed intake of more than 1000 mg/day in order to prevent (further) bone loss. During a follow-up process the patient's understanding of prevention advice and treatment administration instructions is checked, the patient is informed about possible treatment changes agreed on with the GP after applying the MAT and possible clinical risk factors like e.g. falls can be identified (Luf 2009).

1.3. Clinical guidelines

Clinical guidelines represent the view of the institute establishing them and are based on the available evidence. Healthcare professionals are expected to fully follow the guidelines although decisions have to be made according to the individual circumstances in individual patients (NICE 2008).

In the UK, two clinical guidelines provide recommendations for the management of osteoporosis in practice:

- Scottish Intercollegiate Guidelines Network (SIGN) Guideline 71: Management of Osteoporosis (2003) and
- National Institute for Health and Clinical Excellence (NICE) Technology Appraisal Guidance 160 *(Alendronate, etidronate, risedronate, raloxifene and strontium ranelate for the primary prevention of osteoporotic fragility fractures in postmenopausal women*) and 161 (*Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women*)

Both deal with the management of osteoporosis and the timely identification of osteoporotic patients and the prevention of osteoporotic fractures in particular (NICE 2008; SIGN 2003). Treatment recommendations are based on meta- analyses, systematic reviews of randomised controlled trials (RCTs), case control and cohort studies, case reports and expert opinions. The level of evidence is categorised into eight different levels, depending on the quality of the source the evidence is based of (e.g. evidence drawn from reviews with high risk of bias is less reliable than evidence from reviews with low risk of bias). Grade of recommendation ranks from A to D, referring to the strength of evidence on which the recommendation is based (SIGN 2003)

1.4. Clinical audit and medication assessment tool (MAT)

NICE defines a clinical audit as a 'quality improvement process that seeks to improve patient care and outcomes'. During the process of a clinical audit, a systematic review of care is conducted. An assessment whether explicit standards are met or not is conducted. These standards are based on the best available evidence. In case the standard is not met, the reason for this non- adherence has to be identified and change has to be implemented. An agreement on change should result in the establishment of an action plan. The audit should be re-conducted in the future In order to sustain improvement (NICE 2002)

A medication assessment tool enables the researcher to conduct an assessment of quality of medicines use. In other words, it represents a systematic approach to measure quality of prescribing. The MAT is comprised of a certain number of criteria; each criterion is based on an evidence based guideline recommendation. Clinical guidelines are nowadays of increasing importance in the delivery of healthcare. The identification of low or intermediate adherence to guideline recommendation can be used as a systematic process to address pharmaceutical care issues in case discussions with prescribers(McAnaw et al. 2003).

In 2007-08, Ms Aisha Al- Harthi, MSc in Clinical Pharmacy student in the University of Strathclyde, developed the first draft of a MAT for osteoporosis (MATosteo) comprising of 20 criteria. In 2008, Eva Past further developed the MAT resulting in 23 criteria (Past 2008). Johanna Schlais modified the MAT in 2008. It was then comprised of 26 criteria (Schlais 2008). In 2009, Anton Luf adapted the MAT to current guideline recommendations, reducing the number of criteria to 21. The current MATosteo, referred to as 'final tool' was further developed by the research group (see appendix 3) and consists of 19 criteria.

1.5. GPASS® and READ codes

GPASS®, the 'General Practice Administration System for Scotland' is a software programme to manage, store and retrieve patient records. It is widely used in Scotland, approximately 80% of Scottish GPs are currently using GPASS®. This IT-system allows to register patients electronically as well as to refer patients to hospitals electronically. GPASS® is liked to laboratories, so laboratory results are received electronically by the GP. Furthermore electronic transfer of prescriptions to pharmacies is emerging. GPASS® puts a barcode on each prescription which is scanned by the pharmacist and stored electronically in the pharmacy (NHSScotland 2009).

READ codes represent clinical terms. Clinical terms are categorised in topics such as 'signs and symptoms', 'treatment and therapies', 'investigations', 'occupations', 'diagnosis', 'drugs' and 'appliances'. Each clinical term is encoded by a unique READ code. READ codes are intended for use by healthcare professionals for clinical application and allow recorded material to be stored and analysed for purposes of audit and statistics (NHSUK 2009). Patient data such as diagnoses, drugs etc is stored in the form of READ codes in the GPASS® software system (NHSScotland 2009).

1.6. Microsoft Access

Microsoft Access® is a database to store and retrieve data. The user can create e.g. tables (enables to store the information in rows and columns) and queries (enables to store information in questions). Data can be stored, manipulated and analysed in an easy way(Harkin et al. 1999).

2- AIMS AND OBJECTIVES

2.1. Aims

The aims of this project wereto

- demonstrate the use of a medication assessment tool for osteoporosis (MAT_{Osteo}) in the evaluation of the level of adherence to osteoporosis guidelines.
- demonstrate inter-rater reliability of the tool
- assess the value of a fracture risk evaluation service provided by community pharmacists

2.2. Objectives

- To undertake a literature review of the epidemiology of osteoporosis and measures taken by public health experts in order to address the disease.
- Revise a MAT_{Osteo} (originally designed by previous researchers) and redesign database protocols. Test the protocols on a GPASS® database and evaluate inter-rater reliability.
- Test the sensitivity of the MAT_{Osteo} in a comparison of patient samples drawn from two clinical settings and further revise the tool as necessary.
- Test on a larger scale audit the revised $MAT_{Osteo.}$ and compare results with those of another student.
- Validate a potential service by which community pharmacists might contribute to osteoporosis detection and management. Propose potential starting points for community pharmacists to get involved in osteoporosis detection and management.

3- STUDY DESIGN

The study is a retrospective survey including the application of a tool designed for medication assessment in the field of osteoporosis.

3.1. Subjects and Settings:

3.1.1. Subjects

3.1.1.1. Patients

Data of two different samples of patients was extracted from GPASS®. The first sample of patients comprised patients from two general practitioner practices in Clydebank and Paisley previously drawn from GPASS® during an earlier project to design the MAT_{Osteo}. Data of a second sample of patients was extracted from GPASS®, patients were recruited from a third practice, a GP practice in Springburn.Inclusion criteria for patients for whom specific guideline criteria are applicable were

- Patients alive who are registered with the GP practice on date
- Patients who are diagnosed with osteoporosis or osteopenia

3.1.1.2. Interviewees

Interviews were conducted with interviewees drawn from community pharmacy, general practice medicine, fracture risk clinics and public health specialists.

3.1.2. Settings

Settings were GP practices that offered permission for the audit. The patients should be situated in general medical practice within Community Health Partnerships in Renfrewshire and/or Greater Glasgow.

Interviews were conducted with interviewees who have been nominated to participate and accepted the invitation, including health care professionals in Glasgow and Malta.

3.1.3. Study site

The project was conducted at the University of Strathclyde, Glasgow, UK.

3.1.4. Investigator

The investigator was a diploma student at the University of Vienna (Austria) and a visiting scholar at the University of Strathclyde, UK.

3.1.5. Supervision

Prof Stephen A Hudson, Professor of Pharmaceutical Care and Dr Julienne Johnson, lecturer in Pharmacy Practice, within the Pharmaceutical Care Health Service Unit at the University of Strathclyde, Glasgow, and Prof Oskar Hoffmann from the Department of Pharmacology and Toxicology, University of Vienna, supervised this project. The research group referred to in this project included the supervisors, the investigator and another student.

3.1.6. Collaborators

Collaborators were Mr Ian Towle, Senior Teaching Fellow within the Pharmaceutical Care Health Service Unit at the University of Strathclyde who enabled the data extraction from site C. Mrs Susan McKellar, research assistant, was involved in the data analysis.

4- METHODS

4.1. Literature research

At first, a literature research was conducted in order to identify current evidence- based recommendations for the treatment and management of osteoporosis. The investigator mainly focussed on the guidelines published by the Scottish Intercollegiate Guidelines Network (SIGN) since they represent the most relevant information source for Scotland. Furthermore the National Institute for Clinical Excellence (NICE) has provided a technological appraisal including guidance both for primary and secondary prevention of osteoporosis. Both of them have also been taken into account. They are valid for the whole of the United Kingdom.

In addition, the database MEDLINE was consulted via the search engine PubMed in order to gain further background information regarding the need of pharmaceutical care in this context. For this purpose, different search keywords were used alone or in various combinations. The results given by PubMed were narrowed down by specification of the keywords as well as by use of the search function on the journal papers homepages.

4.2. Medication assessment tool- MATosteo

A medication assessment tool (MAT) for the management of osteoporosis was designed by previous researchers. Originally developed by Aisha Al- Harthi in 2008, MATosteo was reviewed by several researchers. Eva Past and Johanna Schlais changed the MAT from originally 20 criteria to 28 respectively 26 criteria (Past 2008; Schlais 2008). In 2009, Anton Luf reviewed the MATosteo, creating a tool comprised of 21 criteria. During this project, the research group further revised the MATosteo. The number of criteria was reduced to 19 criteria.

The MAT is a criterion based tool, each criterion representing a certain guideline recommendation. Each criterion consists of two parts termed **qualifier** and *standard* (see example below). The qualifying statement identifies patients who are eligible for application of the standard. The standard expresses the action that should be implemented in those patients who meet the requirements defined within the qualifier.

Example for a MAT- criterion:

A patient with a diagnosis of disease X…	**qualifier**
…should be prescribed the drug Y.	standard

To each criterion six answer categories were possible (Yes, unjustified non-adherence, justified non-adherence, insufficient data on the standard, insufficient data on the qualifier and not applicable). After applying the MAT criteria to the data set, two main values were calculated: adherence to the requirements set up in the standard and applicability to the qualifying statement. Adherence and applicability were calculated by using the following formulas:

$$Adherence = \frac{\sum Yes}{\sum Yes, No(U), IDS} \times 100$$

Equation 1

$$Applicability = \frac{\sum Yes, No(U), IDS}{n} \times 100$$

Equation 2

(95% confidence intervals; 'n' representing the total number of criteria)

The level of adherence was ranked arbitrarily as follows:

≥70% **High** level of adherence

50-69.9% **Intermediate** level of adherence

<50% **Low** level of adherence

The following table shows six possible answers to the MAT criteria.

Table 4 Six answer-categories to MAT criteria

Answer	Explanation
Not applicable – NA	The patient does not meet the qualifying statement. He/she is not diagnosed with disease X.
Yes	A certain treatment recommended by the guidelines is implemented in eligible patients. The patient with disease X receives drug Y.
No, unjustified – No(U)	The action was not implemented. The patient with disease X does not receive drug Y and there is no explicitly documented reason for the non-prescription.
No, justified – No(J)	The action was not implemented but the prescriber reported an explicit reason (i.e. a justification) for not complying with the standard. The patient with disease X does not receive drug Y for a justified reason.
Insufficient data on the qualifier - IDS	There is not enough information available whether the patient meets the requirements set up in the qualifier. The investigator cannot identify if the patient was actually diagnosed with disease X. Therefore it cannot be ascertained if the standard was implemented correctly.
Insufficient data on the standard – IDQ	There is not enough information available if the action was implemented. The investigator cannot identify if drug Y was prescribed.

4.3. Data Collection

In Scotland patients' data is stored in GPASS®. This software program enables the quick accessibility of recorded data.The data is listed in chronological order and can be ranked easily according to the information needed like e.g. age, sex, medication, READ codes etc. The extracted data was sorted and downloaded into an Access database by using Microsoft queries, which have been especially created for GPASS®. The inclusion criteria for patients for whom specific guideline criteria were applicable were:

- Patients alive who are registered with the GP practice on date
- Patients who are diagnosed with osteoporosis or osteopenia

Three GP practices within Greater Glasgow offered permission for the audit. 319 patients were applicable to a clinical audit of adherence to specific guidelines. Data including sex, age, medication, DEXA scans, sustained fractures, alcohol consumption, BMI and clinical conditions like chronic kidney disease (CKD), rheumatoid arthritis, Morbus Crohn, thrombosis etc and parameters like e.g. GRF were extracted from

GPASS® and stored in Microsoft Excel® spreadsheets before being imported to a Microsoft Access® database.

The data collection has caused certain difficulties since many clinical parameters like e.g. GFR and T-Scores were not accessible.

4.4. Data analysis

The data analysis was performed by using the Microsoft Access® form 'Query Builder'. This form has been designed previously during the course of a different project by Tobias Dreischulte. It represents a tool, which enables the investigator to analyze, store and retrieve patient data (see section 4.5.). The instructions, how to apply Microsoft Access® to the sample of patient data, have been previously designed by Johanna Schlais in 2008 in form of so called 'Database protocols'. These database protocols enable independent researchers to apply the MAT to various sets of data. The use of database protocols guarantees results showing reproducibility not varying from researcher to researcher. The database protocols were redesigned and adapted to the needs of the 'Query Builder', which was applied in this context for the first time. In addition further changes were done upon the data base protocol in order to clarify and shorten it and a manual how to use the 'Query Builder' was created in order to ensure reproducibility of results achieved by successive researchers. The newly designed database protocols were tested on a GPASS® database.

Two independent researchers applied the revised MAT to the same set of data in order to evaluate inter-rater reliability. Sensitivity of the MAT was tested on three patient samples. All examinations were performed in Microsoft Access® and the results stored and further calculated in Microsoft Excel®.

4.5. Query Builder

As mentioned before, the Query Builder is a Microsoft Access® form which enables the researcher to retrieve information whether a single patient or a sample of patients are adherent to a certain statement set up in guideline recommendation. Certain specific data can be accessed rapidly, but before applying the Query Builder to the dataset, appropriate tables containing all the data intended to be assessed have to be created.

As first step, the appropriate READ codes representing diagnosis, clinical conditions, drugs and clinical investigations which were relevant in the context of this project were identified and a table in Microsoft Excel®created. The READ codes were drawn from the Internet. Due to the existence of subsets of READ codes, so called 'MAT Data items' were created in order to eliminate the task of scanning the data for all kind of

subtypes of READ codes. For each subset of READ Codes, a MAT data item summarizing different READ Codes with the same meaning was created.

Table 5 Example for MAT data items

READ Code	Description	MAT Data item
N3305	Drug-induced osteoporosis	Osteoporosis
N330C	Osteoporosis localized spine	Osteoporosis
N3318	Osteoporosis + Pathological fracture of lumbar vertebrae	Osteoporosis
N3319	Osteoporosis + Pathological fracture of thoracic vertebrae	Osteoporosis
N331A	Osteoporosis + Pathological fracture of cervical vertebrae	Osteoporosis

A table containing the patients' patient keys, READ codes encoding all kinds of patient information and the date on which the record was made on GPASS® was created. The Query Builder is a very efficient, but sensitive tool and depends largely on consistency in terms of nomenclature. For this reason it is necessary to term the created table 'Patients: NHS Read codes_QOF and MAT data items_tbl'. The table was created in Microsoft Excel®.

Table 6 Examples for: Patients: NHS Read codes_QOF and MAT data items_tbl

PatientKey	ReadCode	MAT Data item	DateRecorded
1103.C8746.Patient	ZQ021	CHD	24/01/2005
1105.C8746.Patient	42W..	DM	17/07/2002

The uncommon spelling 'ReadCode' without capital letters and a space between the two terms results from the sensitivity of the Query Builder concerning changes in naming.

Furthermore the table 'Patients: Drug History_tbl' was created in Microsoft Excel® containing patientkey, drug name, drug category, preparation, dose and frequency.

Table 7 Examples for: 'Patients: Drug History_tbl'

PatientKey	drug_name	drug_category	preparation	dose	frequency
1035.C8746.Patient	Omeprazole	PPI	CAPS 10MG	1 Cap	In the morning
1033.C8746.Patient	Furosemide	Loop diuretics	TABS 40MG	2 Tabs	In the morning

In the same manner the table 'Patients: Investigations_tbl' was created. For each subset of values a MAT data item was created. Besides patientkey and data item this table is composed of the value and the unit measure of the individual investigation as well as of the date at which the investigation had taken place. e.g.:

Table 8 Examples for table 'Patients: Investigations_tbl'

PatientKey	data_item	Value	Unit ofMeasure	DateRecorded
1033.C8746.Patient	Overweight	34.21	kg/m2	14.06.2005
1051.C8746.Patient	BMI	16.29	kg/m2	07.12.2007

Again the uncommon spelling results from the necessity of adhering to the spelling set up in the Query Builder.

The created tables were imported to Microsoft Access®.

4.4. Database Protocols

The database protocols have been designed in order to enable the application of the MATosteo to patient data drawn from GPASS®, a software program enabling storage and management of patient data. For each MAT criterion a separate database protocol exists. The individual database protocols were merged into one entire protocol containing the instructions how to apply the 19 criteria of the MAT to an individual sample of patients. In a previous project conducted by Johanna Schlais, READ codes were used to identify eligible patients who were meeting the qualifier and/or standard. Patient data is stored in form of READ codes in the GPASS® system. A patient with a diagnosis of osteoporosis would not be recorded as 'osteoporotic' or 'osteoporosis', but

with the READ code 'N330' encoding osteoporosis. Similarly, READ codes are used to encode all kind of other diseases and conditions, drugs that were prescribed in a patient as well as investigations conducted. A disadvantage of processing patient via the use of READ codes is the existence of subsets of READ codes. As shown in the example below, there are 18 different subtypes of READ codes encoding for a DEXA scan performed on spine or hip. The research group agreed on merging subsets of READ codes and on creating so call 'MAT data items' simplifying the database protocols.

In former database protocols, patients who were adherent to the requirements of qualifier and/or standard were identified by accessing 'queries' within Microsoft Access®. Queries had to be built up by using READ codes in order to identify patients receiving certain drugs, diagnosed with certain diseases or conditions etc. Using the 'Query Builder' simplified this since it was not necessary anymore to run large number of queries as required by previous database protocols.

Table 9Database protocol of a MAT criterion designed by J. Schlais

Criterion 4		
Measurement of the BMD by DEXA scan *Is performed at least at the two specific sites – namely anteroposterior spine and hip*		
Identify patients, who comply with qualifier as follows (Denominator):		
Identify patients with a diagnosis of osteoporosis/osteopenia		
Step 1	Inclusion of osteoporosis	
	READ code [N330.., NyuBC]	**GPASS sampling**
DEXA scan is performed at least the two specific sites (Numerator)		
Step 2	Inclusion of those with measurement of the BMD by DEXA scan – anteroposterior spine and hip	
	Apply a Query using READ code [58F, 66U6, 58EG, 58EH, 58EC, 58ED, 58EE, 58EF, 58EG, 58EH, 58EI, 58EJ, 58EL, 58EM, 58EN, 58EK, 58EN, 58EM]	**Access Query, Manually**

This criterion deals with the evidence- based recommendation that measurement of BMD should be performed at two specific sites, namely spine and hip in order to achieve reliable results. It represents a retrospective assessment whether osteoporotic or osteopenic patients have been diagnosed according to guideline recommendation. A

query was applied for this criterion by using several READ codes expressing various methods of BMD- measurement. Individual patients had to be examined manually by comparing the dates on which the examinations had been performed in order to find out whether the DEXA scan had been performed at both sites.

Table 10 Database protocol of the same criterion in the new draft

Criterion 2 Measurement of the BMD by DEXA scan *Is performed at least at the two specific sites – namely anteroposterior spine and hip*		
Step	**What?**	**How?**
Step 1	Identify patients with a measured BMD by DEXA scan measured on two specific sites	**Use** form 'Query maker' in Microsoft Access® **Select** in 'Read code' field: • 'Hip scan' for criterion 1 • 'Lumbar scan' for criterion 2 **Press** 'view' **Create** a new query by using 'design view' **Select '**tbl_temp' **Apply '**patientKey', c1[1], c2[1], d1, d2 **In 'SQL view' change** 'and' to 'or' → [(((tbl_temp.c1)="1")) **OR** (((tbl_temp.c2)="1"));]
Step 2	Identify Yes, No(U)	**Export** results to Microsoft Excel® ➔ Patients with a DEXA scan performed on two specific sites at the *same day!*= Yes ➔ Patients with a DEXA scan performed on only one site or with DEXA scans performed on two specific sites but not at the same day= No(U) ➔ No(J)=0 (there is no justification for non-adherence)

The step of GPASS® sampling was excluded since patient suffering from osteoporosis and osteopenia had been identified previously on GPASS® via use of READ codes and had been stored in appropriate tables within the Query Builder. Similarly, information concerning individual BMD-measurements in individual patients had been stored in tables. This information can now be accessed at this stage by selecting the terms 'Hip scan' and 'Lumbar scan' for the criteria- fields of the so called READ code-

field of the 'Query Builder'. By pressing the icon 'view', hip- and spine-scans on eligible patients are displayed. Unfortunately it is necessary to run a query in order to specify the results. By changing the 'AND' in the SQL- View to 'OR', all performed scans are displayed. Otherwise only patients who indeed have had scans performed on both sides would be displayed. That way it is also possible to indicate non-adherent patients who had a scan performed only on one site. This step might just be excluded in case the investigator does not request the information mentioned before.

4.5. Validation of a potential community pharmacy-service

A validation of a potential community pharmacy-based service for detection and management of osteoporosis was conducted via performance of interviews with healthcare specialists form community pharmacy, general practice medicine, fracture risk clinics and public health specialists in order to assess whether an application of MATosteo together with a fracture risk assessment score can provide a feasible and reliable audit delivered by community pharmacists alongside with GPs. For this purpose, a certain interview schedule was designed to gain relevant information from healthcare specialists.

5- RESULTS

5.1. Revision of MATosteo

The draft of the MATosteo designed by Anton Luf was further revised mainly in terms of wording and numbering. Criterion 1 was reworded from 'A patient diagnosed with osteoporosis *has been assessed by DEXA scan*' to 'A patient diagnosed with osteoporosis *has a recorded DEXA scan to confirm osteoporosis*' in order to point out the diagnostic background of the DEXA scan.

In former criterion 6, which was renumbered to criterion 10 teriparatide as well as contraindications to teriparatide were added to the list of different agents eligible for osteoporosis treatment.

Former criteria 14, 15 and 16, each of them assessing the prescribing of a single bisphosphonate, namely alendronate, risedronate and etidronate, were combined to criterion 14 of the final draft. This criterion enables the investigator to scan a patient's prescription records for those three bisphosphonates as well as to determine whether a patient was prescribed the preferred choice by checking manually the dates on which the individual bisphosphonate has been prescribed.

Former criterion 19 dealing with the prescribing of raloxifene and strontium ranelate in postmenopausal women who are intolerant to bisphosphonates and requiring secondary prevention of fractures, was renumbered to 17. Strontium ranelate was removed from this criterion since its use is assessed on sufficiently in criterion 16.The condition 'with a diagnosis of osteoporosis' formally required by the qualifier was removed. The condition 'with at least one osteoporotic fracture' was reworded to 'is receiving it for secondary prevention' and moved from the qualifier to the standard, as well as the requirement 'has an identifiable reason for not being prescribed a bisphosphonate'.

In criterion 18, which deals with the prescribing of teriparatide, the requirement 'postmenopausal woman diagnosed with osteoporosis' was removed since the age, which is required in order to receive teriparatide, includes being postmenopausal (55 and older).The term 'who has an contraindication to strontium ranelate' was removed since possible contraindications to strontium ranelate are pregnancy and

breastfeeding, conditions practically impossible in patients receiving teriparatide due to the age required for the prescription of teriparatide, namely 55 and over.

Similar changes were done to criterion 19 dealing with the prescribing of calcitonin.

The following table indicates the revision of MATosteo in detail by comparing the final draft, which was agreed on by the research group with the previous draft produced by Anton Luf.

Table 11 Comparison MATosteo final draft with draft Anton Luf

Criterion	Draft Anton Luf	Final draft	Comments
1	**A patient with a diagnosis of osteoporosis** has been assessed by DEXA scan [Justification for not referring to a DEXA Scan Patient ≥ 60 years and ≥ 2 vertebral fractures imply a diagnosis of osteoporosis or a postmenopausal woman ≥ 75 years and two or more independent clinical risk factors for fracture or indicators of low BMD] **Independent clinical risk factors** ❑ low body mass index defined as less than 22 kg/m² ❑ ankylosing spondylitis ❑ Crohn's disease ❑ conditions that result in prolonged immobility ❑ untreated premature menopause **Indicators for low BMD** ❑ parental history of hip fracture, ❑ alcohol intake of 4 or more units/d ❑ rheumatoid arthritis	**A patient with a diagnosis of osteoporosis** has a recorded DEXA Scan to confirm osteoporosis [Justification for not being assessed by DEXA scan to confirm osteoporosis Patient ≥ 60 years and ≥ 2 vertebral fractures imply a diagnosis of osteoporosis or a postmenopausal woman ≥ 75 years and two or more independent clinical risk factors for fracture or indicators of low BMD] **Independent clinical risk factors** ❑ low body mass index defined as less than 22 kg/m² ❑ ankylosing spondylitis ❑ Crohn's disease ❑ conditions that result in prolonged immobility ❑ untreated premature menopause **Indicators for low BMD** ❑ parental history of hip fracture, ❑ alcohol intake of 4 or more units/d ❑ rheumatoid arthritis	Thewording of the criterion was slightly changed in order to point out the diagnostic background of the DEXA scan.

2	**Measurement of the BMD by DEXA scan** is performed at least at the two specific sites – namely, anteroposterior spine and hip.	The same	
3	**A patient with a recorded diagnosis of osteoporosis** is prescribed supplementary calcium (±vitamin D). [Justification for non-prescribing calcium and vitamin D: There is a record that the patient has an adequate dietary intake of calcium and no vitamin D deficiency.]	The same	
4	**A patient with a recorded diagnosis of osteoPENIA** is prescribed supplementary calcium (± vitamin D) for the prevention of osteoporosis. [Justification for non-prescribing calcium and vitamin D: There is a record that the patient has an adequate dietary intake of calcium and no vitamin D deficiency.]	The same	
5	**A patient with confirmed vitamin D deficiency or aged ≥ 65** is prescribed vitamin D.	The same	
6	**A patient with osteoporosis and NOT prescribed any of the following:**	**A patient prescribed supplementary calcium**	The criterion was revised concerning contents and numbering. Teriparatide

	bisphosphonates, raloxifene, strontium ranelate or calcitonin has a recorded contra-indication to each agent (see below) [Contraindications to bisphosphonates are: ☐ oesophageal strictures or achalasia ☐ inability to remain upright for > 30 min after ingestion ☐ hypocalcaemia ☐ osteomalacia (etidronate) ☐ moderate renal impairment (CrCl < 35 mL/min) ☐ pregnancy and breast feeding] [Contraindications to raloxifene are: ☐ past/present venous thromboembolic events ☐ hepatic impairment ☐ cholestasis ☐ severe renal impairment (CrCl < 10 mL/min) ☐ endometrial cancer ☐ uterine bleeding ☐ pregnancy and breast feeding] [Contraindications to strontium ranelate are: ☐ pregnancy and breast feeding ☐ hypersensitivity] [Contraindications to calcitonin are: ☐ hypocalcaemia ☐ hypersensitivity]	is prescribed a daily dose of 500 – 1500 mg calcium.	and contraindications to teriparatide were added to the list. See criterion 10 final draft. Former criterion 6 in the draft Luf is now criterion 10.
7	**A patient prescribed supplementary calcium** is prescribed a daily dose of 500 – 1500 mg calcium.	**A patient prescribed vitamin D** is prescribed a daily dose of 10 – 20 μg (400 - 800 IU) vitamin D.	Criteria 7 and 8 remained identical concerning contents but were changed regarding numbering from former 7 in draft Luf to 6 in the final draft respectively 8 to 7.

8	**A patient prescribed vitamin D** is prescribed a daily dose of 10 – 20 μg (400 - 800 IU) vitamin D.	**Apatientwith a recorded diagnosis of osteoporosis** is prescribed an oral bisphosphonate as first-line therapy. Recorded reasons for non-conformance (justification):	As mentioned before, criterion 8 draft Luf represents criterion 7 final draft. Criterion 8 of the final draft was changed concerning numbering, it is consistent with criterion 10 draft Luf.
9	**A patient with osteoporosis and NOT prescribed any of the following: bisphosphonates, raloxifene, strontium ranelate or calcitonin** is prescribed ≥1000mg calcium plus 800 IU vitamin D per day	**A patient with a recorded diagnosis of osteoPENIA** is prescribed an oral bisphosphonate as first-line therapy. Recorded reasons for non-conformance (justification):	See criterion 11. Contents and wording remained identical, numbering was changed from former 9 to 11.
10	**Apatientwith a recorded diagnosis of osteoporosis** is prescribed an oral bisphosphonate as first-line therapy. Recorded reasons for non-conformance (justification):	**A patient with osteoporosis and NOT prescribed any of the following: bisphosphonates, raloxifene, strontium ranelate, calcitonin or teriparatide** has a recorded contra-indication to each agent (see below) [Contraindications to bisphosphonates are: ☐ oesophageal strictures or achalasia ☐ inability to remain upright for > 30 min after ingestion ☐ hypocalcaemia	Criteron 10 draft Luf represents criterion 8 final draft. Contents and wording remained identical. Criterion 10 in the final draft represents criterion 6 draft Luf. Teriparatide and contraindications to teriparatide were added to the list.

		☐ osteomalacia (etidronate) ☐ moderate renal impairment (CrCl < 35 mL/min) ☐ pregnancy and breast feeding] [Contraindications to raloxifene are: ☐ past/present venous thromboembolic events ☐ hepatic impairment ☐ cholestasis ☐ severe renal impairment (CrCl < 10 mL/min) ☐ endometrial cancer ☐ uterine bleeding ☐ pregnancy and breast feeding] [Contraindications to strontium ranelate are: ☐ pregnancy and breast feeding ☐ hypersensitivity] [Contraindications to calcitonin are: ☐ hypocalcaemia ☐ hypersensitivity] [Contraindications to teriparatide are: ☐ pre-existing hypercalcaemia ☐ skeletal malignancies or bone metastases ☐ metabolic bone diseases ☐ including Paget's disease and hyperparathyroidism ☐ unexplained raised alkaline phosphatase ☐ previous radiation therapy to the skeleton]	
11	**A patient with a recorded diagnosis of osteoPENIA** is prescribed an oral bisphosphonate as first-line therapy. Recorded reasons for non-conformance (justification):	**A patient with osteoporosis and NOT prescribed any of the following: bisphosphonates, raloxifene, strontium ranelate or calcitonin** is prescribed ≥1000mg calcium plus 800 IU vitamin D per day	Numbering was changed from former 11 to 9. Criterion 11 of the final draft represents criterion 9 draft Luf.

12	**A patient who is prescribed a bisphosphonate** has no reason *on record* to avoid bisphosphonates. [Reasons to avoid bisphosphonates are: ❑ contraindication to bisphosphonates o oesophageal strictures or achalasia o inability to remain upright for > 30 min after ingestion o hypocalcaemia o osteomalacia (etidronate) o moderate renal impairment (CrCl < 35 mL/min) o pregnancy and breast feeding ❑ inability to comply with the instructions for use of bisphosphonates o ingestion on an empty stomach o washing the medication down with 250 ml water o avoidance of food for 30 min o avoidance of lying flat within 30 min of ingestion ❑ unsatisfactory response to bisphosphonates o another fracture occurs o decrease in BMD despite adherence to treatment ❑ intolerance to bisphosphonates o oesophageal ulceration o erosion or stricture o severe lower GI symptoms] o	The same	
13	**A patient receiving treatment for osteoporosis/osteopenia**	The same	

	is prescribed a standard dose regimen.		

❑ **Prevention (in osteopenia)**	❑ **Treatment (of osteoporosis)**
Postmenopausal Osteoporosis	
❑ Alendronic acid	
5 mg daily PO	10 mg daily or 70 mg once weekly PO
❑ Disodium etidronate	
400 mg for 14 days PO; 1,25 g calcium carbonate for 76 days PO	400 mg for 14 days PO, 1,25 g calcium carbonate for 76 days PO
❑ Ibandronic acid (not in guidelines)	
	150 mg once a month PO or 3 mg every 3 months IV
❑ Risedronate sodium	
5 mg daily PO	5 mg daily PO or 35 mg weekly PO
❑ Calcitonin	
	200 units daily intranasally
❑ Raloxifene	
60 mg daily PO	60 mg daily PO
❑ Strontium ranelate	
	2 g daily PO
❑ Teriparatide	
	20 micrograms daily, for a maximum duration of treatment of 18 months
Osteoporosis in men	
❑ Alendronic acid	
	10 mg daily PO
Glucocorticoid-induced Osteoporosis	
❑ Alendronic acid	
5 mg daily PO	5 mg daily PO
❑ Disodium etidronate	
400 mg for 14 days PO, 1,25 g calcium carbonate for 76 days PO	400 mg for 14 days PO, 1,25 g calcium carbonate for 76 days PO

	❑ Risedronate sodium 5 mg daily PO ❑ Teriparatide 20 micrograms daily, for a maximum duration of treatment of 18 months		
14	**A postmenopausal woman when started on bisphosphonate therapy** was initiated on alendronate.	**A patient with osteoporosis on bisphosphonate therapy** is on the preferred choice* * 1- Alendronate, 2-risedronate, 3-intermittent cyclical etidronate	Criteria 14, 15 and 16 of draft Luf were merged to criterion 14 in the final draft. Whereas it has initially been investigated separately on alendronate, risedronate and etidronate, criterion 14 now focuses equally on each of them. The criterion audits at the same whether a patient is receiving alendronate, risedronate OR etidronate. If this was the case, the investigator had to check manually the dates of the prescrption in order to confirm adherence to the order set up in guidelines recommendation (alendronate in the first place, risedronate as a second choice and etidronate as a third).
15	**A postmenopausal woman diagnosed with osteoporosis/osteopenia and not treated with alendronate** is prescribed risedronate.	**A patient who is on long-term glucocorticoid therapy** **(≥ 7.5 mg prednisolone or equivalents for ≥ 3 months)** is prescribed a bisphosphonate.	See criterion 14 final draft. Criterion 15 of the final draft represents criterion 17 draft Luf. Contents and wording remained identical.

16	**A postmenopausal woman with ≥ 2 vertebral fractures and NOT treated with alendronate or risedronate** is prescribed intermittent cyclical etidronate[1].	**A postmenopausal woman prescribed strontium ranelate** has an identifiable reason for not being prescribed a bisphosphonate Reasons for non-use of bisphosphonates are ❑ contraindication to bisphosphonates (see 12) ❑ inability to comply with the recommendations for use of bisphosphonates (see 12) ❑ intolerance to bisphosphonates (see12)]	Criterion 16 draft Luf: See criterion 14 final draft. Criterion 16 of the final draft represents criterion 18 draft Luf. The condition 'with a diagnosis of osteoporosis' formally required by the qualifier, was removed. The condition 'being prescribed strontium ranelate' was moved from the standard to the qualifier, the condition 'having an identifiable reason for not being prescribed a bisphosphonate' was moved from the qualifier to the standard.
17	**A patient who is on long-term glucocorticoid therapy** **(≥ 7.5 mg prednisolone or equivalents for ≥ 3 months)** is prescribed a bisphosphonate.	**A postmenopausal woman prescribed raloxifene** is receiving it for secondary prevention and has an identifiable reason for not being prescribed a bisphosphonate [Reasons for non-use of bisphosphonates are ❑ contraindication to bisphosphonates (see 12) ❑ inability to comply with the recommendations for use of bisphosphonates (see 12) ❑ intolerance to bisphosphonates (see 12)]	Criterion 17 draft Luf was changed in aspects of numbering. Former criterion 17 draft Luf is now criterion 15 in the final draft. Criterion 17 final draft was derived from criterion 19 draft Luf. The condition 'with a diagnosis of osteoporosis' formally required by the qualifier was removed. The condition 'with at least one osteoporotic fracture' was reworded to 'is receiving it for secondary prevention'

			and moved from the qualifier to the standard, as well as the requirement 'has an identifiable reason for not being prescribed a bisphosphonate'. Strontium ranelate was removed from this criterion since its use is assessed on sufficiently in criterion 16.
18	**A postmenopausal woman with a diagnosis of osteoporosis, who has an identifiable reason for not being prescribed a bisphosphonate** is prescribed strontium ranelate. [Reasons for non-use of bisphosphonates are Contraindications to bisphosphonates ❑ contraindication to bisphosphonates (see 12) ❑ inability to comply with the recommendations for use of bisphosphonates (see 12) ❑ intolerance to bisphosphonates (see12)]	**A patient prescribed teriparatide** is prescribed it for secondary prevention and meets at least one of the following 2 criteria ❑ **has a reason to avoid bisphosphonates (See 12)** ❑ **has an intolerance to strontium ranelate** o persistent nausea o persistent diarrhoea And has DEXA scan assessment that puts them in one the following groups ❑ **aged ≥ 65 years with a T-Score ≤ -4 SD** ❑ **aged ≥ 65 years with a T-Score ≤ -3.5 SD and has more than two fractures** ❑ **aged 55-64 years with a T-Score ≤ -4 and has more than two fractures**	See criterion 16 final draft. Criterion 18 of the final draft is derived from criterion 20 draft Luf. The requirement 'postmenopausal woman diagnosed with osteoporosis' was removed since the age, which is required in order to receive teriparatide, includes being postmenopausal (55 and older). The term 'with at least one osteoporotic fracture' was reworded to 'is receiving it for secondary prevention'. The action, that a patient is receiving teriparatide was moved from the standard to the qualifying statement since it is easier to assess its use in the first place instead of assessing reasons to avoid bisposphonates, intolerance to strontium ranelate etc before. The term 'who has an contraindication to strontium ranelate' was removed since contraindications to strontium ranelate would be pregnancy and breastfeeding, a condition that is practically impossible in patients receiving teriparatide since they have to be of

			a certain age, namely 55 and over.
19	**A postmenopausal woman diagnosed with osteoporosis with at least one osteoporotic fractures who has an identifiable reason for not being prescribed a bisphosphonate** is prescribed strontium ranelate or raloxifene. [Reasons for non-use of bisphosphonates are Contraindications to bisphosphonates ❑ contraindication to bisphosphonates (see 12) ❑ inability to comply with the recommendations for use of bisphosphonates (see 12) ❑ intolerance to bisphosphonates (see 12)]	**A patient prescribed calcitonin** is prescribed it for secondary prevention after bisphosphonate, raloxifene or strontium ranelate have been tried or have reasons for excluding from consideration [Reasons for non-use of bisphosphonates are ❑ contraindication to bisphosphonates (see 12) ❑ inability to comply with the recommendations for use of bisphosphonates (see 12) ❑ intolerance to bisphosphonates (see 12)]	Criterion 19 draft Luf correlates with criterion 17 of the final draft. See criterion 17 final draft. Contents of criterion 19 of the final draft were derived from former criterion 21 Luf. The action, that a patient is prescribed calcitonin, was moved from the standard to the qualifying statement since it is easier to assess whether a patient is receiving calcitonin then to assess the existence of possible contraindications etc in eligible patients. The requirement of being postmenopausal and being diagnosed with osteoporosis were removed since having sustained osteoporotic fractures is qualification that needs to be fulfilled for being prescribed calcitonin. The condition 'postmenopausal woman' was removed since calcitonin is also indicated for the secondary prevention of osteoporosis in men. The term 'not treated with a bisphosphonate, raloxifene or strontium ranelate' was reworded to 'is prescribed … after bisphosphonate, raloxifene or strontium ranelate have been tried or have reasons for excluding from

			consideration' in order to clarify the motive for not prescribing any of these drugs.
20	**A postmenopausal woman diagnosed with osteoporosis and at least one osteoporotic fractures** **who has either** ❑ **a reason to avoid bisphosphonates (See 12)** ❑ **a contraindication to strontium ranelate** o pregnancy o breast-feeding ❑ **an intolerance to strontium ranelate** o persistent nausea o persistent diarrhoea **and who is either** ❑ **aged ≥ 65 years with a T-Score ≤ -4 SD** ❑ **aged ≥ 65 years with a T-Score ≤ -3.5 SD and has more than two fractures** ❑ **aged 55-64 years with a T-Score ≤ -4 and has more than two fractures** is prescribed teriparatide.		See criterion 18 final draft
21	**A postmenopausal woman diagnosed with osteoporosis with at least one vertebral fracture and NOT treated with a bisphosphonate, raloxifene or strontium ranelate** is prescribed calcitonin.		See criterion 19 final draft.

5.2. Overall adherence and applicability of the total study sample

Measurable endpoints of the study were the identification whether medication use in osteoporosis is according to the guidelines used in this study or not. The guidelines used were SIGN 71 (2003) and NICE 160 and 161 (2008). The application of MATosteo to patient data of three different GPs enabled the assessment and identification of applicability and adherence to guideline recommended treatment and treatment strategies in eligible patients. Furthermore this audit allowed the evaluation and comparison of quality of prescribing in patients located in different GPs. The following tables show demographic patient information of the three GPs.

Table 12 Demographics GP A

Patient subgroup	Number of patients
Total number of patients	464
Osteoporotic patients	138
Osteopenic patients	16
Men	13
Women	141
Male osteoporotic patients	12
Female osteoporotic patients	126
Male osteopenic patients	1
Female osteopenic patients	15
Postmenopausal	139

Table 13 Demographics GP B

Patient subgroup	Number of patients
Total number of patients	62
Osteoporotic patients	62
Osteopenic patients	0
Men	7
Women	55
Male osteoporotic patients	7
Female osteoporotic patients	55
Male osteopenic patients	0
Female osteopenic patients	0

Postmenopausal	54

Table 14 Demographics GP C

Patient group	Number of patients
Total number of patients	103
Osteoporotic patients	59
Osteopenic patients	44
Men	7
Women	96
Male osteoporotic patients	5
Female osteoporotic patients	54
Male osteopenic patients	2
Female osteopenic patients	42
Postmenopausal	94

The following tables show overall adherence and applicability of the total study sample to each criterion. Adherence and applicability are reported for each patient sample (each GP) separately as well as for all three GPs together. For each criterion, the number of applicable patients was calculated by summing up 'Yes'-, 'No, unjustified'- and 'Insufficient data on the standard'- answers. Percentage of applicability was calculated for each criterion. Adherence to each criterion was calculated by dividing the number of 'Yes- answers' by the number of applicable patients, multiplied with 100. Furthermore the 95% confidence interval was calculated.

5.2.1. Applicabilty

Applicability was observed to be very low in criteria 1 and 4. These criteria deal with osteopenic patients. Numbers of osteopenic patients were very low in the study sample, which might result from the fact that there is not enough importance attached with this disease, its diagnosis and implications.

For criteria including a high number of subheadings a significantly low applicability was shown, which results from the difficulty to meet every single requirement set up in concerned criteria. Criterion 12 for example, includes a high number of subheadings:

A patient who is prescribed a bisphosphonate

has no reason *on record* to avoid bisphosphonates.

In order to fulfil the requirements set up in the standard, a patient has to meet at least one statement of the four groups (subheadings) indicated below:

- contraindication to bisphosphonates:
  - oesophageal strictures or achalasia
  - inability to remain upright for > 30 min after ingestion
  - hypocalcaemia
  - osteomalacia (etidronate)
  - moderate renal impairment (CrCl < 35 mL/min)
  - pregnancy and breast feeding
- inability to comply with the instructions for use of bisphosphonates
  - ingestion on an empty stomach
  - washing the medication down with 250 ml water
  - avoidance of food for 30 min
  - avoidance of lying flat within 30 min of ingestion
- unsatisfactory response to bisphosphonates
  - another fracture occurs
  - decrease in BMD despite adherence to treatment
- intolerance to bisphosphonates
  - oesophageal ulceration
  - erosion or stricture
  - severe lower GI symptoms]

In criterion 15, applicability was reported to be 0 in most cases, a result from the fact that there was only one patient with long-term prescription of oral glucocorticoids found in the patient sample. Attention might have to be drawn to inhalative glucocorticoids, but assessment of patients prescribed the latter were not included in this project since inhalative administration of steroids is not explicitly recommended by guidelines to be accompanied by preventive osteoporosis treatment.

In criterion 16, applicability was found to be very low, resulting from the fact that only very few patients (3 out of 319) were prescribed strontium ranelate although it is recommended as treatment alternative in patients who are not eligible for bisphosphonate therapy.

Applicability in criterion 17 was 0 since there were no patients found to receive raloxifene in the patient sample. Subsequently the term ‘no result’ had to be reported for adherence.

In criterion 18, ‘no result’ had to be reported for adherence since there were no applicable patients who were prescribed teriparatide.

‘No result’ due to the non-existence of applicable patients was also reported for criterion 19 since there were no patients receiving calcitonin.

5.2.2. Overall adherence-practice A

In practice A, overall adherence to guideline recommendation was observed to be 65.8%.

For 6 out of 19 criteria high level of adherence (70% and over) was reported. In 7 criteria level of adherence was found to be intermediate (50-69.9%) and in 2 criteria it was low (below 50%). In 4 criteria, 'no result' was reported, since there were no applicable patients.

Criteria indicating high level of adherence were criteria 7 and 8 (in patients receiving calcium respectively vitamin D, the appropriate dose is prescribed) with 98,8% respectively 98.7% of adherence. Furthermore adherence was high in criterion 12 with 83.0% (patients receiving antiresorptive or osteoanabolic treatment do not have a contraindication to this treatment). Similarly criterion 13 (patients prescribed treatment for osteoporosis are prescribed a standard regimen) was highly adhered to with 86.2%. Criterion 14 showed 87.8% of adherence (patients receiving a bisphosphonate receive the preferred choice). The criterion with the highest level of adherence was criterion 16 with 100% of adherence. This criterion deals with the requirement that patients who are prescribed strontium ranelate have to present a contraindication for bisphosphonates.

Low level of adherence was reported for criterion 2 with 34.4% requiring DXA scans on two specific sites. Furthermore criterion 9 was shown to be poorly adhered to, requiring prescription of calcium and vitamin D in untreated patients with only 20.4% of adherence.

For criteria 1, 4, 5, 6, 10 and 11 intermediate adherence was reported, ranking from 55.1 to 60.8%. These criteria require diagnosis of osteoporosis to be set up by DEXA scan, supplementary calcium to be prescribed in osteoporotic and osteopenic patients, vitamin D to be prescribed in patients with vitamin D deficieny or over the age of 65, prescription of appropriate treatment in patients diagnosed with osteoporosis as well as prescribing of bisphosphonates as first line therapy for osteoporosis and osteopenia.

For criteria 15, 17, 18 and 19 'no result' was reported, since there were no patients found to receive long-term oral glucocorticoid therapy, raloxifene, teriparatide or calcitonin.

Table 15 Overall adherence practice A

Practice A (154 patients)	**N/A**	**Yes**	**No(J)**	**No(U)**	**IDS**	**IDQ**	**Applicable**	**Adherence**
n= 2926 criteria	**%**	**%**	**%**	**%**	**%**	**%**	**Applicability**	**(CI 95%)**
1 **Patient with a diagnosis of osteoporosis** has a recorded DEXA scan	22/154 14.3%	77	6	55	0	0	132/154 85.7%	77/132 58.3% (49.9-66.7)
2 **Patient with measured BMD by DEXA scan** has measures takenat spine and hip	61/154 39.6%	32	0	55	6	0	93/154 60.4%	32/93 34.4% (24.7-44.1)
3 **Patient with osteoporosis** is prescribed supplementary calcium	16/154 10.4%	76	0	62	0	0	138/154 89.6%	76/138 55.1% (46.8-63.4)
4 **Osteopenic patient** is prescribed supplementary calcium	138/216 89.6%	9	0	7	0	0	16/154 10.4%	9/16 56.3% (32-80.6)
5 **Patient with confirmed vitamin D deficiency or age ≥ 65years** is prescribed vitamin D	30/154 19.5%	73	0	51	0	0	124/154 80.5%	73/124 58.9% (50.2-67.6)

Practice A (154 patients)		**N/A**	**Yes**	**No(J)**	**No(U)**	**IDS**	**IDQ**	**Applicable**	**Adherence**
n= 2926 criteria		**%**	**%**	**%**	**%**	**%**	**%**	**Applicability**	**(CI 95%)**
6	**Patient with osteoporosis** is treated with antiresorptive/osteoanabolic agent (Biphopshonates, raloxifene, strontium ranelate, calcitonin or teriparatide)	16/154 10.4%	84	0	54	0	0	138/154 89.6%	84/138 60.8% (52.7-68.9)
7	**Patient prescribed calcium** is prescribed 500-1500 mg	69/154 44.8%	84	0	1	0	0	85/154 55.2%	84/85 98.8% (96.5-101.1)
8	**Patient prescribed vitamin D** is prescribed 400-800 IU	76/154 49.4%	77	0	1	0	0	78/154 50.6%	77/78 98.7% (96.2-101.2)
9	**Patient with osteoporosis untreated byantiresorptive/anabolic agent** *(BPs, raloxifene, strontium ranelate or calcitonin)* is prescribed >=1000mg calcium plus 800 IE vitamin D	100/154 64.9%	11	0	42	1	0	54/154 35.1%	11/54 20.4% (9.7-31.1)
10	**Patient with osteoporosis** is prescribed an oral BP as first-line therapy	16/154 10.4%	81	0	57	0	0	138/154 89.6%	81/138 58.7% (50.5-66.9)
11	**Osteopenic patient** is prescribed an oral BP as first-line therapy (Canadian guidelines only)	138/154 89.6%	9	0	7	0	0	16/154 10.4%	9/16 56.3% (32-80.6)

Practice A (154 patients)		**N/A**	**Yes**	**No(J)**	**No(U)**	**IDS**	**IDQ**	**Applicable**	**Adherence**
n= 2926 criteria		**%**	**%**	**%**	**%**	**%**	**%**	**Applicability**	**(CI 95%)**
12	**Patient treated with antiresorptive/osteoanabolic agent** has no contra-indication on record (Biphopshonates, raloxifene, strontium ranelate, calcitonin or teriparatide	60/154 39%	78	0	16	0	0	94/154 61%	78/94 83.0% (75.4-90.6)
13	**Patient receiving treatment for osteopenia/osteoporosis** is prescribed a standard dose regimen	60/154 39%	81	0	10	3	0	94/154 61%	81/94 86.2% (79.2-93.2)
14	**A patient with osteoporosis on bisphosphonate therapy** is on the preferred choice* * 1- Alendronate, 2-risedronate, 3-intermittent cyclical etidronate	72/154 46.8%	72	0	10	0	0	82/154 53.2%	72/82 87.8% (80.8-94.8)
15	**A patient who is on long-term glucocorticoid therapy** **(≥ 7.5 mg prednisolone or equivalents for ≥ 3 months)** is prescribed a bisphosphonate	154/154 100%	0	0	0	0	0	0/154 0%	nr

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Practice A (154 patients)		**N/A**	**Yes**	**No(J)**	**No(U)**	**IDS**	**IDQ**	**Applicable**	**Adherence**
n= 2926 criteria		**%**	**%**	**%**	**%**	**%**	**%**	**Applicability**	**(CI 95%)**
16	**A postmenopausal woman prescribed strontium ranelate** has an identifiable reason for not being prescribed a bisphosphonate	152/154 98.7%	2	0	0	0	0	2/154 1.3%	2/2 100.0%
17	**A postmenopausal woman prescribed raloxifene** is receiving it for secondary prevention	154/154 100%	0	0	0	0	0	0/154 0%	nr

Practice A (154 patients) **n= 2926 criteria**	**N/A** **%**	**Yes** **%**	**No(J)** **%**	**No(U)** **%**	**IDS** **%**	**IDQ** **%**	**Applicable** **Applicability**	**Adherence** **(CI 95%)**
18 **A patient prescribed teriparatide** is prescribed it for secondary prevention and meets at least one of the following 2 criteria ❑ **has a reason to avoid bisphosphonates (See 12)** ❑ **has an intolerance to strontium ranelate** o persistent nausea o persistent diarrhoea And has DEXA scan assessment that puts them in one the following groups ❑ **aged ≥ 65 years with a T-Score ≤ -4 SD** ❑ **aged ≥ 65 years with a T-Score ≤ -3.5 SD and has more than two fractures** ❑ **aged 55-64 years with a T-Score ≤ -4 and has more than two fractures**	154/154 100%	0	0	0	0	0	0/154 0%	nr

Practice A (154 patients) **n= 2926 criteria**	**N/A** **%**	**Yes** **%**	**No(J)** **%**	**No(U)** **%**	**IDS** **%**	**IDQ** **%**	**Applicable** **Applicability**	**Adherence** **(CI 95%)**
19 **A patient prescribed calcitonin** is prescribed it for secondary prevention after bisphosphonate, raloxifene or strontium ranelate have been tried or have reasons for excluding from consideration [Reasons for non-use of bisphosphonates are ❑ contraindication to bisphosphonates (see 12) ❑ inability to comply with the recommendations for use of bisphosphonates (see 12) ❑ intolerance to bisphosphonates (see 12)]	154/154 100%	0	0	0	0	0	0/154 0%	nr
Overall **(%)**	1642	846	6	428	10	0	1284	846/1284 65.8% (62.3-69.3)

N/A: not applicable; **No(J):** justified non-adherence to the guideline; **No(U):** unjustified non-adherence to the guideline; **IDS:** insufficient data on the standard; **IDQ:** insufficient data on the qualifier; **CI:** confidence interval; **S1:** Search 1;**nr:** no result

5.2.3. Overall adherence-practice B

In practice B, overall adherence to the clinical guidelines used in this study was observed to be 52.1%.

Level of adherence was high (70% and over) in 4 out of 19 criteria, intermediate (50-69.9%) in 3 criteria and low (below 50%) in 4 criteria. For 6 criteria 'no result' was reported for adherence since there were no patients applicable to the qualifying statements.

Criteria presenting significantly high level of adherence were criteria 7 and 8 with 100% respectively 94.1% of adherence. These criteria represent the requirement, that patients who are prescribed calcium respectively vitamin D should be prescribed the appropriate dose. Furthermore criterion 13 was observed to be highly adhered to with 74.5%, requiring prescription of standard dose regimens in osteoporosis treatment. Criterion 14 as well showed high level of adherence with 83.9%. This criterion checks whether patients who are prescribed a bisphosphonate are on the preferred choice.

Criteria with significantly low level of adherence were criteria 1 and 2 with 1.6% respectively 0%. These criteria represent the requirement that assessment of BMD should be performed via DXA scan on two specific sites. There was only one patient in practice B found to have a diagnosis of osteoporosis set up via DXA scan which results from the fact that there were no DXA- facilities available in practice Bwhich is located in a deprived area within Greater Glasgow. Within patients' records the term 'bone density measurement' was found in most cases, a term that is most likely to refer to BMD assessment via radiography or some other technique.

For criterion 3, which requires the prescribing of calcium in all patients diagnosed with osteoporosis, a low adherence of only 38.7% was reported. Furthermore criterion 12 was observed to be poorly adhered to with 41.9%. This criterion requires that patients who are prescribed antiresorptive or osteoanabolic treatment must not have a contraindication to these treatment options.

For criteria 5,6 and 10 intermediate level of adherence was observed within a range from 50 to 59.6%. These criteria deal with the prescribing of supplementary vitamin D in patients above the age of 64, prescribing of treatment in osteoporotic and osteopenic patients respectively the prescribing of bisphosphonates as first line treatment in osteoporosis-patients.

Since there were no osteopenic patients within this patient sample, no patients were applicable to criteria 4 and 11 and 'no result' was reported for adherence. There were no patients on long-

term oral glucocorticoid therapy, strontium ralenate, raloxifene, teriparatide or calcitonin. Hence, there are no results for adherence in criteria 15, 16, 17, 18 and 19.

Table 16 Overall adherence practice B

Practice B (62 patients)	**N/A**	**Yes**	**No(J)**	**No(U)**	**IDS**	**IDQ**	**Applicable**	**Adherence**
n= 1178 criteria	**%**	**%**	**%**	**%**	**%**	**%**	**Applicability**	**(CI 95%)**
1 **Patient with a diagnosis of osteoporosis** has a recorded DEXA scan	0/62 0%	1	0	54	7	0	62/62 100%	1/62 1.6% (-1.5-4.7)
2 **Patient with measured BMD by DEXA scan** has measures takenat spine and hip	51/62 82.3%	0	0	1	10	39	11/62 17.7%	0/11 0%
3 **Patient with osteoporosis** is prescribed supplementary calcium	0/62 0%	24	0	38	0	0	62/62 100%	24/62 38.7% (26.5-50.9)
4 **Osteopenic patient** is prescribed supplementary calcium	62/62 100%	0	0	0	0	0	0/62 0%	nr
5 **Patient with confirmed vitamin D deficiency or age ≥ 65years** is prescribed vitamin D	15/62 24.2%	28	0	19	0	0	47/62 75.8%	28/47 59.6% (45.5-73.7)

Practice B (62 patients)		**N/A**	**Yes**	**No(J)**	**No(U)**	**IDS**	**IDQ**	**Applicable**	**Adherence**
n= 1178 criteria		**%**	**%**	**%**	**%**	**%**	**%**	**Applicability**	**(CI 95%)**
6	**Patient with osteoporosis** is treated with antiresorptive/osteoanabolic agent (Biphopshonates, raloxifene, strontium ranelate, calcitonin or teriparatide)	0/62 0%	31	0	31	0	0	62/62 100%	31/62 50.0% (37.6-62.4)
7	**Patient prescribed calcium** is prescribed 500-1500 mg	28/62 45.2%	34	0	0	0	0	34/62 54.8%	34/34 100.0%
8	**Patient prescribed vitamin D** is prescribed 400-800 IU	28/62 45.2%	32	0	2	0	0	34/62 54.8%	32/34 94.1% (86.2-100.2)
9	**Patient with osteoporosis untreated byantiresorptive/anabolic agent** *(BPs, raloxifene, strontium ranelate or calcitonin)* is prescribed >=1000mg calcium plus 800 IE vitamin D	31/62 50%	12	0	19	0	0	31/62 50%	12/31 38.7% (21.6-55.8)
10	**Patient with osteoporosis** is prescribed an oral BP as first-line therapy	0/62 0%	31	0	31	0	0	62/62 100%	31/62 50.0% (37.6-62.4)
11	**Osteopenic patient** is prescribed an oral BP as first-line therapy (Canadian guidelines only)	62/62 0%	0	0	0	0	0	0/62 0%	nr

Practice B (62 patients)		**N/A**	**Yes**	**No(J)**	**No(U)**	**IDS**	**IDQ**	**Applicable**	**Adherence**
n= 1178 criteria		**%**	**%**	**%**	**%**	**%**	**%**	**Applicability**	**(CI 95%)**
12	**Patient treated with antiresorptive/osteoanabolic agent** has no contra-indication on record (Biphopshonates, raloxifene, strontium ranelate, calcitonin or teriparatide	31/62 50%	13	0	5	13	0	31/62 50%	13/31 41.9% (24.5-59.3)
13	**Patient receiving treatment for osteopenia/osteoporosis** is prescribed a standard dose regimen	11/62 17.7%	38	0	5	8	0	51/62 82.3%	38/51 74.5% (62.5-86.5)
14	**A patient with osteoporosis on bisphosphonate therapy** is on the preferred choice* * 1- Alendronate, 2-risedronate, 3-intermittent cyclical etidronate	31/62 50%	26	0	5	0	0	31/62 50%	26/31 83.9% (71-96.8)
15	**A patient who is on long-term glucocorticoid therapy** **(≥ 7.5 mg prednisolone or equivalents for ≥ 3 months)** is prescribed a bisphosphonate.	62/62 100%	0	0	0	0	0	0/62 0%	nr

Practice B (62 patients) **n= 1178 criteria**	**N/A** **%**	**Yes** **%**	**No(J)** **%**	**No(U)** **%**	**IDS** **%**	**IDQ** **%**	**Applicable** **Applicability**	**Adherence** **(CI 95%)**
16 **A postmenopausal woman prescribed strontium ranelate** has an identifiable reason for not being prescribed a bisphosphonate	62/62 100%	0	0	0	0	0	0/62 0%	Nr
17 **A postmenopausal woman prescribed raloxifene** is receiving it for secondary prevention	62/62 100%	0	0	0	0	0	0/62 0%	**Nr**
18 **A patient prescribed teriparatide** is prescribed it for secondary prevention and meets at least one of the following 2 criteria ❑ **has a reason to avoid bisphosphonates (See 12)** ❑ **has an intolerance to strontium ranelate** o persistent nausea o persistent diarrhoea And has DEXA scan assessment that puts them in one the following groups ❑ **aged ≥ 65 years with a T-Score ≤ -4 SD** ❑ **aged ≥ 65 years with a T-Score ≤ -3.5 SD and has more than two fractures** ❑ **aged 55-64 years with a T-Score ≤ -4 and has more than two fractures**	62/62 100%	0	0	0	0	0	0/62 0%	nr

Practice B (62 patients) **n= 1178 criteria**	**N/A** **%**	**Yes** **%**	**No(J)** **%**	**No(U)** **%**	**IDS** **%**	**IDQ** **%**	**Applicable** **Applicability**	**Adherence** **(CI 95%)**
19 **A patient prescribed calcitonin** is prescribed it for secondary prevention after bisphosphonate, raloxifene or strontium ranelate have been tried or have reasons for excluding from consideration [Reasons for non-use of bisphosphonates are ❑ contraindication to bisphosphonates (see 12) ❑ inability to comply with the recommendations for use of bisphosphonates (see 12) ❑ intolerance to bisphosphonates (see 12)]	62/62 100%	0	0	0	0	0	0/62 0%	nr
Overall **(%)**	660	270	0	210	38	39	518	270/518 52.1% (47.8-56.4)

N/A: not applicable; **No(J):** justified non-adherence to the guideline; **No(U):** unjustified non-adherence to the guideline; **IDS:** insufficient data on the standard; **IDQ:** insufficient data on the qualifier; **CI:** confidence interval; **S1:** Search 1; **nr:** no result

5.2.4. Overall adherence-practice C

In practice C, overall adherence to guideline recommendation was observed to be 61.4%.

For 5 out of 19 criteria adherence was found to be of high level, 6 criteria showed intermediate and 5 criteria low level of adherence. In three criteria, no results could be reported since there were no patients applicable.

Significantly high adherence was observed in criteria 7 and 8 with 100% both. These criteria require the prescribing of calcium and vitamin D in appropriate dosage. Furthermore for criteria 15 and 16 it was reported that adherence to guidelines recommendation was 100%. However, in both criteria only one patient was applicable to the qualifier (patients prescribed long-term oral glucocorticoid therapy respectively strontium ranelate). In both cases guideline recommendation (prescribing of bisphosphonate prevention in steroid patients respectively prescribing of strontium ranelate exclusively in patients with a contraindication to bisphosphonates) was implemented.

Significantly low level of adherence was observed in criterion 2 with 10.8%. This criterion requires the performance of DXA scan on two specific sites. Furthermore criterion 11 was reported to be poorly adhered to with 23.3.%. Criterion 11 requires bisphosphonate therapy to be first line treament in patients with osteopenia. Similarly low adherence (30.2%) was shown for criterion 4, which requires prescribing of supplementary calcium in osteopenic patients. Criterion 9 and 12 were found to be poorly adhered to with 40.9 respectively 47.9%. These criteria check if osteoporotic and osteopenic patients who are not receiving pharmacological osteoporosis treatment are prescribed calcium and vitamin D respectively if patients who actually do receive treatment do not have a contraindication to the latter.

For criteria 1, 3, 5, 6, 10 and 13 intermediate level of adherence was reported.

There were no patients applicable in criteria 17, 18 and 19, hence there could be no result reported.

Table 17 Overall adherence practice C

Practice C (103 patients)		**N/A**	**Yes**	**No(J)**	**No(U)**	**IDS**	**IDQ**	**Applicable**	**Adherence**
n= 1957		**%**	**%**	**%**	**%**	**%**	**%**	**Applicability**	**(CI 95%)**
1	**Patient with a diagnosis of osteoporosis** has a recorded DEXA scan	44/103 42.7%	37	1	17	5	0	59/103 57.3%	37/59 62.7% (50.4-75.0)
2	**Patient with measured BMD by DEXA scan** has measures takenat spine and hip	66/103 64.1%	4	0	33	0	5	37/103 35.9%	4/37 10.8% (0.8-20.8)
3	**Patient with osteoporosis** is prescribed supplementary calcium	43/103 41.7%	38	0	22	0	0	60/103 58.3%	38/60 63.3% (51.1-75.5)
4	**Osteopenic patient** is prescribed supplementary calcium	60/103 58.3%	13	0	30	0	0	43/103 41.7%	13/43 30.2% (16.5-43.9)
5	**Patient with confirmed vitamin D deficiency or age ≥ 65years** is prescribed vitamin D	34/103 33%	41	0	28	0	0	69/103 67%	41/69 59.4% (47.8-70.8)

Practice C (103 patients) **n= 1957**		**N/A** **%**	**Yes** **%**	**No(J)** **%**	**No(U)** **%**	**IDS** **%**	**IDQ** **%**	**Applicable** **Applicability**	**Adherence** **(CI 95%)**
6	**A patient with osteoporosis** is treated with an antiresorptive/osteoanabolic agent	48/103 46,6%	38	5	12	5	0	55/103 53,4%	38/55 69,1% (56,9-81,3)
7	**A patient prescribed supplementary calcium** is prescribed a daily dose of 500-1500 mg calcium	52/103 50.5%	51	0	0	0	0	51/103 49.5%	51/51 100.0%
8	**A patient prescribed vitamin D** is prescribed a daily dose of 10 – 20 μg (400 - 800 IU) vitamin D	53/103 51.5%	50	0	0	0	0	50/103 48.5%	50/50 100.0%
9	**Patient with osteoporosis untreated by antiresorptive/osteoanabolic agent** is prescribed >=1000 mg calcium plus 800 IE vitamin D	81/103 78.6%	9	0	13	0	0	22/103 21.4%	9/22 40.9% (20.4-61,4)
10	**A patient with osteoporosis is prescribed an oral bisphosphonate as first-line therapy**	49/103 47.6%	37	6	12	5	0	54/103 52.4%	37/54 68.5% (56.1-80.9)

Practice C (103 patients) **n= 1957**		**N/A** **%**	**Yes** **%**	**No(J)** **%**	**No(U)** **%**	**IDS** **%**	**IDQ** **%**	**Applicable** **Applicability**	**Adherence** **(CI 95%)**
11	**A patient with osteopenia is prescribed an oral bisphosponate as first-line therapy**	60/103 58.3%	10	0	33	0	0	43/103 41.7%	10/43 23.3% (10.7-35.9)
12	**A patient who is prescribed a antiresorptive/osteoanabolic agent** has no contraindication on record	55/103 53.4%	23	0	2	23	0	48/103 46.6%	23/48 47.9% (33.8-62.0)
13	**Patient receiving treatment for osteopenia/osteoporosis** is prescribed a standard dose regimen	55/103 53.4%	31	0	15	2	0	48/103 46.7%	31/48 64.6% (51.1-78.1)
14	**A patient with osteoporosis on bisphosphonate therapy** is on the preferred choice* • 1- Alendronate, 2-risedronate, 3-intermittent cyclical etidronate •	66/103 64.1%	32	0	5	0	0	37/103 35.9%	32/37 86.5% (75.5-97.5)

Practice C (103 patients) **n= 1957**		**N/A** **%**	**Yes** **%**	**No(J)** **%**	**No(U)** **%**	**IDS** **%**	**IDQ** **%**	**Applicable** **Applicability**	**Adherence** **(CI 95%)**
15	**A patient who is on long-term glucocorticoid therapy** **(≥ 7.5 mg prednisolone or equivalents for ≥ 3 months)** is prescribed a bisphosphonate.	102/103 99%	1	0	0	0	0	1/103 1%	1/1 100.0%
16	**A postmenopausal woman prescribed strontium ranelate** has an identifiable reason for not being prescribed a bisphosphonate	102/103 99%	1	0	0	0	0	1/103 1%	1/1 100.0%
17	**A postmenopausal woman prescribed raloxifene** is receiving it for secondary prevention	103/103 100%	0	0	0	0	0	0/103 0%	nr

Practice C (103 patients) **n= 1957**	**N/A** **%**	**Yes** **%**	**No(J)** **%**	**No(U)** **%**	**IDS** **%**	**IDQ** **%**	**Applicable** **Applicability**	**Adherence** **(CI 95%)**
18 **A patient prescribed teriparatide** is prescribed it for secondary prevention and meets at least one of the following 2 criteria ☐ **has a reason to avoid bisphosphonates (See 12)** ☐ **has an intolerance to strontium ranelate** ☐ persistent nausea ☐ persistent diarrhoea And has DEXA scan assessment that puts them in one the following groups ☐ **aged ≥ 65 years with a T-Score ≤ -4 SD** ☐ **aged ≥ 65 years with a T-Score ≤ -3.5 SD and has more than two fractures** ☐ **aged 55-64 years with a T-Score ≤ -4 and has more than two fractures**	103/103 100%	0	0	0	0	0	0/103 0%	nr

Springburn (103 patients) **n= 1957**	**N/A** **%**	**Yes** **%**	**No(J)** **%**	**No(U)** **%**	**IDS** **%**	**IDQ** **%**	**Applicable** **Applicability**	**Adherence** **(CI 95%)**
19 **A patient prescribed calcitonin** is prescribed it for secondary prevention after bisphosphonate, raloxifene or strontium ranelate have been tried or have reasons for excluding from consideration [Reasons for non-use of bisphosphonates are ☐ contraindication to bisphosphonates (see 12) ☐ inability to comply with the recommendations for use of bisphosphonates (see 12) ☐ intolerance to bisphosphonates (see 12)]	103/103 100%	0	0	0	0	0	0/103 0%	nr
Overall **(%)**	1279/1957 65.4%	416	12	222	40	5	678/1957 34.6%	416/678 61.4% (57.7-65.1)

N/A: not applicable; **No(J):** justified non-adherence to the guideline; **No(U):** unjustified non-adherence to the guideline; **IDS:** insufficient data on the standard; **IDQ:** insufficient data on the qualifier; **CI:** confidence interval; **S1:** Search 1; **nr**: no result

5.2.5. Overall-adherence- total patient sample

In the total patient sample, overall adherence to the clinical guidelines used in this project was observed to be 61.7%, which represents intermediate level of adherence (50-69.9%).

In 6 out of 19 criteria guideline recommendations were found to be highly adhered to, in 5 criteria adherence was intermediate. 5 criteria were reported to be only poorly adhered to. For 3 criteria it was not possible to report a result.

Criteria with significantly high level of adherence were criteria 7, 8, 15 and 16. Criteria 7 and 8 check if patients who are prescribed supplementary calcium and vitamin D are receiving the appropriate dose. In criterion 15 (bisphosphonate prevention for patients on long-term oral steroids) only patient was applicable, hence adherence was going to be either 0% or 100% with a probability of 50% for both cases. Similarly in criterion 16, only three patients were applicable (prescribed strontium ranelate). Since all of them met the standard (presented a contraindication to bisphosphonates), adherence was 100%.

Criteria presenting significantly low level of adherence were criteria 1, 2, 4, 9 and 11. Criteria 1 and 2 requiring BMD assessment via DEXA at spine and hip were shown to be adhered to in 45.5 respectively 25% of applicable patients. Criterion 4 requires prescribing of supplementary calcium in osteopenic patients and was adhered in only 37% of applicable patients.

For 5 criteria (3, 5, 6, 10 and 12) level of adherence was observed to be intermediate within a range from 53.1 to 65.9%.

In criteria 17, 18 and 19 there could be no results found since there were no patients receiving raloxifene, teriparatide or calcitonin.

Table 18 Overall adherence total patient sample

Total (319 patients)		**N/A**	**Yes**	**No(J)**	**No(U)**	**IDS**	**IDQ**	**Applicable**	**Adherence**
n= 6061 criteria		**%**	**%**	**%**	**%**	**%**	**%**	**Applicability**	**(CI 95%)**
1	**Patient with a diagnosis of osteoporosis** has a recorded DEXA scan	66/319 20.7%	115	7	126	12	0	253/319 79.3%	115/253 45.5% (40.5- 50.5%)
2	**Patient with measured BMD by DEXA scan** has measures takenat spine and hip	178/319 55.8%	36	0	89	16	44	141/319 44.2%	36/141 25.5% (18.3-32.7)
3	**Patient with osteoporosis** is prescribed supplementary calcium	59/319 18.5%	138	0	122	0	0	260/319 81.5%	138/260 53.1% (47-59.2)
4	**Osteopenic patient** is prescribed supplementary calcium	1	22	0	37	0	0	59/319 18.5%	22/59 37.3% (25-59.6)
5	**Patient with confirmed vitamin D deficiency or age ≥ 65years** is prescribed vitamin D	79/319 24.8%	142	0	98	0	0	240/319 75.2%	142/240 59.2% (53-65.4)

Total (319 patients)		**N/A**	**Yes**	**No(J)**	**No(U)**	**IDS**	**IDQ**	**Applicable**	**Adherence**
n= 6061 criteria		**%**	**%**	**%**	**%**	**%**	**%**	**Applicability**	**(CI 95%)**
6	**Patient with osteoporosis** is treated with antiresorptive/osteoanabolic agent (Biphopshonates, raloxifene, strontium ranelate, calcitonin or teriparatide)	64/319 20.1%	153	5	97	5	0	255/319 79.9%	153/255 60% (54.0-66.0)
7	**Patient prescribed calcium** is prescribed 500-1500 mg	149/319 46.7%	169	0	1	0	0	170/319 53.3%	169/170 99.4% (98.2-100.6)
8	**Patient prescribed vitamin D** is prescribed 400-800 IU	157/319 49.2%	159	0	3	0	0	162/319 50.8%	159/162 98.1% (96-100.2)
9	**Patient with osteoporosis untreated byantiresorptive/anabolic agent** *(BPs, raloxifene, strontium ranelate or calcitonin)* is prescribed >=1000mg calcium plus 800 IE vitamin D	212/319 66.5%	32	0	74	1	0	107/319 33.5%	32/107 29.9% (21.2-38.6)
10	**Patient with osteoporosis** is prescribed an oral BP as first-line therapy	65/319 20.4%	149	6	100	5	0	254/319 79.6%	149/254 58.6% (52.5-64.7)

Total (319 patients)		**N/A**	**Yes**	**No(J)**	**No(U)**	**IDS**	**IDQ**	**Applicable**	**Adherence**
n= 6061 criteria		**%**	**%**	**%**	**%**	**%**	**%**	**Applicability**	**(CI 95%)**
11	**Osteopenic patient** is prescribed an oral BP as first-line therapy (Canadian guidelines only)	260/319 81.5%	19	0	40	0	0	59/319 18.5%	19/59 32.2% (20.3-44.1)
12	**Patient treated with antiresorptive/osteoanabolic agent** has no contra-indication on record (Biphopshonates, raloxifene, strontium ranelate, calcitonin or teriparatide	146/319 45.8%	114	0	23	36	0	173/319 54.23%	114/173 65.9% (58.8-73.0)
13	**Patient receiving treatment for osteopenia/osteoporosis** is prescribed a standard dose regimen	126/319 39.5%	150	0	30	13	0	193/319 60.5%	150/193 77.7% (71-84.4)
14	**A patient with osteoporosis on bisphosphonate therapy** is on the preferred choice* * 1- Alendronate, 2-risedronate, 3-intermittent cyclical etidronate	169/319 53%	130	0	20	0	0	150/319 47%	130/150 86.7% (81.3-92.1)

Total (319 patients)		**N/A**	**Yes**	**No(J)**	**No(U)**	**IDS**	**IDQ**	**Applicable**	**Adherence**
n= 6061 criteria		**%**	**%**	**%**	**%**	**%**	**%**	**Applicability**	**(CI 95%)**
15	**A patient who is on long-term glucocorticoid therapy** **(≥ 7.5 mg prednisolone or equivalents for ≥ 3 months)** is prescribed a bisphosphonate.	318/319 99.7%	1	0	0	0	0	1/319 0.3%	1/1 100.0%
16	**A postmenopausal woman prescribed strontium ranelate** has an identifiable reason for not being prescribed a bisphosphonate	316/319999. 1%	3	0	0	0	0	3/319 0.9%	3/3 100.0%
17	**A postmenopausal woman prescribed raloxifene** is receiving it for secondary prevention	319/319 1%	0	0	0	0	0	0/319 0%	nr

Total (319 patients)	**N/A**	**Yes**	**No(J)**	**No(U)**	**IDS**	**IDQ**	**Applicable**	**Adherence**
n= 6061 criteria	**%**	**%**	**%**	**%**	**%**	**%**	**Applicability**	**(CI 95%)**
18 **A patient prescribed teriparatide** is prescribed it for secondary prevention and meets at least one of the following 2 criteria ❑ **has a reason to avoid bisphosphonates (See 12)** ❑ **has an intolerance to strontium ranelate** o persistent nausea o persistent diarrhoea And has DEXA scan assessment that puts them in one the following groups ❑ **aged ≥ 65 years with a T-Score ≤ -4 SD** ❑ **aged ≥ 65 years with a T-Score ≤ -3.5 SD and has more than two fractures** ❑ **aged 55-64 years with a T-Score ≤ -4 and has more than two fractures**	319/319 100%	0	0	0	0	0	0/319 0%	nr

Total (319 patients)		**N/A**	**Yes**	**No(J)**	**No(U)**	**IDS**	**IDQ**	**Applicable**	**Adherence**
n= 6061 criteria		**%**	**%**	**%**	**%**	**%**	**%**	**Applicability**	**(CI 95%)**
19	**A patient prescribed calcitonin** is prescribed it for secondary prevention after bisphosphonate, raloxifene or strontium ranelate have been tried or have reasons for excluding from consideration [Reasons for non-use of bisphosphonates are ❑ contraindication to bisphosphonates (see 12) ❑ inability to comply with the recommendations for use of bisphosphonates (see 12) ❑ intolerance to bisphosphonates (see 12)]	319/319 100%	0	0	0	0	0	0/319 0%	nr
Overall		3581/6061	1532	18	860	88	44	2480/6061	1532/2480
(%)		59.1%						40.9%	61.7% (59.8-63.6)

N/A: not applicable; **No(J):** justified non-adherence to the guideline; **No(U):** unjustified non-adherence to the guideline; **IDS:** insufficient data on the standard; **IDQ:** insufficient data on the qualifier; **CI:** confidence interval; **S1:** Search 1; **nr:** no result

The following tables show ranking of level of adherence to each criterion in practice A, B and C as well as of the whole study sample.

In practice A, 6 criteria were reported to be highly adhered to with a mean of 92.4%. Intermediate level of adherence was observed in 7 criteria with a mean of 57.7%. In 2 criteria adherence was found to be low with a mean of 27.4%. In 4 criteria no results could be reported since there were no patients applicable to these criteria.

Table 19 Ranking in level of adherence practice A

Ranking	Level of adherence	Criterion number and description	Adherence	Applicability
1	High	C16: Patient prescribed strontium ranelate has a reason to avoid bisphosphonates	100%	1.3%
2		C 7: Patient prescribed supplementary calcium is prescribed the appropriate dose	98.8%	55.2%
3		C 8: Patient prescribed supplementary vitamin D is prescribed the appropriate dose	98.7%	50.6%
4		C 14: Patient on a bisphosphonate is prescribed the preffered choice	87.8%	53.2%
5		C 13: Patient prescribed osteoporosis treatment is prescribed standard dose regimen	86.2%	61%
6		C 12: Patient prescribed antiresorptive/osteoanabolic treatment has no contraindication to the agent	83.0%	61%
7	Intermediate	C 6: Patient diagnosed with osteoporosis is prescribed treatement	60.8%	89.6%
8		C 5: Patient with vitamin D deficieny or aged over 65 is prescribed vitamin D	58.9%	80.5%
9		C 10: Osteporotic patient is prescribed a bisphosphonate as first line therapy	58.7%	89.6%
10		C 1: Patient with a diagnosis of osteoporosis was diagnosed via DEXA scan	58.3%	85.7%
11		C 4: Osteopenic patient is prescribed supplementary calcium	56.3%	10.4%
12		C 11: Osteopenic patient prescribed bisphosphonate as first line therapy	56.3%	10.4%
13		C 3: Osteoporotic patient prescribed supplementary calcium	55.1%	89.6%
14		C 2: DEXA scan performed at two specific sites (spine and hip)	34.4%	60.4%

15	Low	C 9: Patients not prescribed antiresorptive/osteoanablic treatment are prescribed calcium and vitamin D	20.4%	0%
-	No result	C 15: Patient on long-term oral steroids receiving a bisphosphonate	-	0%
-		C 17: Patient prescribed raloxifene is prescribed it for secondary prevention	-	0%
-		C 18: Patient prescribed teriparatide meets requirements for being prescribed teriparatide	-	0%
-		C 19: Patient prescribed calcitonin meets requirements for being prescribed calcitonin	-	0%

In practice B, high adherence was reported for 4 criteria with a mean of 88.1%. Intermediate adherence was observed in 3 criteria with a mean of 53.3%. 5 criteria were found to be poorly adhered to with a mean of 24.2%. In 7 criteria no results could be found since there were no applicable patients.

Table 20 Ranking in level of adherence practice B

Ranking	Level of adherence	Criterion number and description	Adherence	Applicability
1	High	C 7: Patient prescribed supplementary calcium	100%	54.8%
2		C 8: Patient prescribed supplementary vitamin D is prescribed the appropriate dose	94.1%	54.8%
3		C 14: Patient on a bisphosphonate is prescribed the preffered choice	83.9%	50%
4		C 13: Patient prescribed osteoporosis treatment is prescribed standard dose regimen	74.5%	82.3%
5	Intermediate	C 5: Patient with vitamin D deficieny or aged over 65 is prescribed vitamin D	59.6%	75.8%
6		C 6: Patient diagnosed with osteoporosis is prescribed treatement	50%	100%
7		C 10: Osteporotic patient is prescribed a bisphosphonate as first line therapy	50%	100%
8		C 12: Patient prescribed antiresorptive/osteoanabolic treatment has no contraindication to the agent	41.9%	50%
9		C 3: Osteoporotic patient prescribed	38,7%	100%

		supplementary calcium		
10	Low	C 9: Patients not prescribed antiresorptive/osteoanablic treatment are prescribed calcium and vitamin D	38.7%	50%
11		C 1: Patient with a diagnosis of osteoporosis was diagnosed via DEXA scan	1.6%	100%
12		C 2: DEXA scan performed at two specific sites (spine and hip)	0%	17.7%
-	No result	C 4: Osteopenic patient is prescribed supplementary calcium	-	0%
-		C 11: Osteopenic patient prescribed bisphosphonate as first line therapy	-	0%
-		C 15: Patient on long-term oral steroids receiving a bisphosphonate	-	0%
-		C 16: Patient prescribed strontium ranelate has a reason to avoid bisphosphonates	-	0%
-		C 17: Patient prescribed raloxifene is prescribed it for secondary prevention	-	0%
-		C 18: Patient prescribed teriparatide meets requirements for being prescribed teriparatide	-	0%
-		C 19: Patient prescribed calcitonin meets requirements for being prescribed calcitonin	-	0%

In practice C, 5 criteria were highly adhered to with a mean of 97.3%. In 6 criteria intermediate adherence was observed with a mean of 64.6%. 5 criteria were found to be of low level of adherence with a mean of 30.6%. In 3 criteria no results could be found due to non-existence of applicable patients.

Table 21 Ranking in level of adherence practice C

Ranking	Level of adherence	Criterion number and description	Adherence	Applicability
1	High	C 7: Patient prescribed supplementary calcium is prescribed the appropriate dose	100%	49.5%
2		C 8: Patient prescribed supplementary vitamin D is prescribed the appropriate dose	100%	48.5%
3		C 15: Patient on long-term oral steroids receiving a bisphosphonate	100%	58.3%
4		C16: Patient prescribed strontium ranelate has a reason to avoid bisphosphonates	100%	1%

5		C 14: Patient on a bisphosphonate is prescribed the preffered choice	86.5%	35.9%
6	Intermediate	C 6: Patient diagnosed with osteoporosis is prescribed treatement	69.1%	53.4%
7		C 10: Osteporotic patient is prescribed a bisphosphonate as first line therapy	68.5%	52.4%
8		C 13: Patient prescribed osteoporosis treatment is prescribed standard dose regimen	64.6%	46.7%
9		C 3: Osteoporotic patient prescribed supplementary calcium	63.3%	58.3%
10		C 1: Patient with a diagnosis of osteoporosis was diagnosed via DEXA scan	62.7%	57.3%
11		C 5: Patient with vitamin D deficieny or aged over 65 is prescribed vitamin D	59.4%	67%
12	Low	C 12: Patient prescribed antiresorptive/osteoanabolic treatment has no contraindication to the agent	47.9%	46.6%
13		C 9: Patients not prescribed antiresorptive/osteoanablic treatment are prescribed calcium and vitamin D	40.9%	46.7%
14		C 4: Osteopenic patient is prescribed supplementary calcium	30.2%	35.9%
15		C 11: Osteopenic patient is prescribed a bisphosphonate as first line therapy	23.3%	1%
16		C 2: DEXA scan performed at two specific sites (spine and hip)	10.8%	1%
-	No result	C 17: Patient prescribed raloxifene is prescribed it for secondary prevention	-	0%
-		C 18: Patient prescribed teriparatide meets requirements for being prescribed teriparatide	-	0%
-		C 19: Patient prescribed calcitonin meets requirements for being prescribed calcitonin	-	0%

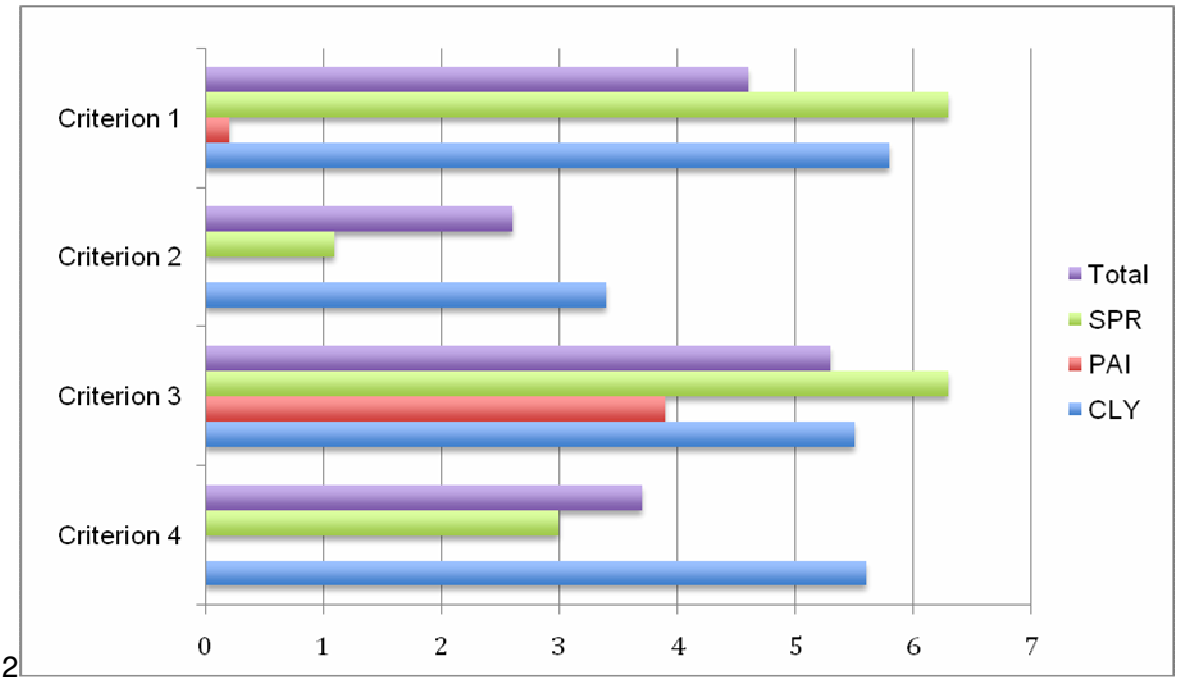
For the whole study sample, 6 criteria were found to be highly adhered to with a mean of 93.7%. In 5 criteria intermediate level of adherence was observed with a mean of. 59.4% Low level of adherence could was found in 5 criteria with a mean of 34.1%. For criteria, no results could be found since there were no patients applicable to these criteria.

Table 22 Ranking in level of adherence total patient sample

Ranking	Level of adherence	Criterion number and description	Adherence	Applicability
1	High	C 15: Patient on long-term oral steroids receiving a bisphosphonate	100%	0.3%
2		C16: Patient prescribed strontium ranelate has a reason to avoid bisphosphonates	100%	0.9%
3		C 7: Patient prescribed supplementary calcium is prescribed the appropriate dose	99.4%	53.3%
4		C 8: Patient prescribed supplementary vitamin D is prescribed the appropriate dose	98.1%	50.8%
5		C 14: Patient on a bisphosphonate is prescribed the preffered choice	86.7%	47%
6		C 13: Patient prescribed osteoporosis treatment is prescribed standard dose regimen	77.7%	60.5%
7	Intermediate	C 12: Patient prescribed antiresorptive/osteoanabolic treatment has no contraindication to the agent	65.9%	79.9%
8		C 6: Patient diagnosed with osteoporosis is prescribed treatement	60%	53.3%
9		C 5: Patient with vitamin D deficieny or aged over 65 is prescribed vitamin D	59.2%	50.8%
10		C 10: Osteporotic patient is prescribed a bisphosphonate as first line therapy	58.6%	33.5%
11		C 3: Osteoporotic patient prescribed supplementary calcium	53.1%	81.5%
12	Low	C 1: Patient with a diagnosis of osteoporosis was diagnosed via DEXA scan	45.5%	79.3%
13		C 4: Osteopenic patient is prescribed supplementary calcium	37.3%	18.5%
14		C 11: Osteopenic patient is prescribed a bisphosphonate as first line therapy	32.2%	18.5%
15		C 9: Patients not prescribed antiresorptive/osteoanablic treatment are prescribed calcium and vitamin D	29.9%	33.5%
16		C 2: DEXA scan performed at two specific sites (spine and hip)	25.5%	44.2%
-		C 17: Patient prescribed raloxifene is prescribed it for secondary prevention	-	0%

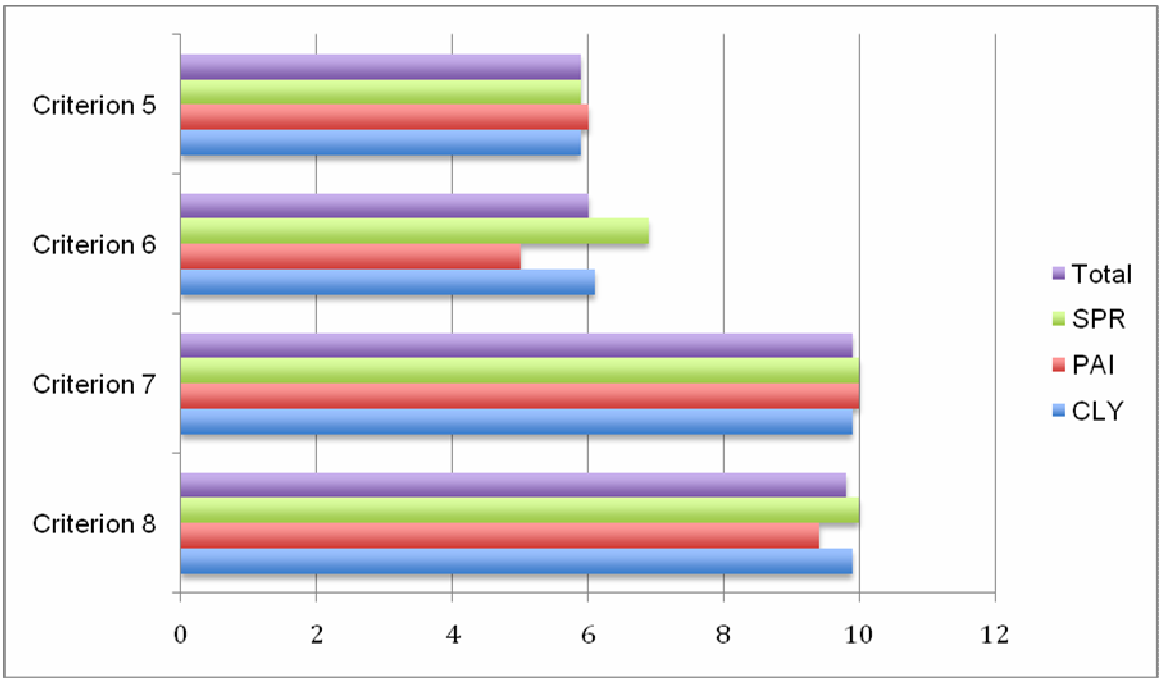
-	No result	C 18: Patient prescribed teriparatide meets requirements for being prescribed teriparatide	-	0%
-		C 19: Patient prescribed calcitonin meets requirements for being prescribed calcitonin	-	0%

The following bar charts were designed to highlight the differences in level of adherence between the three GPs. Adherence was observed to be particularly low in GP B, especially in criteria 1 (1.6%) and 2 (0%) dealing with DEXA scans. Criteria dealing with osteopenic patients (4 and 11) could not be applied to this patient sample since it was solemnly comprised of osteoporotic patients while there were no patients diagnosed with osteopenia. ForGP C particularly low adherence was reported for criterion 2, requiring diagnosis by DEXA scan performed at two specific sites. In all other criteria level of adherence was more or less similar, except for an especially high adherence in GP A for criterion 12 requiring no contraindications on record for patients receiving antiresorptive/ osteoanabolic agents.

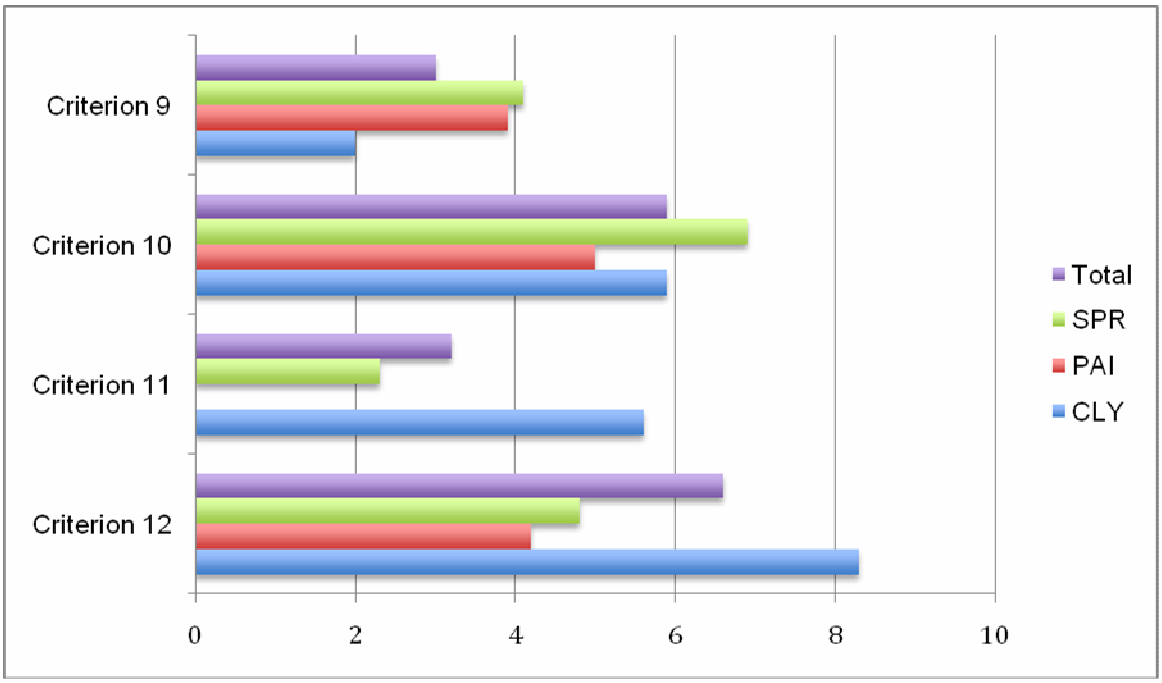


2

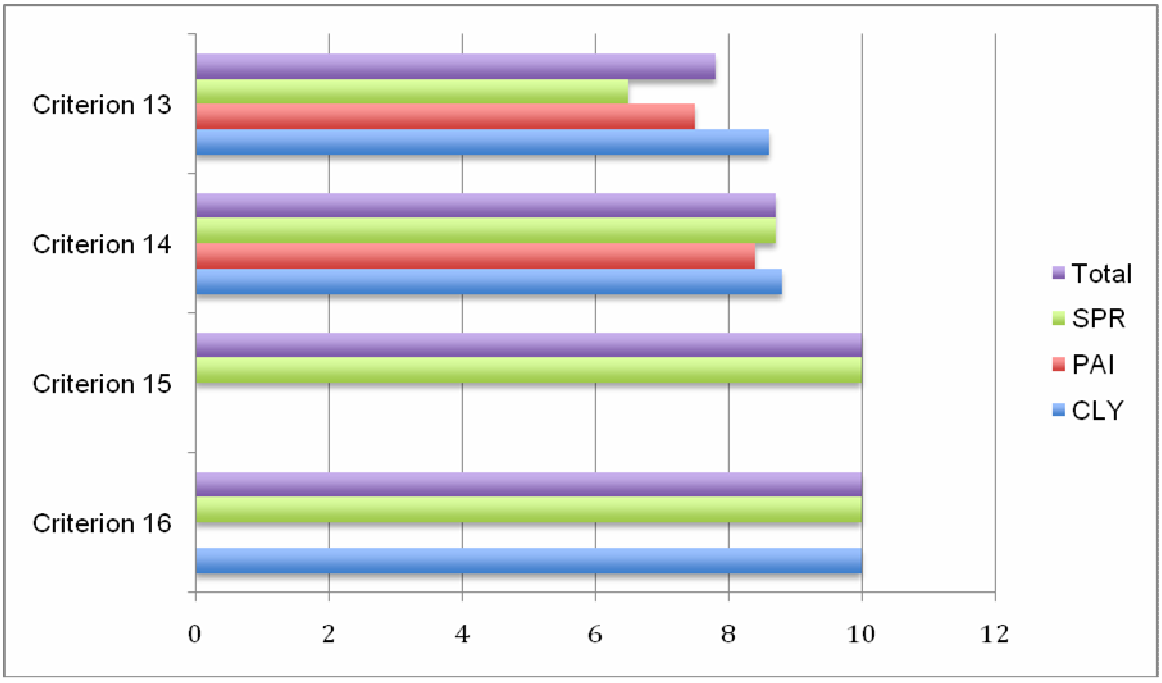
Bar chart 1 Adherence to criteria 1-4



Bar chart 2 Adherence to criteria 5-8



Bar chart 3 Adherence to criteria 9-12

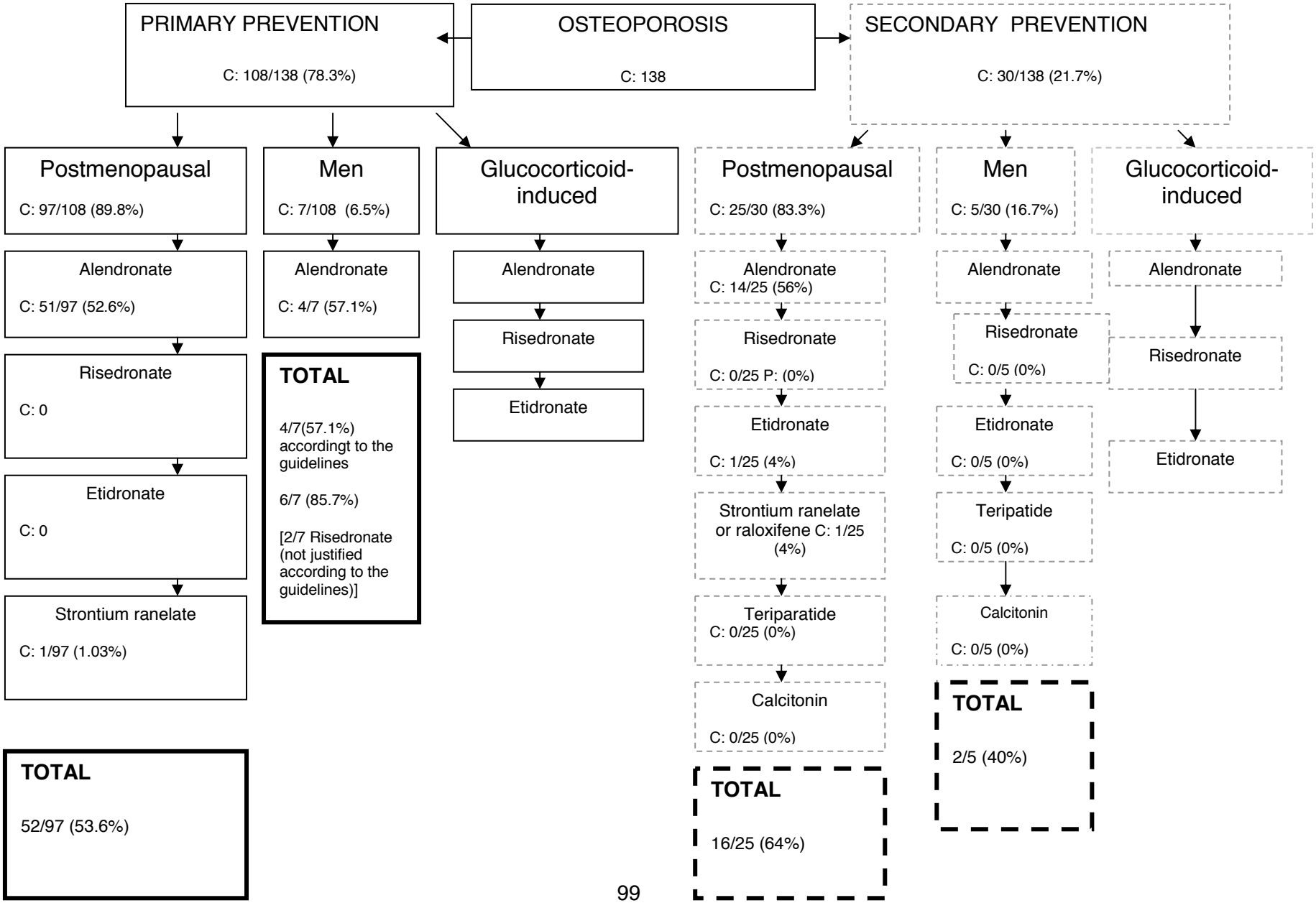


Bar chart 4 Adherence to criteria 13-16

For criteria 17, 18 and 19 there could be no result reported since there were no patients applicable to these criteria.

The following flowcharts show adherence to the clinical guidelines used in this project (SIGN 71 and NICE 160 and 161) concerning preferred order in treatment options in both primary and secondary prevention of osteoporosis in postmenopausal women, men and patients with glucocorticoid- induced osteoporosis drawn from GP A and B.

Table 23 Flowchart practice A



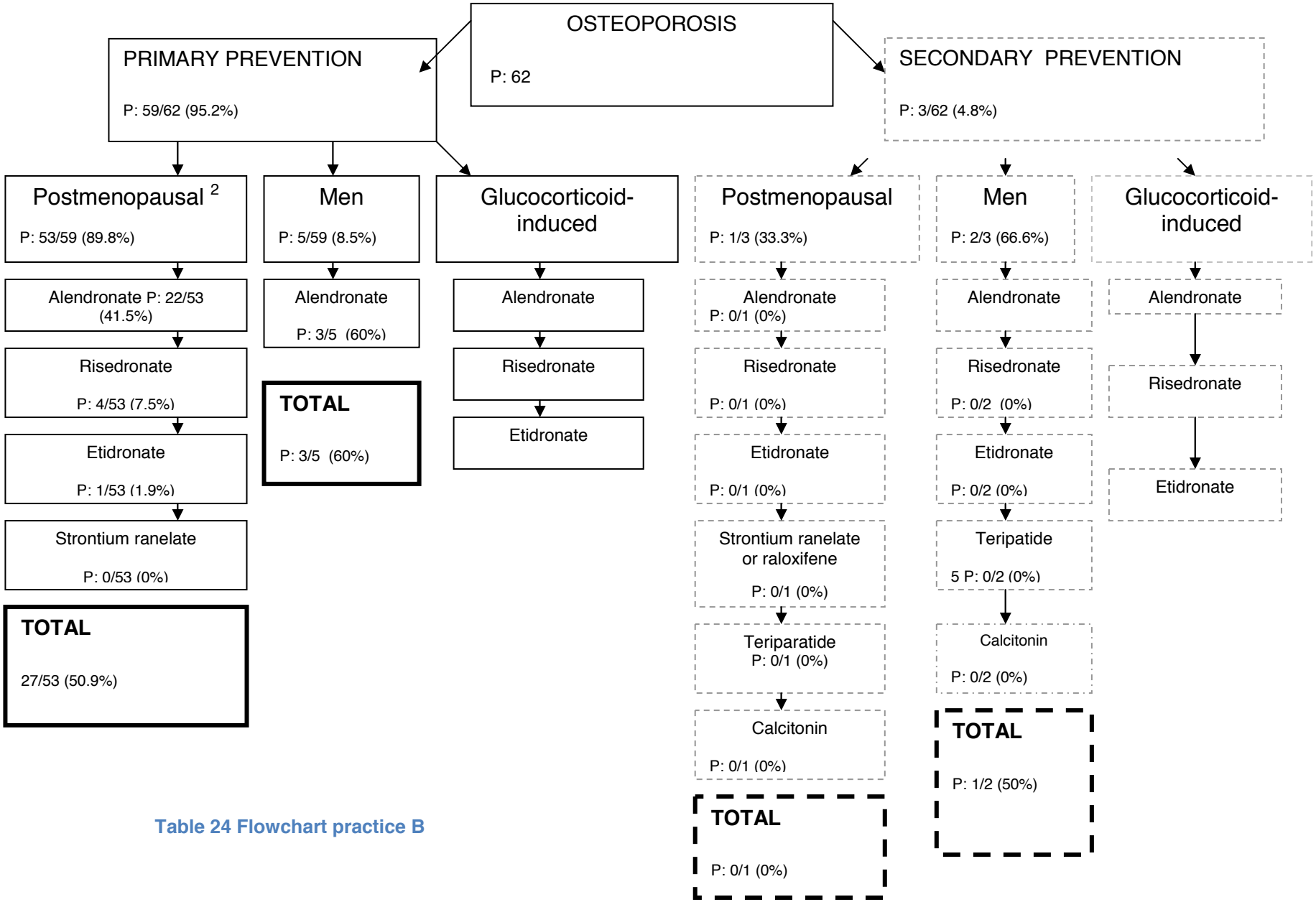


Table 24 Flowchart practice B

5.3. Inter-rater reliability testing

Inter-rater reliability testing of the MATosteo was conducted by two independent researchers and showed mean agreements of 99% for both applicability and adherence. Calculations were performed for the patient samples drawn from GP A and B, using the draft of MATosteo preceding the final tool, which was comprised of 21 criteria instead of 19. Minimum agreement in applicability was 90%, maximum 100% shown in 15 out of 21 criteria. Minimum adherence was 95% with 100% shown in 18/21 criteria. Total agreement in 'Yes'- results was achieved in 18 out of 21 criteria with a mean agreement of 99.6%. The two researchers fully agreed in terms of justified non-adherences in 21 out of 21 criteria. Concerning unjustified non-adherence, total agreement was achieved in 19 criteria with a mean agreement of 99.9%. See appendix 5.

5.4. Results of the validation of a potential community pharmacy- based service for the management of osteoporosis- Interviews

Health care specialists stated that the population did not have enough knowledge about osteoporosis, especially not about the implications of the disease, although there seemed to be a certain awareness of osteoporosis since many people have relatives or friends who are sufferers. Information provided about the disease by community pharmacists and in general was reported to be insufficient. An increase in provision of information through e.g. leaflets was confirmed to encourage more patients to refer themselves for diagnosis. It was reported that public health campaigns, nationally as well as locally have not yet taken place in Glasgow respectively Scotland but would contribute to create knowledge and awareness among patients. Interviewees suggested pharmacists to contribute in a public health campaign via speaking to patients, providing leaflets and posters.

Furthermore it was affirmed that an assessment of patients' knowledge would improve treatment outcomes. Use of questionnaires or checklists including risk factors like prior fracture, age, gender, family history, drug use like steroids, early menopause etc alongside with the indication of the appropriate action that should be taken, was confirmed to be capable of increasing identification rates in osteoporosis. The FRAX® tool was reported to be a useful tool which could be applied by community pharmacists to calculate fracture probability in patients in order to give appropriate advice or refer for diagnosis. Nevertheless it is not widely used in Glasgow due to the existence of the

DADS (direct access DEXA service) criteria that are basically equivalent to the FRAX® criteria. However, the FRAX® tool was reported to be of use in the making of treatment decisions in osteopenic patients whether to initiate treatment or not. Time was reported to be the limitating factor for calculation of fracture probability by using the FRAX® via community pharmacists.

Health care specialists stated that pharmacists did not sufficiently focus on the connection between diet, exercise, smoking etc and osteoporosis in the provision of health education and recommendation. It was reported that neither general medical practitioners nor community pharmacists provided sufficient support in medicines compliance to osteoporosis treatment. Interviewees affirmed that it would be useful to create a standard procedure for patients receiving osteoporosis treatment in order to increase the number of compliant patients. Health care specialists referred to the existence of a service intended for delivery by community pharmacists to follow up patients prescribed osteoporosis treatment. It was stated that only very few pharmacists actually were doing it. Implementation of measures to encourage pharmacists to provide long-term support was appreciated.

Interviewees reported that community pharmacists were usually not able to identify the duration of a patient's oral steroid therapy and were therefore incapable of indicating that the patient was suggested for bisphosphonate therapy. Hence, a service delivered by community pharmacies capable of identifying issues such as steroid patients not receiving preventive treatment for osteoporosis, was appreciated.

Measurement of adherence to clinical guidelines in osteoporosis patients was found to be unnecessary by several interviewees. From their point of view treatment was initiated exclusively by specialists 'who usually operate according to guideline recommendation'. Interviewees estimated adherence to guideline recommended prescribing to be approximately 80%.

5.5. Results literature review: Measures to address osteoporosis- current strategies and projects

5.5.1. Falls prevention- A Glasgow model of care

In Glasgow a Pharmacist-led model of care is targeting the problem of falls prevention. This model of care represents a systematic multidisciplinary approach to the problem of patients falling and sustaining fractures and was suggested by health care professionals to be incorporated into the NHS Primary and Secondary Care systems. Glasgow has a funded Strategy for Osteoporosis and Falls Prevention (see section

5.5.2.). The model is based on more than 60 randomised trials of interventions to prevent falls (Lowrie 2008). It consists on identification and referral of patients living in the community who are over the age of 65 and have fallen in the past year via community pharmacists. The patient's contact details are transferred to the Home Falls Prevention Programme (HFPP) who arranges an appointment with a worker trained in multidimensional risk assessment who will undertake a screening visit at the patient's home in order to identify risk factors for falling, especially environmental risk factors (Lowrie 2008).

The community pharmacist can refer patients to the HFPP or the patients can refer themselves. Onward referral from the HFPP to the pharmacy is also taking place in case a patient is receiving more than three repeat medicines and agrees to a medication review (Lowrie 2008). The medication review is a key intervention within the model besides the identification of high-risk patients. Such medication reviews used to be delivered by falls-specialist pharmacists, but now they are increasingly delivered by the community pharmacist nominated by the patient, which creates a perfect follow- up scenario since the community pharmacist is in regular contact with the patient and can identify ongoing problems and intervene. The medication review is a structured discussion between the pharmacist and the patient respectively his or her carer and tackles issues such as a patient's condition, medicines and expectations. A main component of the review is the identification of drugs increasing the risk of falling. Centrally acting drugs or drugs affecting blood pressure contribute to the risk of falling via mechanism like sedation, orthostatic hypotension, confusion, blurred vision etc especially when four or more drugs are taken at the same time(Lowrie 2008).

The review may include a withdrawal of potentially fall inducing drugs or a dose reduction. If the pharmacist delivering the review is a supplementary prescriber, changes to treatment are can be done immediately. Otherwise suggestions are made to the GP or consultant. Onward referral to other health or social care partners may take place following the review. The medication review should lead to an agreement to change in treatment between pharmacist and patient. The pharmacist will follow up any recommended changes in order to ensure the patient understood, accepted and adheres to them (Lowrie 2008).

5.5.2. NHS Greater Glasgow: Strategy for Osteoporosis and Falls Prevention

This strategy is a sub set of the Glasgow City Older People's strategic framework and has been developed by the multidisciplinary Osteoporosis and Falls Steering group, which was comprised of representatives of geriatric medicine, osteoporosis services, allied health professionals, public health, planning and local authority social work. It was implemented in 2006. The aim of the strategy was to *'reduce the number of falls which result in serious injury and ensure effective treatment and rehabilitation for those who have fallen*' by

- Prevention (including the prevention and treatment of osteoporosis
- Improving the diagnosis, care and treatment of those who have fallen
- Rehabilitation and long term support (NHS 2006)

Sub groups of health care professionals participated in the development of the strategy. Those were the Care Homes Subgroup, the Home Falls Subgroup, the Hospital Subgroup, the Osteoporosis subgroup and the Physical Activity subgroup. The focus of the strategy was put onto several target groups,

- the population as a whole
- individuals at risk of falling
- individuals at risk of injury from falling
- individuals at risk of fracture and
- individuals affected psychologically by falls (NHS 2006)

I: Approach to prevent falls in the general population

1.: Public Health Approach

The approach to reduce the incidence and impact of falls in the general population was based on actions to 'encourage appropriate weight-bearing and strength enhancing physical activity, promote health eating (including adequate intake of calcium) and reduce smoking'. The National Osteoporosis Society recommends in its Primary Care Strategy for Osteoporosis and Falls of 2002 the following life stage approach:

Table 26 Lifestyle recommendations according to age

Life stage	Area for action
From conception to school age	Maternal well being
	Healthy diet
	Adequate safe sunshine exposure
	Adequate weight bearing physical activity
School age	Healthy diet
	Adequate safe sunshine exposure
	Adequate weight bearing physical activity
	Avoidance of smoking
	Caution about excessive dieting and athletic amenorrhoea
Young adults	Women with amenorrhoea/early menopause
	Healthy diet
	Adequate safe sunshine exposure
	Adequate weight bearing physical activity
	Avoidance of smoking
	Caution about excessive dieting and athletic amenorrhoea
	Alcohol within recommended safe limits
Adults at midlife	Women at menopause
	Healthy diet
	Adequate safe sunshine exposure
	Adequate weight bearing physical activity
	Avoidance of smoking
	Caution about excessive dieting and athletic amenorrhoea
	Alcohol within recommended safe limits
65+	Selective case finding for people at high risk of osteoporosis
	Falls prevention measures
	Healthy diet
	Adequate safe sunshine exposure
	Adequate weight bearing physical activity
	Avoidance of smoking
	Alcohol within recommended safe limits

2.: Local health promotion strategies

National school meal guidelines 'Hungry for Success' were implemented in Primary Schools to provide assured availability of adequately calcium containing food. The NHS Greater Glasgow reformulated its Food and Health Policy to establish new standards for nutrition in hospitals, which focussed on the adequate calcium and vitamin D intake in continuing care beds for older people (NHS 2006).

II: Preventing falls in individuals at home

There are several places where a patient who has fallen can be referred to:

- the Interdisciplinary Response and Intervention Service (IRIS)
- the Discharge and Rehabilitation Team (DART)
- the Community Older People's Teams (COPTs)
- the Day Hospital
- the Home Falls Prevention Programme
- Falls clinics

During a pilot falls project to which patients were referred to via GPs, health, social workers, carers and self-referal, a screening tool for risk factors and a plan for appropriate interventions were developed. A trained OT support worker under the supervision of a clinical lead undertakes the screening of all patients who are referred to the service. The screening tool includes short assessment tools like mini mental state, timed up and go (TUAG), Hospital Anxiety and Depression Scale. The assessment enables the service to refer patients appropriately for further assessment and/or intervention to

- DXA scan
- Physiotherapy/ exercise programme
- Day Hospital review
- Pharmacy-medication review
- Optometry
- Podiatry

- Occupational Therapy

The service includes a Falls Administration Centre, which enables the gathering of basic information about the patient and the direct referral to the appropriate service (NHS 2006).

Outpatient Falls Clinics

In Greater Glasgow there are five outpatient falls clinics. Patients with syncope (transient loss of consciousness), complex pharmacology and 2 or more falls with preceding symptoms are referred to an outpatient falls clinic. The clinics undertake a medical review with 'Falls Screening Documentation', which is provided by the Home Falls Prevention service. Following this consultants etc from the hospital meet to discuss and agree on an appropriate action plan (NHS 2006).

Standardised exercise programme

Referral to exercise programmes is based on the individual patient's conditions. All hospitals run exercise programmes. Programmes will be increased to ten weeks and delivered on a twice-weekly basis. These will be physiotherapy led for the first six weeks and then coach- led. On discharge, patients will be referred into level 1. Community programmes take place in community based centres throughout NHS Greater Glasgow. Falls prevention programmes are run alongside with the exercise programme. Many patients, particularly the elderly ones, require transportation to the centres or hospital where their exercise programme is taking place. This is provided by ambulance transportation for patients attending the hospital based programme or the level 1 programme (NHS 2006).

Table 27 Patient specific exercise programmes

Programme	Target group
Hospital based	Suitable for frail, functionally dependent individuals who require high level of supervision
Level 1(Community based)	Suitable for patients who are slightly more independent
Level 2 (Community based)	Higher level balance activities for functionally independent patients
Level 3 (Hospital based osteoporosis class)	Primarily for the postmenopausal osteoporosis group. Also suitable for low risk fallers.
Level 4	Primarily for the postmenopausal osteoporosis group. Also suitable for independent older individuals for prevention purposes.
Exercise booklet/video (basic seated warm up and exercises in sitting and standing)	Suitable for all patients. (This will be used in care homes settings as a home based physical intervention). Plus separate osteoporosis video.

Community pharmacies

The majority of Glasgow's community pharmacists have received training to identify patients who are at risk of osteoporosis and/or falling, to deliver medication reviews and to provide support in medication compliance with osteoporosis treatment. The contract for community pharmacies offers a potential possibility for patient contacts and continuity and consistency in long-term support of patients receiving osteoporosis and/or who are at risk of falling. As mentioned before, the community pharmacy contribution consists on

- identifying patients/customers at risk of falling
- offering relevant and appropriate information
- referring to the Home Falls Prevention Programme,
- delivering medication reviews for patients referred by the HFPP

Pharmacists also deliver medication reviews in falls clinics in collaboration with secondary care based pharmacists. This provides the additional benefit of linking the community pharmacy with the clinical setting and enables a pre- as well as a post-clinic appointment with the community pharmacist (NHS 2006).

Direct Access to DXA services

All patients who have fallen are assessed for risk factors of osteoporosis according to the criteria used for the Direct Access DXA service (DADS) (NHS 2006).

Preventing falls in patients who live in care homes

Many inhabitants of care homes frail, ill and/or have mobility problems. Every inhabitant who has recently fallen is provided with a 'Falls Action Plan'. This plan includes documentation of a patient's individual environmental/personal and communication needs, any behaviours leading to falls as well as aids and equipment to prevent falls. Each care home reviews all falls on a three- monthly cycle or more frequently if required. Action plans for inhabitants who fall frequently, might be reviewed. Guidance for equipment to reduce risk of falls was established. This guidance includes seating, bed rails, non-slip mats, lap straps and low-level beds or mattresses. Hip protectors might protect residents who fall and might be implemented. Older people living in care homes receive calcium and vitamin D supplementations. Residents who present the following problems associated with falls risk are referred to the appropriate service in order to reduce the risk of falling:

- problems in gait, balance, mobility and muscle weakness
- osteoporosis risk
- perceived functional ability and fear relating to falling
- visual impairment
- cognitive impairment (will be referred for neurological examination)
- urinary incontinence
- medications increasing the risk of falling (NHS 2006)

Staff of care homes is trained to deliver exercise programmes for the residents. The programme is based on the exercise book and video. Residents who are functionally more able should attend the level 1 class in the nearest community. Furthermore the staff receives training concerning the identification of environmental risk factors, identification of personal risks and the use of mobility aids (NHS 2006).

Falls prevention co- coordinators should be employed in order to increase the awareness of falls prevention and management and to support the care home in the

development and the review of falls action plans as well provide help in patients eligible for hip protectors(NHS 2006).

Preventing falls in patients in hospitals

In the clinical setting, 'Hospital Falls Coordinators' ensure that all wards carry out effective risk assessment and appropriate interventions and provide staff and patient education. Furthermore equipment and hip protectors are overviewed. Patients with gait problems are referred to physiotherapy and receive a structured exercise plan. Patients who fall and do not fracture are referred for osteoporosis risk assessment via DADS criteria (NHS 2006).

6- DISCUSSION

Osteoporosis is an asymptomatic disease that often remains undiagnosed and untreated, resulting in mortality, morbidity and impaired quality of life, socially, emotionally and financially (Lewiecki 2009a). It has been predicted that in 20 years' time approximately one quarter of the European population will be above the age of 65 (Woolf and Akesson 2003). The fact that incidence in fractures increases with age combined with the expanding population of elderly people results in a growing burden of osteoporosis. Therefore progress in diagnosis and identification of individuals at high fracture risk is crucial. Even though evidence based interventions for diagnosis, prevention and treatment of the disease exist, it has been observed that they are not applied in clinical practice or only to a certain, small extent (Woolf and Akesson 2003).

An adequate intake of calcium and vitamin D is regarded as baseline therapy for both prevention as well as treatment of osteoporosis (Lewiecki 2009b). Elderly people in particular are considered for calcium and vitamin D supplementation (Woolf and Akesson 2003). Assessment of the patient sample in this study showed that guideline recommendations concerning calcium and vitamin D are only poorly adhered to. Oral bisphosphonates are considered to be first line therapy for osteoporosis. However their use may be limited due to gastrointestinal side effects (Lewiecki 2009a). Assessment of the patient data in this project showed that treatment alternatives such as alternative oral bisphosphonates, i.v. bisphosponates, strontium ranelate, raloxifene, calcitonin or teriparatide are only very rarely prescribed.

Pharmacological interventions to prevent fractures are most clinically and cost effective when targeted at people who are at highest risk of sustaining fractures. Individuals who are at highest risk can be identified via previous fractures and low bone density since they are strong risk factors for sustaining a subsequent fracture. Combining these with other risk factors allows the identification of those patients who are at highest risk. Management of high-risk patients should be according to their risks and needs (Woolf and Akesson 2003). Drug intolerance, complexity of dosing regimens and poor understanding of the benefits and risks of the treatment are the major limitations in osteoporosis treatment. Therefore there is a substantial need for effective strategies to maximize compliance, long-term tolerance and persistence with therapy (Lewiecki 2009a). To sum up, there is a substantial need for development of strategies to

address osteoporosis, to screen and identify more individuals who are at high risk, to give systematic patient specific advice, to provide individual patient-specific treatment, to follow up treatment and ensure long-term efficacy, tolerance and safety of treatment.

Assessment of patient data of osteoporosis and osteopenia patients in this project showed that 40% of patients are receiving no treatment at all although they are eligible for treatment and although alternative treatment options exist. In many patients there could be no documented reason such as e.g. a contraindication to a certain agent found to justify this non-prescribing of both first line and second line therapy. Prescribing of supplementary calcium and vitamin D was observed to be low, especially in osteopenic patients. 30% of patients eligible for osteoporosis treatment but not receiving antiresorptive or osteoanablioc treatment were not prescribed supplementary calcium and vitamin D.

6.1. Problems and challenges within the conduction of the study

Major limitation to the feasibility of the implementation of MATosteo was the accessibility of patient data. Crucial information such as results from certain investigations was not accessible for the researcher on GPASS®. There was no access to actual T- Scores (BMD measurement values), so there could be no judgement made whether a diagnosis of osteoporosis or osteopenia was reliable and set up according to WHO-criteria or not. Furthermore lab results such as Creatinine Clearance (CrCl) were not accessible. In many cases documentation was restricted to an entry of ‘chronic kidney disease’ or ‘chronic kidney disease stage 3’ or ‘chronic kidney disease stage 4’. Therefore the investigator was not able to determine whether a patient presents an explicit contraindication to bisphosphonates respectively raloxifene or not.

Bisposphonates are contraindicated in patients presenting a CrCl below 35 ml/min, which represents a stage within CKD stage 3. Raloxifene is contraindicated in patients with a CrCl below 10 ml/min (CKD stage 4). In some cases serum creatinine was reported which does not allow an explicit categorisation of renal impairment. Another problem was the inconsistency in documentation regarding wording. For example there could be entries of ‘chronic renal failure’, ‘renal impairment’, ‘chronic kidney disease’, ‘CKD’ and ‘Serum Creatinine raised’. All these terms represent the same condition and aggravate the data extraction from GPASS®. In many cases documentation was

incomplete. Documentation of 'HRT' did not allow the investigator to determine whether a woman was receiving hormone replacement therapy for alleviation of postmenopausal symptoms or for osteoporosis treatment. Furthermore gaps in documentation were discovered in weight and height. Body mass index (BMI) was hardly ever documented.

A correct data collection is crucial for the accurate conduction of the study. Due to the reasons mentioned before the data collection has to be conducted by trained stuff presenting certain background information in pharmacology and the software system GPASS®.

6.2. Adherence of the GP clinics to guideline recommendation

The purpose of this study was to evaluate the extent to which prescribers handle medicine use according to guideline recommendation. Overall adherence of 61.7% to clinical guidelines for the management of osteoporosis represents intermediate level of adherence. This information might be a first stage to take steps to increase guideline adherence in osteoporosis management. Local health specialists estimated adherence to guideline recommended prescribing to be approximately 80%, which has been shown to be not the case with a mean of only 60%.

6.2.1. Calcium and vitamin D

The study revealed that level of adherence to guideline recommendation in prescribing of supplementary calcium and vitamin D is insufficient. Within the total study sample only 53.1% of patients with osteoporosis and 37.3% of patients with osteopenia were prescribed calcium. 59.2% of patients aged 65 and over were prescribed vitamin D. 29.9% of patients with osteoporosis who were not receiving antiresorptive/ osteoanabolic treatment, were prescribed supplementary calcium and vitamin D meaning that approximately 70% of patients with osteoporosis remain completely untreated.

For GP A significantly high adherence was observed in criteria 7 and 8 stating that prescribed dosing regimens in calcium and vitamin D prescriptions are correct. In 84 out of 85 respectively 77 out of 78 patients the correct dosage was prescribed. However, applicability in these criteria was shown to be only 55.2% respectively 50.6%. This means that only 85 out of eligible 154 (55.2%) patients were prescribed calcium and 78 out of 154 (50.6%) were prescribed vitamin D. Although calcium and vitamin D supplementation is regarded as baseline therapy in the prevention and treatment of

osteoporosis and osteopenia (Lewiecki 2009a), the number of patients receiving supplements is significantly low with approximately a half of eligible patients.

Similarly forGP B adherence to criteria 7 and 8 was 100% and 94.1% with 34 out of 34 and 32 out of 32 patients. Again, applicability to these criteria was only 54.8% since only 34 out of 62 (54.8%) were prescribed supplementary calcium and vitamin D.

For GP C criteria 7 and 8 were adhered to by 100% with 51 out of 51 and 50 out of 50 patients. However the patient sample drawn from GP C was comprised of 103 patients, all of them eligible for calcium and vitamin D supplementation, meaning that approximately 50% of patients were missed for supplementation.

Although in most calcium and vitamin D prescriptions the appropriate dosage is prescribed, approximately half of eligible osteoporotic and osteopenic patients are not receiving supplementary calcium and vitamin D at all. For GP B criterion 3 requiring supplementary calcium in osteoporotic patients was only met by 24 out of 62 applicable (osteoporotic) patients (38.7%), a fact that indicates significant insufficiency in prescribing of supplementary calcium. For GP C only 30.2% of osteopenic patients were found to receive calcium.

For criterion 9 requiring prescribing of supplementary calcium and vitamin D in osteoporotic patients who are not receiving any treatment (antiresorptive or osteoanabolic), adherence was found to be only 29.9% (20.4% (11/54) for GP A, 38.7% (12/31) for GP B and 40.9% (9/22) for GP C).

Besides low rate in prescriptions, incompliance to regular intake of and vitamin D might also contribute to the non- adherence to supplementation of calcium and vitamin D. Since long-term prescriptions have to be picked up at the GP every month it might be possible that patients are merely incompliant to supplements and do not pick up their prescription on a monthly basis which would result in a non-existing of an active prescription record. This might be misinterpreted by the investigator as a non-existence of a prescription. The investigator suggests to conduct further research within the field of compliance in order to identify the underlying reason for the significantly low adherence to supplementation, especially in patients who do not present an active prescription record for any kind of osteoporosis treatment.

Similarly as for calcium and vitamin D supplementation, in antiresorptive and osteoanabolic treatment it has been found that appropriate dosages were prescribed. For GP A 81 (86.2%) of 94 applicable patients were prescribed the appropriate dose regimen. Similarly 74.5% adherence (38 out of 51 applicable patients) was reported for

GP B. However, rates of actual prescribing of treatment were found to be rather insufficient.

6.2.2. Antiresorptive/ osteo-anabolic treatment

Although local health specialists estimated adherence in prescribing to be around 80%, the study showed that only 60% of osteoporosis-patients of the total study sample were actually prescribed antiresorptive/ osteoanabolic treatment. This percentage represents intermediate level of adherence to guideline recommendation.

There were 58.6% of patients with osteoporosis and only 32.3% of patients with osteopenia were observed to receive a bisphosphonate as first line therapy, suggesting that osteopenic patients remain significantly undertreated.

Some 65.9% of patients receiving treatment had no contraindications to these agents on records, a percentage that is apparently too low. Criterion 12 requires that patients receiving antiresorptive or osteoanabolic treatment do not have a contraindication to those agents. 94 out of 154 (61%) patients were applicable to this requirement (prescribed either antiresorptive or osteoanbolic treatment), 78 out of those 94 patients were adherent to the standard and did not have a contraindication on record.

Criterion 14 requires that osteoporotic patients on bisphosphonate therapy should be on the preferred choice (alendronate or alternatively risedronate or as third choice etidronate). 72 patients out of 82 patients prescribed a bisphosphonate were adherent to the standard. Adherence to this criterion is 87.8%. Similarly adherence was 83.9% for GP B (26 out of 31 patients) and 86.5% for GP C (32 out of 37 applicable patients). Adherence of 100% in patients drawn from GP C was reported for criterion 16, requiring a prescription of strontium ranelate exclusively for patients who have a contraindication to bisphosphonates.

There were only 2 patients prescribed strontium ranlelate, both of them presenting an identifiable reason to avoid bisposphonate therapy. Similarly for GP C one patient presenting a reason to avoid bisphosphonates was prescribed strontium ranelate, so adherence was 100%. Furthermore 100% was reported for criterion 15 for GP C. This criterion requires bisphosphonate prevention for patients receiving long-term steroid therapy. There was one patient receiving long-term steroids, he was prescribed a bisphosphonate.

Given the fact that various alternatives in antiresorptive and osteoanabolic treatment exist, contraindications in individual patients to certain medications can be taken into account and appropriate, alternative treatment options for each patient can be found. No patients were found to receive iv bisphosphonates, only 9 out of 319 patients were prescribed risedronate respectively etidronate. Only 3 out of 319 patients were found to receive strontium ranelate. There have been no patients on raloxifene, teriparatide or calcitonin. These facts suggest that rates in prescribing of alternative treatment options should be increased.

6.2.3. DEXA scan

Significantly low adherence in all three GPs was reported for criteria 1 and 2 requiring diagnosis of osteoporosis to be set up via DEXA scan (criterion 1) at two specific sites (criterion 2). For the requirement set up in criterion 1 stating that a patient with osteoporosis should have a recorded DEXA scan adherence was observed to be 45.5%. In criterion 2 suggesting that a DEXA scan should be performed at two specific sites, namely spine and hip at the same date, adherence was even less with 25.5%.

These findings suggest that diagnosing in osteoporosis is not necessarily reliable since the recommended action (performance of DEXA scan at spine and hip) is only taken in very few patients.

Whereas adherence in criterion 1 was 58.3% in GP A (77/132) and 62.7% in GP C (37/59), it was only 1.6% in GP B (1 patient out of 62 osteoporotic patients diagnosed via DEXA scan). This might be due to the fact that GP B is located in a rather deprived area within Greater Glasgow did not have access to DEXA scan facilities for a long time. However the requirement for performance of DEXA scans on two specific sites, namely spine and hip (criterion 2), was poorly adhered to in all three GPs. In GP A 32 out of 93 applicable patients (34.4%) adhered to guideline recommendation, 0% in GP B and 4 out of 37 applicable patients (10.8%) in GP C.

6.2.4. Non-significant results

Several criteria presenting high levels of adherence were found to be not necessarily of statistical significance due to very low numbers of applicable patients.

For example: ‘A patient receiving strontium ranelate has a contraindication to bisphosphonates’. For this criterion, level of adherence was reported to be 100%. However applicability was only 0.9 with only 3 out of 319 patients who were actually prescribed strontium ranlelate.

Similarly for criterion 15 ('A patient receiving long-term oral glucocorticoid therapy is prescribed a bisphosphonate) level of adherence was 100%. As in the criterion mentioned before, applicability was extremely low with only 0.3% since there was only 1 out of 319 patients receiving long-term oral steroid therapy and therefore meeting the qualifying statement.

This shows that the results from the statistical analysis have to be handled with care and interpreted carefully. Significantly high levels of adherence are not necessarily statistically meaningful, applicability has to be taken into account as well.

6.3. Contribution of the pharmacist

The community setting represents an ideal location to assess the risk of various diseases in random customers.

Pharmacists can participate in the management and prevention of osteoporosis via e.g. providing relevant lifestyle advice, helping to find the optimal medication for the individual patient, supporting long-term compliance with osteoporosis treatment or/and reviewing a patient's medication since they are experts within the field of pharmacotherapy and drugs. The community pharmacist is situated in the ideal position to provide the aspects mentioned before since he or she is in constant and regular contact with patients. Awareness of the risk and consequences of osteoporosis as well as adequate training in order to gain the skills required to deliver pharmaceutical care for the management of osteoporosis are crucial preconditions for pharmacists.

In the clinical setting, the clinical pharmacist has to have full access to a patient's diagnosis, laboratory results and other information in order to be able to provide a medication review and to share his or her knowledge of drug therapy in the most beneficial way for the patient (SIGN 2003). Hence interdisciplinary teamwork among doctors and pharmacists is crucial. Furthermore this interdisciplinary team consists of nurses, nutritionists and technicians. This aspect of pharmaceutical care is mainly taking place in the hospital since the clinical pharmacist has most access to a patient's information. This is (at least so far) unlikely to be the case for community pharmacists whose access to a patient's recorded diagnosis and other information is very restricted or even non-existing. Given the availability of certain data, medication reviews can also be delivered by a community pharmacist.

6.4. Strenghts and limitations of this project

A clear strength of this study is that guideline recommendation for the management and prevention of osteoporosis was derived from the latest version of relevant guidance.

MATosteo has been developed in a multi-stage process, which allowed the research group to review and revise the tool in order to obtain the most relevant draft presenting highest practicability, applicability and feasibility for its use in practice.

The tool was applied to patients located within three different GPs and applied by two independent researchers in order to assess inter-rater reliability of the tool. It was shown that MATosteo represents a reliable tool, which provides reproducible and reliable results when applied by different researchers. Furthermore application of the tool was found to be not too time-consuming.

A limitation of the project is that the local Glasgow guidelines were not included. It might be useful to conduct a survey to measure adherence to these local guidelines.

The tool does not cover management of chronic and acute pain of osteoporotic fractures, which is a crucial aspect of osteoporosis therapy.

MATosteo cannot be applied by untrained staff, a pharmacological background was identified to be crucial precondition since appropriate knowledge is necessary for the data collection as well as for interpretation of medical history of individual patients (e.g. knowledge of medical conditions representing a contraindication for bisphosphonate therapy).

6.5. Proposals for future research

The investigator suggests to conduct a survey on the correlation between patient education (modifiable risk factors, instructions for use of bisphosphonates, necessity of calcium and vitamin D supplementation) and compliance respectively outcomes of treatment since the problem of compliance might be a major factor contributing to low adherence to guideline recommendation.

This study revealed that lately licensed treatment options (iv bisphosphonates, teriparatide, calcitonin) are not integrated into osteoporosis treatment. Identification of possible reasons as well as creation of measures to allow integration of these treatment options might be issues for future research.

7- CONCLUSION

MATosteo has been shown to be a useful tool in the evaluation of level of adherence to clinical guidelines. The application of the MAT by two independent researchers to the same set of patient data indicated reliability of the MAT in the administration to electronical medical records. MATosteo represents a sensitive tool, which can be used for comparison of prescribing in different clinical settings as well as for a large-scale audit of medication use.

The assessment of the patient data of the three GP practices revealed an overall non-adherence to guideline recommendation of 38.3%. These findings represent a first stage in identifying and addressing pharmaceutical care issues in the management of osteoporosis. Identification of low guideline adherence in patients could be discussed with the responsible GP in order to optimize beneficial treatment effects for patients. Adherence to guideline recommendation was particularly low in the prescribing of supplementary calcium and vitamin D and the diagnosing via specific DEXA scan. Low level of adherence to calcium and vitamin D supplementation might partly result from non-compliance. Further research should be conducted in this field of compliance. Osteopenia was found to remain significantly undertreated. Methods to arise awareness of this issue and to draw the attention to osteopenic patients who are suggested to receive certain treatment in order to prevent the development of osteoporosis should be established. Furthermore it has been detected that prescribing of alternative treatment options like iv bisphosphonates or strontium ranelate is practically non-existing. These findings might be used as a starting point for pharmacoeconomical research.

A community pharmacy based service to identify patients at high risk for osteoporosis and fractures was found to be useful and feasible. Community pharmacists are considered to be skilled and capable of contributing in the detection and management of osteoporosis. Furthermore community pharmacists are located in an ideal position for delivery of such a service as they are in constant contact with patients. As possible start points a fracture risk assessment in individual patients via the Internet tool FRAX®, provision of relevant advise and referral according to the calculated risk as well as assessment of quality of prescribed medication were identified. Furthermore pharmacists could participate in falls prevention in case appropriate training is provided. The limitating factor for the implementation of a pharmaceutical care tool for community pharmacy interventions in osteoporosis was identified to be bringing up

extra time for the delivery of such a service. This was reported to be solvable by reimbursing community pharmacists for the delivery of the service, as it is the case for e.g. provision of smoking cessation advises.

REFERENCES

Aktories, K., Förstermann, U., Hofman, F., and Forth, W. (2005). Allgemeine und spezielle Pharmakologie und Toxikologie.

Barrett-Connor, E., Siris, E.S., Wehren, L.E., Miller, P.D., Abbott, T.A., Berger, M.L., Santora, A.C., and Sherwood, L.M. (2005). Osteoporosis and fracture risk in women of different ethnic groups. J Bone Miner Res *20*, 185-194.

Berenguer, B., La Casa, C., de la Matta, M.J., and Martin-Calero, M.J. (2004). Pharmaceutical care: past, present and future. Curr Pharm Des *10*, 3931-3946.

Bitsch, T. (1997). Klinikleitfaden Rheumatologie, Vol 2.Auflage.

Blahos, J. (2007). Treatment and prevention of osteoporosis. Wien Med Wochenschr *157*, 589-592.

BNF (2009). British National Formulary 57. In BNF 57.

Chakkalakal, D.A. (2005). Alcohol-induced bone loss and deficient bone repair. Alcohol Clin Exp Res *29*, 2077-2090.

Chatziavramidis, A., Mantsopoulos, K., Gennadiou, D., and Sidiras, T. (2008). Intranasal complications in women with osteoporosis under treatment with nasal calcitonin spray: case reports and review of the literature. Auris Nasus Larynx *35*, 417-422.

Cipolle, R.J., Strand, L.M., and Morley, P.C. (2004). Pharmaceutical care practice: The clinician's guide.

Compston, J.E. (2001). Sex steroids and bone. Physiol Rev *81*, 419-447.

Copeland, C., and Worsley, A. (2009). Osteoporosis features of disease and diagnosis. Clinical Pharmacist *1*, 4.

Cummings, S.R., and Melton, L.J. (2002). Epidemiology and outcomes of osteoporotic fractures. Lancet *359*, 1761-1767.

Faulkner, K.G. (2005). The tale of the T-score: review and perspective. Osteoporos Int *16*, 347-352.

Harkin, S., Gerhart, T., and Hansen, K. (1999). Using Microsoft Access 2000, 1. edn (MacMillan Computer Publishing, Que corporation).

Hartikainen, S., Lönnroos, E., and Louhivouri, K. (2007). Medication as a Risk Factor for Falls: Critical Systematic Review. Journal of Gerontology: MEDICAL SCIENCES *62A*.

Hepler, C.D., and Strand, L.M. (1990). Opportunities and responsibilities in pharmaceutical care. Am J Hosp Pharm *47*, 533-543.

Hettenkofer, H.J. (1998). Rheumatologie, Vol 3.Auflage.

Hirschhorn, J.N., and Gennari, L. (2008). Bona fide genetic associations with bone mineral density. N Engl J Med *358*, 2403-2405.

Hoidrup, S., Prescott, E., Sorensen, T.I., Gottschau, A., Lauritzen, J.B., Schroll, M., and Gronbaek, M. (2000). Tobacco smoking and risk of hip fracture in men and women. Int J Epidemiol *29*, 253-259.

Jehle, P.M., and Pfeilschifter, J. (2009). [Osteoporosis - Which therapy is confirmed?]. Internist (Berl).

Kanis, J.A. (2002). Diagnosis of osteoporosis and assessment of fracture risk. Lancet *359*, 1929-1936.

Kanis, J.A., Johnell, O., Oden, A., Johansson, H., and McCloskey, E. (2008a). FRAX and the assessment of fracture probability in men and women from the UK. Osteoporos Int *19*, 385-397.

Kanis, J.A., McCloskey, E.V., Johansson, H., Strom, O., Borgstrom, F., and Oden, A. (2008b). Case finding for the management of osteoporosis with FRAX--assessment and intervention thresholds for the UK. Osteoporos Int *19*, 1395-1408.

Karsdal, M.A., Henriksen, K., Arnold, M., and Christiansen, C. (2008). Calcitonin: a drug of the past or for the future? Physiologic inhibition of bone resorption while sustaining osteoclast numbers improves bone quality. BioDrugs *22*, 137-144.

Kazakia, G.J., and Majumdar, S. (2006). New imaging technologies in the diagnosis of osteoporosis. Rev Endocr Metab Disord *7*, 67-74.

Kenneth, D.W., and Klesges, R.C. (2001). A Meta-Analysis of the Effects of Cigarette Smoking on Bone Mineral Density. Calcif Tissue Int *68*.

Korpelainen, R., Keinanen-Kiukaanniemi, S., Heikkinen, J., Vaananen, K., and Korpelainen, J. (2006). Effect of impact exercise on bone mineral density in elderly women with low BMD: a population-based randomized controlled 30-month intervention. Osteoporos Int *17*, 109-118.

Law, A.V., and Shapiro, K. (2005). Impact of a community pharmacist-directed clinic in improving screening and awareness of osteoporosis. J Eval Clin Pract *11*, 247-255.

Law, M.R., and Hackshaw, A.K. (1997). A meta-analysis of cigarette smoking, bone mineral density and risk of hip fracture: recognition of a major effect. BMJ *315*, 841-846.

Lewiecki, E.M. (2009a). Current and emerging pharmacologic therapies for the management of postmenopausal osteoporosis. J Womens Health (Larchmt) *18*, 1615-1626.

Lewiecki, E.M. (2009b). Managing osteoporosis: challenges and strategies. Cleve Clin J Med *76*, 457-466.

Li, C., Paris, O., Siegel, S., Roschger, P., Paschalis, E., Klaushofer, K., and Fratzl, P. (2009a). Strontium is Incorporated Into Mineral Crystals Only in Newly Formed Bone During Strontium Ranelate Treatment. J Bone Miner Res.

Li, M., Xing, X.P., Zhang, Z.L., Liu, J.L., Liu, D.G., Xia, W.B., and Meng, X.W. (2009b). Infusion of ibandronate once every 3 months effectively decreases bone resorption markers and increases bone mineral density in Chinese postmenopausal osteoporotic women: a 1-year study. J Bone Miner Metab.

Lowrie, R. (2008). Pharmacy and the falling elderly: from evidence base to model of care, R. Lowrie, ed.

Luf, A. (2009).

Mauck, K.F., and Clarke, B.L. (2006). Diagnosis, screening, prevention, and treatment of osteoporosis. Mayo Clin Proc *81*, 662-672.

McAnaw, J., Hudson, S., and MCGlynn, S.T. (2003). Development of an evidence-based medication assessment tool to demonstrate the quality of drug therapy use in patients with heart failure. . International Journal of Pharmacy Practice R17.

Migliaccio, S., Brama, M., and Malavolta, N. (2009). Management of glucocorticoids-induced osteoporosis: role of teriparatide. Ther Clin Risk Manag *5*, 305-310.

Miller, P.D. (2008). Anti-resorptives in the management of osteoporosis. Best Pract Res Clin Endocrinol Metab *22*, 849-868.

Morgan, S.L., and Kitchin, B. (2008). Osteoporosis: handy tools for detection, helpful tips for treatment. J Fam Pract *57*, 311-320.

Naylor, K.E., Clowes, J.A., Finigan, J., Paggiosi, M.A., Peel, N.F., and Eastell, R. (2009). The effect of cessation of raloxifene treatment on bone turnover in postmenopausal women. Bone.

NHS (2006). Strategy for Osteoporosis and Falls Prevention, N.H.S.G. Glasgow, ed.

NHSScotland (2009). GPASS- Clinical Software.

NHSUK (2009). NHS- Connecting for Health, N. UK, ed.

NICE (2002). Principles of best practice in clinical audit.

NICE (2004). NICE 21: Assessment and prevention of falls in elderly people, N.I.f.H.a.C. Excellence, ed.

NICE (2008). Alendronate, etidronate, risedronate, raloxifene and strontium ranelate for the primary prevention of osteoporotic fragility fractures in postmenopausal women. In NICE technology appraisal guidance 160, N.I.f.H.a.C. Excellence, ed. (NICE).

NOS (2009), N.O. Society, ed.

Past, E. (2008). The implementation of evidence based practice in osteoporosis treatement and prevention: Development of a medication assessment tool (Vienna, University of Vienna).

Peters, M.L., Leonard, M., and Licata, A.A. (2001). Role of alendronate and risedronate in preventing and treating osteoporosis. Cleve Clin J Med *68*, 945-951.

Reginster, J. (2007). Managing the osteoporotic patient today. Bone *40*, 12-18.

Reid, I.R. (2008). Anti-resorptive therapies for osteoporosis. Semin Cell Dev Biol *19*, 473-478.

Rey, J.R., Cervino, E.V., Rentero, M.L., Crespo, E.C., Alvaro, A.O., and Casillas, M. (2009). Raloxifene: mechanism of action, effects on bone tissue, and applicability in clinical traumatology practice. Open Orthop J *3*, 14-21.

Roux, C., and Thomas, T. (2008). Optimal use of FRAX. Joint Bone Spine.

Schettler, G., and Greten, H. (1998). Innere Medizin, Vol 9.Auflage.

Schlais, J. (2008). Evaluation of implementation of evidence-based practice in the treatment and prevention of osteoporosis (Glasgow, University of Strathclyde).

Siegenthaler, W., Kaufmann, W., Hornbostel, H., and Waller, H.D. (1992). Lehrbuch der Inneren Medizin, Vol 3. Auflage.

SIGN (2003). SIGN 71: Management of osteoporosis- A national clinical guideline, S.I.G. Network, ed.

Silverman, S. (2009). Selecting patients for osteoporosis therapy. J Bone Miner Res *24*, 765-767.

Snelling, A.M., Crespo, C.J., Schaeffer, M., Smith, S., and Walbourn, L. (2001). Modifiable and nonmodifiable factors associated with osteoporosis in postmenopausal women: results from the Third National Health and Nutrition Examination Survey, 1988-1994. J Womens Health Gend Based Med *10*, 57-65.

Sontag, A., Wan, X., and Krege, J.H. (2009). Benefits and risks of raloxifene by vertebral fracture status. Curr Med Res Opin.

Strand, L.M., Cipolle, R.J., Morley, P.C., and Perrier, D.G. (1991). Levels of pharmaceutical care: a needs-based approach. Am J Hosp Pharm *48*, 547-550.

Styrkarsdottir, U., Halldorsson, B.V., Gretarsdottir, S., Gudbjartsson, D.F., Walters, G.B., Ingvarsson, T., Jonsdottir, T., Saemundsdottir, J., Center, J.R., Nguyen, T.V., Bagger, Y., Gulcher, J.R., Eisman, J.A., Christiansen, C., Sigurdsson, G., Kong, A., Thorsteinsdottir, U., and Stefansson, K. (2008). Multiple genetic loci for bone mineral density and fractures. N Engl J Med *358*, 2355-2365.

Tamura, Y., Okinaga, H., and Takami, H. (2004). Glucocorticoid-induced osteoporosis. Biomed Pharmacother *58*, 500-504.

WHO (2003). Prevention and management of osteoporosis. In Technical report series 921, W.H. Organization, ed. (Geneva).

Woolf, A.D., and Akesson, K. (2003). Preventing fractures in elderly people. BMJ *327*, 89-95.

APPENDICES

APPENDIX 1: PROJECT PROTOCOL

Study Protocol

Implementation of a pharmaceutical care tool to guide community pharmacy interventions in osteoporosis

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Academic supervisor Prof Stephen Hudson

Co-Supervisors Dr B Julienne Johnson,

Ao Univ. Prof. Oskar Hoffmann

Collaborators Ian Towle, Susan McKellar, Karin Doblhammer, Anton Luf

Proposed duration of the project:

The project should be completed within four months

1. Introduction

1.1. Definition

Osteoporosis is a systematic skeletal disease characterized by low bone density and micro architectural deterioration of bone tissue with a consequent increase of bone fragility.

Low bone density occurs with advancing age [1]. By the third decade of life there is a gradual loss of bone mass [2]. But since it remains asymptomatic in many cases, it is not usually diagnosed until fractures occur [1]. Since life expectancy is increasing and the number of elderly people is rising, osteoporosis will become a global problem within the next decades [3].

1.2. Prevalence/Epidemiology

Approximately one in three women and one in twelve men over the age of 50 are likely to suffer an osteoporotic fracture [5].Osteoporosis is more common in women due to the lower bone peak mass [1] and the decrease in oestrogen production after the menopause [2]. Osteoporotic fragility fractures occur most commonly in the vertebrae, hip and wrist and cause disability, pain, reduced quality of life and are associated with increased mortality and morbidity [2].

Osteoporosis can be divided in two categories, primary and secondary osteoporosis. Primary osteoporosis is usually associated with age and/or sex (postmenopausal women). Secondary osteoporosis occurs when an underlying disease (e.g. hypogonadism), deficiencies (e.g. malnutrition) or drugs (e.g. glucocorticoids) cause osteoporosis. Further risk factors for osteoporosis are a low body mass index, smoking, excessive alcohol intake, decreased physical activity and low dietary intake of calcium [4].

2. Research Question, Aims and Objectives

2.1. Research questions

1. Can a medication assessment tool for osteoporosis (MAT_{Osteo}) reliably be administered to computerised medical records?

2. Is the MAT_{Osteo} asensitive tool for comparing prescribing practices in different clinical settings?

3. Does the MAT_{Osteo} together with a fracture risk assessment score offer a potential osteoporosis service for provision from a community pharmacy?

2.2. Aims:

- To demonstrate the use of a medical assessment tool for osteoporosis (MAT_{Osteo}) in the evaluation of the level of adherence to osteoporosis guidelines.

- To demonstrate the inter-rater reliability of such a tool.

- To assess the value of a fracture risk evaluation service provided by community pharmacists

2.3. Objectives:

- To undertake a literature review of the epidemiology of osteoporosis and measures taken by public health experts in order to address the disease.

- To revise a MAT_{Osteo} (originally designed by previous researchers) and redesign database protocols. Test the protocols on a GPASS® database and evaluate inter-rater reliability.

- Test the sensitivity of the MAT_{Osteo} in a comparison of patient samples drawn from two clinical settings and further revise the tool as necessary.

- Test on a larger scale audit the revised $MAT_{Osteo.}$ *Each student take one patient sample and compare with the other student.*

- Validate a potential service by which community pharmacists might contribute to osteoporosis detection and management.Propose potential starting points for community pharmacists to get involved in osteoporosis detection and management.

3. Study Design, Subjects and Settings

3.1. Study Design:

Retrospective survey including the application of a tool designed for medication assessment in the field of osteoporosis

3.2. Subjects and Settings:

3.2.1. Subjects:

1. Patients from two practices in Clydebank and Paisley previously used in an earlier project to design the MAT_{Osteo}
2. Patients recruited from a third practice to be compared with those from a fourth
3. Interviewees (4-6) drawn from community pharmacy, general practice medicine, fracture risk clinics and public health specialists

The inclusion criteria for patients for whom specific guideline criteria are applicable are:

- Patients alive who are registered with the GP practice on date
- Patients who are diagnosed with osteoporosis or osteopenia

3.2.2. Settings:

- GP practices offering permission for the audit. The patients should be situated in general medical practice within Community Health Partnerships in Renfrewshire and/or Greater Glasgow.
- Interviewees who have been nominated to participate and accepted the invitation

4. Methods

To undertake a literature review of the epidemiology of osteoporosis and measures taken by public health experts in order to address the disease

For the purpose of this project information was gathered by using journal papers accessed via databases (e.g. PubMed®, Medlineplus® and ClinicalTrials.gov).

The number of articles presented was narrowed down by using a combination of certain keywords. Useful articles were identified by reading abstracts.

MAT_{Osteo} which will be tested regarding reliability is based on Scottish Intercollegiate Network (SIGN) 71 and National Institute for Clinical Excellence (NICE) guidelines.

To revise a MAT_{Osteo} (originally designed by previous researchers) and redesign database protocols. Test the protocols on a GPASS® database and evaluate inter-rater reliability.

MAT_{Osteo} will be tested by analysing data drawn from Clydebank GP and Paisley GP. The patients' files will be manipulated by using Microsoft Access® and Microsoft Excel® to extract the patients' data and compare only project related information according to database protocols designed by previous researchers. [7]

Microsoft Access® is a database to store and retrieve data. [7, 9] The user can create e.g. tables (enables to store the information in rows and columns) and queries (enables to store information in questions). [7, 9] Data can be stored, manipulated and analysed in an easy way. [7, 9]

These two elements will be used to build up a relationship between the data. [7]

After entering the data into Microsoft Access® database, this data is stored in a table. [7, 9]But in general tables are not used to interact with the data directly. [7, 9] Therefore the researcher may use queries. [7, 9]

Statistical analysis will be done by using SPSS.

Test the sensitivity of the MAT_{Osteo} in a comparison of patient samples drawn from two clinical settings and further revise the tool as necessary.

Test on a larger scale audit the revised $MAT_{Osteo.}$ Each student take one patient sample and compare with the other students.

Ian Towle will provide help in order to collect data of two or more GPs within Greater Glasgow and Clyde by withdrawing it from GPASS®.

MAT_{Osteo} will be tested by analysing data drawn from Clydebank GP and Paisley GP. The patients' files will be manipulated by using Microsoft Access® and Microsoft Excel® to extract the patients' data and compare only project related information according to database protocols designed by previous researchers.

Statistical analysis will be done by using SPSS.

Validate a potential service by which community pharmacists might contribute to osteoporosis detection and management.Propose potential starting points for community pharmacists to get involved in osteoporosis detection and management

References

1. World Health Organisation (WHO), *Prevention and Management of Osteoporosis: Report of a WHO scientific group*
   2003

2. National Institute for Health and Clinical Excellence (NICE) 161
   Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women

   October 2008

   Available from www.nice.org.uk

3. C. Cooper *Epidemiology of Osteoporosis* , Osteoporosis International, 1999
4. Alana C. Serota *Osteoporosis (Secondary)* 2006 accessible via eMedicine
5. Scottish Intercollegiate Guidelines Network (SIGN) 71 *Management of Osteoporosis* June 2003
6. Eva Past *The implementation of evidence-based practice in osteoporosis treatment and prevention: Development of a Medication Assessment Tool in Pharmacy* 2007 University of Strathclyde, Glasgow
7. Johanna Schlais *Evaluation of implementation of evidence-based practice in the treatment and prevention of osteoporosis* 2008 MSc thesis University of Strathclyde, Glasgow
8. GPASS®, General Practice Administration System for Scotland
   accessible at www.gpass.scot.nhs.uk

9. Harkin S., Gerhart T., Hansen K. *Using Microsoft Access 2000.* 1st ed. USA: A division of Macmillan Computer Publishing. Que Corporation: 1999

APPENDIX 2: MATosteo ANTON LUF

Medication Assessment Tool for use in osteoporosis/osteopenia (MAT_{Osteo}) – Draft Anton Luf

Patient Code:

Date and setting:

Key for the six answer categories:

NA	Not applicable
Yes	Standard is adhered to in eligible patients
No(J)	No, but justified
No(U)	No, unjustified
ID_Q	Insufficient data to address the qualifying statement
ID_S	Insufficient data to address the standard statement

Definitions:

Osteoporosis	… is defined as a value of bone mineral density at least 2.5 standard deviations below the young adult mean (T-score $\leq$ - 2.5).
Osteopenia	… is defined as a value of bone mineral density between 1 and 2.5 standard deviations below the young adult mean (T-score < - 1 and > - 2.5).
DEXA scan	Dual-energy X-ray absorptiometry is a method to assess the bone mineral density. The result is expressed in relation to the young adult mean (T-score) in standard deviation units.
BMD	Bone mineral density (g/cm^2) = Bone mineral content (g/cm) / width at the scanned line (W)

References:

1 Scottish Intercollegiate Guidelines Network (SIGN). Management of Osteoporosis 71 (April 2004 Update)

2 National Institute for Clinical Excellence (NICE). Alendronate, etidronate, risedronate, raloxifene, strontium ranelate for the primary prevention of osteoporotic fragility fractures in postmenopausal women Technology Appraisal TA160, October 2008

3 National Institute for Clinical Excellence (NICE). Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women Technology Appraisal TA161, October 2008

4 Summary of the 2002 Canadian Guidelines for the Diagnosis and Management of Osteoporosis (2005 Update)

5 British National Formulary (BNF) 56, September 2008

	NA	Yes	No (J)	No (U)	ID_Q	ID_S	Ref
Diagnosis of osteoporosis/osteopenia							
1 A patient with a diagnosis of osteoporosis has been assessed by DEXA scan [Justification for not referring to a DEXA Scan Patient ≥ 60 years and ≥ 2 vertebral fractures imply a diagnosis of osteoporosis or a postmenopausal woman ≥ 75 years and two or more independent clinical risk factors for fracture or indicators of low BMD]	☐	☐	☐	☐	☐	☐	1,2,3
2 Measurement of the BMD by DEXA scan is performed at least at the two specific sites – namely, anteroposterior spine and hip.	☐	☐	☐	☐	☐	☐	1
Calcium and vitamin D supplementation							
3 A patient with a recorded diagnosis of osteoporosis	☐	☐	☐	☐	☐	☐	1

Independent clinical risk factors

- ❑ low body mass index defined as less than 22 kg/m²
- ❑ ankylosing spondylitis
- ❑ Crohn's disease
- ❑ conditions that result in prolonged immobility
- ❑ untreated premature menopause

Indicators for low BMD

- ❑ parental history of hip fracture,
- ❑ alcohol intake of 4 or more units/d
- ❑ rheumatoid arthritis

	is prescribed supplementary calcium (±vitamin D). [Justification for non-prescribing calcium and vitamin D:There is a record that the patient has an adequate dietary intake of calcium and no vitamin D deficiency.]							
4	**A patient with a recorded diagnosis of osteoPENIA** is prescribed supplementary calcium (± vitamin D) for the prevention of osteoporosis. [Justification for non-prescribing calcium and vitamin D: There is a record that the patient has an adequate dietary intake of calcium and no vitamin D deficiency.]	☐	☐	☐	☐	☐	☐	**4**
5	**A patient with confirmed vitamin D deficiency or aged ≥ 65** is prescribed vitamin D.	☐	☐	☐	☐	☐	☐	**1**
6	**A patient with osteoporosis and NOT prescribed any of the following: bisphosphonates, raloxifene, strontium ranelate or calcitonin** has a recorded contra-indication to each agent (see below) [Contraindications to bisphosphonates are: ☐ oesophageal strictures or achalasia ☐ inability to remain upright for > 30 min after ingestion ☐ hypocalcaemia ☐ osteomalacia (etidronate) ☐ moderate renal impairment (CrCl < 35 mL/min) ☐ pregnancy and breast feeding] [Contraindications to raloxifene are: ☐ past/present venous thromboembolic events ☐ hepatic impairment ☐ cholestasis ☐ severe renal impairment (CrCl < 10 mL/min) ☐ endometrial cancer ☐ uterine bleeding ☐ pregnancy and breast feeding] [Contraindications to strontium ranelate are: ☐ pregnancy and breast feeding ☐ hypersensitivity] [Contraindications to calcitonin are: ☐ hypocalcaemia ☐ hypersensitivity]	☐	☐	☐	☐	☐	☐	**1,2,5**
7	**A patient prescribed supplementary calcium** is prescribed a daily dose of 500 – 1500 mg calcium.	☐	☐	☐	☐	☐	☐	**1,4**

8	**A patient prescribed vitamin D** is prescribed a daily dose of 10 – 20 μg (400 - 800 IU) vitamin D.	☐	☐	☐	☐	☐	☐	**1**
9	**A patient with osteoporosis and NOT prescribed any of the following: bisphosphonates, raloxifene, strontium ranelate or calcitonin** is prescribed ≥1000mg calcium plus 800 IU vitamin D per day	☐	☐	☐	☐	☐	☐	**1**
10	**Apatientwith a recorded diagnosis of osteoporosis** is prescribed an oral bisphosphonate as first-line therapy. Recorded reasons for non-conformance (justification): _____	☐	☐	☐	☐	☐	☐	**1,4**
11	**A patient with a recorded diagnosis of osteoPENIA** is prescribed an oral bisphosphonate as first-line therapy. Recorded reasons for non-conformance (justification): _____	☐	☐	☐	☐	☐	☐	**4**
12	**A patient who is prescribed a bisphosphonate** has no reason *on record* to avoid bisphosphonates. [Reasons to avoid bisphosphonates are: ❑ **contraindication to bisphosphonates** o oesophageal strictures or achalasia o inability to remain upright for > 30 min after ingestion o hypocalcaemia o osteomalacia (etidronate) o moderate renal impairment (CrCl < 35	☐	☐	☐	☐	☐	☐	**1,2,5**

mL/min)
- pregnancy and breast feeding

- inability to comply with the instructions for use of bisphosphonates
  - ingestion on an empty stomach
  - washing the medication down with 250 ml water
  - avoidance of food for 30 min
  - avoidance of lying flat within 30 min of ingestion

- unsatisfactory response to bisphosphonates
  - another fracture occurs
  - decrease in BMD despite adherence to treatment

- intolerance to bisphosphonates
  - oesophageal ulceration
  - erosion or stricture
  - severe lower GI symptoms]

		NA	Yes	No (J)	No (U)	ID_Q	ID_S	Ref
13	**A patient receiving treatment for osteoporosis/osteopenia** is prescribed a standard dose regimen.	☐	☐	☐	☐	☐	☐	**1,5**
14	**A postmenopausal woman when started on bisphosphonate therapy** was initiated on alendronate.	☐	☐	☐	☐	☐	☐	**2,3**
15	**A postmenopausal womandiagnosed with osteoporosis/osteopenia and not treated with alendronate** is prescribed risedronate.	☐	☐	☐	☐	☐	☐	**1**

❑ **Prevention (in osteopenia)**	❑ **Treatment (of osteoporosis)**
Postmenopausal Osteoporosis	
❑ Alendronic acid	
5 mg daily PO	10 mg daily or 70 mg once weekly PO
❑ Disodium etidronate	
400 mg for 14 days PO; 1,25 g calcium carbonate for 76 days PO	400 mg for 14 days PO, 1,25 g calcium carbonate for 76 days PO
❑ Ibandronic acid (not in guidelines)	
	150 mg once a month PO or 3 mg every 3 months IV
❑ Risedronate sodium	
5 mg daily PO	5 mg daily PO or 35 mg weekly PO
❑ Calcitonin	
	200 units daily intranasally
❑ Raloxifene	
60 mg daily PO	60 mg daily PO
❑ Strontium ranelate	
	2 g daily PO
❑ Teriparatide	
	20 micrograms daily, for a maximum duration of treatment of 18 months
Osteoporosis in men	
❑ Alendronic acid	
	10 mg daily PO
Glucocorticoid-induced Osteoporosis	
❑ Alendronic acid	
5 mg daily PO	5 mg daily PO
❑ Disodium etidronate	
400 mg for 14 days PO, 1,25 g calcium carbonate for 76 days PO	400 mg for 14 days PO, 1,25 g calcium carbonate for 76 days PO
❑ Risedronate sodium	
5 mg daily PO	
❑ Teriparatide	
	20 micrograms daily, for a maximum duration of treatment of 18 months

16	**A postmenopausal woman with ≥ 2 vertebral fractures and NOT treated with alendronate or risedronate** is prescribed intermittent cyclical etidronate[2].	☐	☐	☐	☐	☐	☐	**1**
		NA	**Yes**	**No (J)**	**No (U)**	**ID_Q**	**ID_S**	Ref
17	**A patient who is on long-term glucocorticoid therapy** **(≥ 7.5 mg prednisolone or equivalents for ≥ 3 months)** is prescribed a bisphosphonate.	☐	☐	☐	☐	☐	☐	**1**
18	**A postmenopausal woman with a diagnosis of osteoporosis, who has an identifiable reason for not being prescribed a bisphosphonate** is prescribed strontium ranelate. [Reasons for non-use of bisphosphonates are Contraindications to bisphosphonates ❑ contraindication to bisphosphonates (see 12) ❑ inability to comply with the recommendations for use of bisphosphonates (see 12) ❑ intolerance to bisphosphonates (see12)]	☐	☐	☐	☐	☐	☐	**2**
19	**A postmenopausal woman diagnosed with osteoporosis with at least one osteoporotic fractures who has an identifiable reason for not being prescribed a bisphosphonate** is prescribed strontium ranelate or raloxifene. [Reasons for non-use of bisphosphonates are Contraindications to bisphosphonates ❑ contraindication to bisphosphonates (see 12) ❑ inability to comply with the recommendations for use of bisphosphonates (see 12) ❑ intolerance to bisphosphonates (see 12)]	☐	☐	☐	☐	☐	☐	**3**

[2] standard dose regimen see criterion 13

20	**A postmenopausal woman diagnosed with osteoporosis and at least one osteoporotic fractures** **who has either** ❑ **a reason to avoid bisphosphonates (See 12)** ❑ **a contraindication to strontium ranelate** o pregnancy o breast-feeding ❑ **an intolerance to strontium ranelate** o persistent nausea o persistent diarrhoea **and who is either** ❑ **aged ≥ 65 years with a T-Score ≤ -4 SD** ❑ **aged ≥ 65 years with a T-Score ≤ -3.5 SD and has more than two fractures** ❑ **aged 55-64 years with a T-Score ≤ -4 and has more than two fractures** is prescribed teriparatide.	☐	☐	☐	☐	☐	☐	**3**
21	**A postmenopausal womandiagnosed with osteoporosis with at least one vertebral fracture and NOT treated with a bisphosphonate, raloxifene or strontium ranelate** is prescribed calcitonin.	☐	☐	☐	☐	☐	☐	**1**

APPENDIX 3: MATosteo FINAL TOOL

Medication Assessment Tool for use in osteoporosis/osteopenia (MAT_{Osteo}) – Final Tool

Patient Code:

Date and setting:

Key for the six answer categories:

NA	Not applicable
Yes	Standard is adhered to in eligible patients
No(J)	No, but justified
No(U)	No, unjustified
ID_Q	Insufficient data to address the qualifying statement
ID_S	Insufficient data to address the standard statement

Definitions:

Osteoporosis	… is defined as a value of bone mineral density at least 2.5 standard deviations below the young adult mean (T-score $\leq$ - 2.5).
Osteopenia	… is defined as a value of bone mineral density between 1 and 2.5 standard deviations below the young adult mean (T-score < - 1 and > - 2.5).
DEXA scan	Dual-energy X-ray absorptiometry is a method to assess the bone mineral density. The result is expressed in relation to the young adult mean (T-score) in standard deviation units.
BMD	Bone mineral density (g/cm^2) = Bone mineral content (g/cm) / width at the scanned line (W)

References:

1 Scottish Intercollegiate Guidelines Network (SIGN). Management of Osteoporosis 71 (April 2004 Update)

2 National Institute for Clinical Excellence (NICE). Alendronate, etidronate, risedronate, raloxifene, strontium ranelate for the primary prevention of osteoporotic fragility fractures in postmenopausal women Technology Appraisal TA160, October 2008

3 National Institute for Clinical Excellence (NICE). Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women Technology Appraisal TA161, October 2008

4 Summary of the 2002 Canadian Guidelines for the Diagnosis and Management of Osteoporosis (2005 Update)

5 British National Formulary (BNF) 56, September 2008

		NA	Yes	No (J)	No (U)	ID_Q	ID_S	Ref
	Diagnosis of osteoporosis/osteopenia							
1	**A patient with a diagnosis of osteoporosis** has a recorded DEXA Scan to confirm osteoporosis [Justification for not being assessed by DEXA scan to confirm osteoporosis Patient ≥ 60 years and ≥ 2 vertebral fractures imply a diagnosis of osteoporosis or a postmenopausal woman ≥ 75 years and two or more independent clinical risk factors for fracture or indicators of low BMD]	☐	☐	☐	☐	☐	☐	1,2,3
	Independent clinical risk factors ❑ low body mass index defined as less than 22 kg/m² ❑ ankylosing spondylitis ❑ Crohn's disease ❑ conditions that result in prolonged immobility ❑ untreated premature menopause **Indicators for low BMD** ❑ parental history of hip fracture, ❑ alcohol intake of 4 or more units/d ❑ rheumatoid arthritis							
2	**Measurement of the BMD by DEXA scan** is performed at least at the two specific sites – namely, anteroposterior spine and hip.	☐	☐	☐	☐	☐	☐	1
	Calcium and vitamin D supplementation							
3	**A patient with a recorded diagnosis of osteoporosis**	☐	☐	☐	☐	☐	☐	1

	is prescribed supplementary calcium (±vitamin D). [Justification for non-prescribing calcium and vitamin D:There is a record that the patient has an adequate dietary intake of calcium and no vitamin D deficiency.]							
4	**A patient with a recorded diagnosis of osteoPENIA** is prescribed supplementary calcium (± vitamin D) for the prevention of osteoporosis. [Justification for non-prescribing calcium and vitamin D: There is a record that the patient has an adequate dietary intake of calcium and no vitamin D deficiency.]	☐	☐	☐	☐	☐	☐	**4**
5	**A patient with confirmed vitamin D deficiency or aged ≥ 65** is prescribed vitamin D.	☐	☐	☐	☐	☐	☐	**1**
6	**A patient prescribed supplementary calcium** is prescribed a daily dose of 500 – 1500 mg calcium.	☐	☐	☐	☐	☐	☐	**1,4**
7	**A patient prescribed vitamin D** is prescribed a daily dose of 10 – 20 μg (400 - 800 IU) vitamin D.	☐	☐	☐	☐	☐	☐	**1**
8	**Apatientwith a recorded diagnosis of osteoporosis** is prescribed an oral bisphosphonate as first-line therapy. Recorded reasons for non-conformance (justification): _____	☐	☐	☐	☐	☐	☐	**1,4**

	NA	**Yes**	**No (J)**	**No (U)**	**ID_Q**	**ID_S**	**Ref**

9 **A patient with a recorded diagnosis of osteoPENIA**

is prescribed an oral bisphosphonate as first-line therapy.

☐ ☐ ☐ ☐ ☐ ☐ **4**

Recorded reasons for non-conformance (justification):

_____

10 **A patient with osteoporosis and NOT prescribed any of the following: bisphosphonates, raloxifene, strontium ranelate, calcitonin or teriparatide**

has a recorded contra-indication to each agent (see below)

[Contraindications to bisphosphonates are:

- ☐ oesophageal strictures or achalasia
- ☐ inability to remain upright for > 30 min after ingestion
- ☐ hypocalcaemia
- ☐ osteomalacia (etidronate)
- ☐ moderate renal impairment (CrCl < 35 mL/min)
- ☐ pregnancy and breast feeding]

[Contraindications to raloxifene are:

- ☐ past/present venous thromboembolic events
- ☐ hepatic impairment
- ☐ cholestasis
- ☐ severe renal impairment (CrCl < 10 mL/min)
- ☐ endometrial cancer
- ☐ uterine bleeding
- ☐ pregnancy and breast feeding]

☐ ☐ ☐ ☐ ☐ ☐ **1,2,5**

[Contraindications to strontium ranelate are:

- ☐ pregnancy and breast feeding
- ☐ hypersensitivity]

[Contraindications to calcitonin are:

- ☐ hypocalcaemia
- ☐ hypersensitivity]

[Contraindications to teriparatide are:

- ☐ pre-existing hypercalcaemia
- ☐ skeletal malignancies or bone metastases
- ☐ metabolic bone diseases
- ☐ including Paget's disease and hyperparathyroidism
- ☐ unexplained raised alkaline phosphatase
- ☐ previous radiation therapy to the skeleton]

11 **A patient with osteoporosis and NOT prescribed any of the following: bisphosphonates, raloxifene, strontium ranelate or calcitonin**

☐ ☐ ☐ ☐ ☐ ☐ **1**

	is prescribed ≥1000mg calcium plus 800 IU vitamin D per day								
12	**A patient who is prescribed a bisphosphonate** has no reason *on record* to avoid bisphosphonates. [Reasons to avoid bisphosphonates are: ❑ **contraindication to bisphosphonates** o oesophageal strictures or achalasia o inability to remain upright for > 30 min after ingestion o hypocalcaemia o osteomalacia (etidronate) o moderate renal impairment (CrCl < 35 mL/min) o pregnancy and breast feeding ❑ inability to comply with the instructions for use of bisphosphonates o ingestion on an empty stomach o washing the medication down with 250 ml water o avoidance of food for 30 min o avoidance of lying flat within 30 min of ingestion ❑ unsatisfactory response to bisphosphonates o another fracture occurs o decrease in BMD despite adherence to treatment ❑ intolerance to bisphosphonates o oesophageal ulceration o erosion or stricture o severe lower GI symptoms]	☐	☐	☐	☐	☐	☐	**1,2,5**

		NA	Yes	No (J)	No (U)	ID_Q	ID_s	Ref
13	**A patient receiving treatment for osteoporosis/osteopenia** is prescribed a standard dose regimen.	☐	☐	☐	☐	☐	☐	**1,5**
14	**A patient with osteoporosis on bisphosphonate therapy** is on the preferred choice* * 1- Alendronate, 2-risedronate, 3-intermittent cyclical etidronate [Preferred order as shown in the drug history]	☐	☐	☐	☐	☐	☐	**2,3**

❑ **Prevention (in osteopenia)**	❑ **Treatment (of osteoporosis)**
Postmenopausal Osteoporosis	
❑ Alendronic acid	
5 mg daily PO	10 mg daily or 70 mg once weekly PO
❑ Disodium etidronate	
400 mg for 14 days PO; 1,25 g calcium carbonate for 76 days PO	400 mg for 14 days PO, 1,25 g calcium carbonate for 76 days PO
❑ Ibandronic acid (not in guidelines)	
	150 mg once a month PO or 3 mg every 3 months IV
❑ Risedronate sodium	
5 mg daily PO	5 mg daily PO or 35 mg weekly PO
❑ Calcitonin	
	200 units daily intranasally
❑ Raloxifene	
60 mg daily PO	60 mg daily PO
❑ Strontium ranelate	
	2 g daily PO
❑ Teriparatide	
	20 micrograms daily, for a maximum duration of treatment of 18 months
Osteoporosis in men	
❑ Alendronic acid	
	10 mg daily PO
Glucocorticoid-induced Osteoporosis	
❑ Alendronic acid	
5 mg daily PO	5 mg daily PO
❑ Disodium etidronate	
400 mg for 14 days PO, 1,25 g calcium carbonate for 76 days PO	400 mg for 14 days PO, 1,25 g calcium carbonate for 76 days PO
❑ Risedronate sodium	
5 mg daily PO	
❑ Teriparatide	
	20 micrograms daily, for a maximum duration of treatment of 18 months

		NA	Yes	No (J)	No (U)	ID_Q	ID_s	Ref
15	**A patient who is on long-term glucocorticoid therapy** **(≥ 7.5 mg prednisolone or equivalents for ≥ 3 months)** is prescribed a bisphosphonate.	☐	☐	☐	☐	☐	☐	1
16	**A postmenopausal woman prescribed strontium ranelate** has an identifiable reason for not being prescribed a bisphosphonate Reasons for non-use of bisphosphonates are ❑ contraindication to bisphosphonates (see 12) ❑ inability to comply with the recommendations for use of bisphosphonates (see 12) ❑ intolerance to bisphosphonates (see12)]	☐	☐	☐	☐	☐	☐	2
17	**A postmenopausal woman prescribed raloxiphene** is receiving it for secondary prevention and has an identifiable reason for not being prescribed a bisphosphonate [Reasons for non-use of bisphosphonates are ❑ contraindication to bisphosphonates (see 12) ❑ inability to comply with the recommendations for use of bisphosphonates (see 12) ❑ intolerance to bisphosphonates (see 12)]	☐	☐	☐	☐	☐	☐	3
18	**A patient prescribed teriparatide** is prescribed it for secondary prevention and meets at least one of the following 2 criteria ❑ **has a reason to avoid bisphosphonates (See 12)** ❑ **has an intolerance to strontium ranelate** o persistent nausea o persistent diarrhoea And has DEXA scan assessment that puts them in one the following groups ❑ **aged ≥ 65 years with a T-Score ≤ -4 SD** ❑ **aged ≥ 65 years with a T-Score ≤ -3.5 SD and has more than two fractures** ❑ **aged 55-64 years with a T-Score ≤ -4 and has more than two fractures**	☐	☐	☐	☐	☐	☐	3

19 **A patient prescribed calcitonin** is prescribed it for secondary prevention after bisphosphonate, raloxifene or strontium ranelate have been tried or have reasons for excluding from consideration

[Reasons for non-use of bisphosphonates are

- ❑ contraindication to bisphosphonates (see 12)
- ❑ inability to comply with the recommendations for use of bisphosphonates (see 12)
- ❑ intolerance to bisphosphonates (see 12)]

APPENDIX 4: DATA BASE PROTOCOLS

CRITERION 1

A patient with a diagnosis of osteoporosis has

been assessed by DEXA scan

Step	**What?**	**How?**
Step 1	Identify patients with a diagnosis of osteoporosis who have been assessed by DEXA scan	**Use** form 'Query maker' in Microsoft Access® **Select** in 'Read code' field: • 'Osteoporosis' for criterion 1 • 'DXA' for criterion 2 • 'DEXA IDS' for criterion 3 **Press** 'view' **Sort** patients by 'Osteoporosis' **Delete** patients who are not osteoporotic (0)
Step 2	Store results in a Microsoft Excel®spreadsheet	**Export** results to Microsoft Excel® **Sort** all resultsby applying the 'sort descending' function **Delete** first row (containing 'c1', 'd1', 'c2'…)
Step 3	Create a new table in Microsoft Access® containing results from step 2	**Select** 'Tables', 'new', 'import table' in order to import the table created in step 2 **Select** 'First Row Contains Headings' during the process of importing **Name** table 'OS and DEXA'
Step 4	Prepare justification search for "No"-results	**Use** form 'Query maker' in Microsoft Access® **Select** in 'Read code' field: • 'Osteoporosis' for criterion 1 • '>=60 years' for criterion 2 • 'Vertebral' for criterion 3 • '>=75 years' for criterion 4 • 'Female' for criterion 5 • 'ICR IND BMD LOW' for criterion 6 **Press** 'view'
Step 5	Identify patients	**Create** new query by using 'design view'

	with osteoporosis, no DEXA scan, >= 60 years and at least two vertebral fractures (Justification A)	**Link** 'tbl_temp' and table 'OS and DEXA' via patientKey. **Apply** 'patientKey', c1[1], c2 [0] (table 'OS an DEXA'), c1 [1], c2 [1],c3 [1] ('tbl_temp') **Run** query 1 **Export** results to Microsoft Excel® For patients with '1' in field c3 ('tbl_temp'): **Check manually** if they sustained more than 2 vertebral fractures by inspecting on the table 'Patients: NHS Read codes_QOF and MAT data items_tbl' (use the search function) ➔ 0 or 1 vertebral fractures: No(U) ➔ 2 or more vertebral fractures No(J)
Step 6	Identify patients with osteoporosis, no DEXA scan, >=75 years, female and at least 2 ICRF or IND for low BMD (Justification B)	**Create** new query by using 'design view' **Link** 'tbl_temp' and table 'OS and DEXA' via patient keys **Apply** 'patientKey', c2 [0] (table 'OS an DEXA'), c4 [1], c5 [1], c6 [1] ('tbl_temp') **Run** query 2 **Export** data to Microsoft Excel® For patients with '1' in field c3 ('tbl_temp'): **Check manually** if they show 2 or more ICRF IND BMD by inspecting on the table 'Patients: NHS Read codes_QOF and MAT data items_tbl' (use the search function) ➔ 0 or 1 ICRF IND BMD: No(U) ➔ 2 or more ICRF IND BMD No(J) Remaining patients with osteoporosis but no DEXA scan: No(U)
Step 7	Interpret results from step 2 (stored in Microsoft Excel®)	➔ Osteoporosis 1, DXA 0 and DEXA IDS 1: =IDS ➔ Osteoporosis 1, DXA 1 and DEXA IDS 0: =YES ➔ Osteoporosis 1, DXA 0 and DEXA IDS 0: See step 5 and 6 for justifications

CRITERION 2

Measurement of the BMD by DEXA scan

Is performed at least at the two specific sites – namely anteroposterior spine and hip

Step	What?	How?
Step 1	Identify patients with a measured BMD by DEXA scan measured on two specific sites	**Use** form 'Query maker' in Microsoft Access® **Select** in 'Read code' field: • 'Hip scan' for criterion 1 • 'Lumbar scan' for criterion 2 **Press** 'view' **Create** a new query by using 'design view' **Select** 'tbl_temp' **Apply** 'patientKey', c1[1], c2[1], d1, d2 **In 'SQL view' change** 'and' to 'or'→ [(((tbl_temp.c1)="1")) **OR** (((tbl_temp.c2)="1"));]
Step 2	Identify Yes, No(U)	**Export** results to Microsoft Excel® ➔ Patients with a DEXA scan performed on two specific sites at the *same day!*= Yes ➔ Patients with a DEXA scan performed on only one site or with DEXA scans performed on two specific sites but not at the same day= No(U) ➔ No(J)=0 (there is no justification for non-adherence)
Step 3	Identify IDS, IDQ	**Use** form 'Query maker' in Microsoft Access® **Select** in 'Read code' field: • 'C2IDSdxa' for criterion 1 • 'DEXA IDS' (is IDQ for this criteria!) for criterion 2 **Press** 'view' **Create** a new query by using 'design view' **Select** 'tbl_temp' **Apply** 'patientKey', c1[1], c2[1] **In 'SQL view' change** 'and' to 'or'→

		[(((tbl_temp.c1)="1")) **OR** (((tbl_temp.c2)="1"));] **Export** results to Microsoft Excel® ➔ IDS= number of patients marked with 1 in column c1 ➔ IDQ= number of patients marked with 1 in column c2

CRITERION 3

Patient with a recorded diagnosis of osteoporosis

Is prescribed supplementary calcium (vitamin D)

Step	**What?**	**How?**
Step 1	Identify patients with a diagnosis of osteoporosis	**Use** form 'Query maker' in Microsoft Access® **Select** in 'Read code' field: • 'Osteoporosis' for criterion 1 **Press** 'view' **Sort** patients by 'Osteoporosis' **Delete** patients who are not osteoporotic (0) **Export** results to Microsoft Excel®. **Name** document 'CLY OS'
Step 2	Create a table containing patients with a diagnosis of osteoporosis	**Use** Microsoft Access® **Select '**Tables', 'New', 'Import Table' **Import** Microsoft Excel®document 'CLY OS' and rename field c1 to 'Osteoporosis' (Table 'CLY OS')
Step 3	Identify patients with a diagnosis of osteoporosis who are prescribed supplementary calcium	**Use** form 'Query maker' in Microsoft Access® **Select** in 'Drug' field/ 'group': • 'Supplement' for criterion 1 **Press** 'view' **Create** new query by using 'desing view' **Select '**tbl_temp' and table 'CLY OS' **Link** tables via 'patientKey' **Apply** 'patientKey', osteoporosis [1] (Table 'CLY OS') and d1 [not like "0"] ('tbl_temp')

		Run query 1 ➔ Number of 'Yes' results
Step 4	Identify patients with a diagnosis of osteoporosis who are not prescribed supplementary calcium	**Create** new query by using 'Find Unmatched Query Wizard' **Select** table 'CLY OS' **Press** 'next' **Select** 'Queries' / 'query 1' **Press** 'next' **Link** tables via 'patientKey' **Press** 'next' **Select** 'patientKey' **Press** 'next' ➔ Number of total 'No' results
Step 5	Search for justifications of non-adherence	**Use** form 'Query maker' in Microsoft Access® **Select** in 'Read code' field: • 'Adequate dietary intake of calcium' for criterion 1 • 'Adequate dietary intake of vitamin D' for criterion 2 **Create** new query by using 'desing view' **Select** 'tbl_temp' and 'CLY_OS Without Matching Query 2' **Link** via 'patientKey' **Apply** 'patientKey', c1[1], c2[1] In 'SQL view' change AND to OR between c1 and c2 **Run** query 3 ➔ Number of justified non-adherence= No(J) ➔ Number of unjustified non-adherence= Number of total No-results- No(J)= No(U)

CRITERION 4

Patient with a recorded diagnosis of osteopenia

Is prescribed supplementary calcium (vitamin D)

Step	**What?**	**How?**
Step 1	Identify patients with a diagnosis of osteopenia	**Use** form 'Query maker' in Microsoft Access® **Select** in 'Read code' field: • 'Osteopenia' for criterion 1 **Press** 'view' **Sort** patients by 'Osteopenia' **Delete** patients who are not osteopenic (0) **Export** results to Microsoft Excel®. **Name** document 'CLY ON'
Step 2	Create a table containing patients with a diagnosis of osteopenia	**Use** Microsoft Access® **Select** 'Tables', 'New', 'Import Table' **Import** Microsoft Excel®document 'CLY ON' and rename field c1 to 'Osteopenia' (Table 'CLY ON')
Step 3	Identify patients with a diagnosis of osteopenia who are prescribed supplementary calcium	**Use** form 'Query maker' in Microsoft Access® **Select** in 'Drug' field/ 'group': • 'Supplement' **Press** 'view' **Create** new query by using 'desing view' **Select** 'tbl_temp' and table 'CLY ON' **Link** tables via 'patientKey' **Apply** 'patientKey', osteopenia [1] (Table 'CLY ON') and d1 [not like "0"] ('tbl_temp') **Run** query 1 ➔ Number of 'Yes' results

Step 4	Identify patients with a diagnosis of osteopenia who are not prescribed supplementary calcium	**Create** new query by using 'Find Unmatched Query Wizard' **Select** table 'CLY ON' **Press** 'next' **Select** queries/ 'query 1' **Press** 'next' **Link** tables via 'patientKey' **Press** 'next' **Select** 'patientKey' **Press** 'next' ➔ Number of total 'No' results
Step 5	Search for justifications of non-adherence	**Use** form 'Query maker' in Microsoft Access® **Select** in 'Read code' field: • 'Adequate dietary intake of calcium' for criterion 1 • 'Adequate dietary intake of vitamin D' for criterion 2 **Create** new query by using 'design view' **Select '**tbl_temp' and 'CLY_ON Without Matching Query 2' **Link** via 'patientKey' **Apply** 'patientKey', c1[1], c2[1] In 'SQL view' change AND to OR between c1 and c2 **Run** query 3 ➔ Number of justified non-adherence= No(J) ➔ Number of unjustified non-adherence= Number of total No-results- No(J)= No(U)

CRITERION 5

A patient with confirmed vitamin D deficiency or aged 65 or older

is prescribed vitamin D

Step	**What?**	**How?**
Step 1	Identify patients with confirmed vitamin D deficiency or aged over 65 *who are prescribed vitamin D*	**Use** form 'Query maker' in Microsoft Access® **Select** in 'Read code' field: • '>=65 years' for criterion 1 • 'Vitamin D deficiency' for criterion 2 **Press** 'view' **Create** new query by using 'design view' **Select** 'tbl_temp' **Apply** 'patientKey', c1[1], c2 [1] In 'SQL view' change AND to OR between c1 and c2 **Run** query 1 **Export** results to Microsoft Excel®. **Name** document 'CLY patients over 65 or vitamin D deficiency'
Step 2	Create a table containing patients aged 65 or older	**Use** Microsoft Access® **Select** 'Tables', 'New', 'Import Table' **Import** Microsoft Excel®document 'CLY patients over 65' and rename field c1 to '>=65 years' and c2 to 'vd deficiency' (table 'CLY patients over 65 or vitamin deficiency')
Step 3	Identify patients aged 65 years or older or with a confirmed vitamin d deficiency who are prescribed vitamin d	**Use** form 'Query maker' in Microsoft Access® **Select** in 'Drug' field/ 'group': • 'Supplement' **Press** 'view' **Create** new query by using 'design view' **Select** 'tbl_temp' and table 'CLY patients over 65 or vitamin deficiency' **Link** tables via 'patientKey' **Apply** 'patientKey' ('CLY patients over 65 or vitamin deficiency') and d1 [not like "0"] ('tbl_temp') **Run** query 2 ➔ Number of Yes results

Step 4	Identify patients aged 65 years or older or with a confirmed vitamin D deficiency who are not prescribed vitamin d	**Create** new query by using 'Find Unmatched Query Wizard' **Select** table 'CLY patients over 65 or vitamin D deficiency' **Press** 'next' **Select** queries/ query 2 **Press** 'next' **Link** tables via 'patientKey' **Press** 'next' **Select** 'patientkey' **Press** 'next' ➔ Number of total No results= No(U) as there is no justification for not prescribing vitamin d in this case

CRITERION 6- SEARCH 1 (excluding ibandronic acid and zoledronic acid because they are not included in the guidelines)

A patient with osteoporosis and NOT prescribed any of the following: bisphosphonates, raloxifene, strontium ranelate or calcitonin

has a recorded contraindication to each agent (see below)

Step	**What?**	**How?**
Step 1	Identify patients NOT treated with bisphosphonate, raloxifene, strontium ranelate, OR calcitonin	**Use** form 'Query maker' in Microsoft Access® **Select** ➔ 'Osteoporosis' for criterion 1 ➔ 'Bisphosphonate' for criterion 2 ➔ 'strontium ranelate' for criterion 3 ➔ 'raloxifene' for criterion 4 ➔ 'calcitonin' for ➔ criterion 5

		Sort patients by 'Osteoporosis' **Delete** patients who are not osteoporotic (0) **Sort** patients by different treatments (bisphosphonates, strontium ranelate, raloxifene, calcitonin) **Delete** patients who are receiving treatment (Mauck and Clarke 2006)
Step 2	Identify patients with contraindications tobisphosphonates, raloxifene, strontium ranelate AND calcitonin <u>which are the following:</u> Bisphosphonates: o Oesophageal strictures and achalasia o Inability to remain upright for > 30 min after ingestion o Hypocalcaemia o Osteomalacia (etidronate) o Moderate renal impairment (CrCl < 35 mL/min) o Pregnancy and breast feeding Raloxifene: o Past/present venous thromboembolic events o Hepatic impairment o Cholestasis o Severe renal impairment (CrCl < 10 mL/min) o Endometrial cancer o Uterine bleeding o Pregnancy and breast feeding Strontium Ranelate: o Pregnancy and breast feeding o Hypersensitivity Calcitonin: o Hypocalcaemia o Hypersensitivity	**Use** form 'Query maker' in Microsoft Access® **Select** ➔ 'Contraindication to bisphosphonates' for criterion 1 ➔ 'Contraindication to strontium ranelate' for criterion 2 ➔ 'Contraindication to raloxifene' for criterion 3 ➔ 'Contraindication to calcitonin' for criterion 4

Step 3	Identify patients with IDS results	**Use** form 'Query maker' in Microsoft Access® **Select** ➔ 'Contraindication to bisphosphonates IDS' for criterion 1 ➔ 'Contraindication to strontium ranelate IDS' for criterion 2 ➔ 'Contraindication to raloxifene IDS' for criterion 3 ➔ 'Contraindication to calcitonin IDS' for criterion 4

CRITERION 6- SEARCH 2 (including ibandronic acid and zoledronic acid because they are authorized by BNF but not by the guidelines)

A patient with osteoporosis and NOT prescribed any of the following: bisphosphonates, raloxifene, strontium ranelate or calcitonin

has a recorded contraindication to each agent (see below)

Step	**What?**	**How?**
Step 1	Identify patients NOT treated with bisphosphonate, raloxifene, strontium ranelate, OR calcitonin	**Use** form 'Query maker' in Microsoft Access® **Select** ➔ 'Osteoporosis' for criterion 1 ➔ 'Bisphosphonate' for criterion 2 ➔ 'Ibandro+Zoledro' for criterion 3 ➔ 'strontium ranelate' for criterion 4 ➔ 'raloxifene' for criterion 5

		➔ 'calcitonin' for criterion 6 **Sort** patients by 'Osteoporosis' **Delete** patients who are not osteoporotic (0) **Sort** patients by different treatments (bisphosphonates, strontium ranelate, raloxifene, calcitonin) **Delete** patients who are receiving treatment (Mauck and Clarke 2006)
Step 2	Identify patients with contraindications tobisphosphonates, raloxifene, strontium ranelate AND calcitonin <u>which are the following:</u> Bisphosphonates: o Oesophageal strictures and achalasia o Inability to remain upright for > 30 min after ingestion o Hypocalcaemia o Osteomalacia (etidronate) o Moderate renal impairment (CrCl < 35 mL/min) o Pregnancy and breast feeding Raloxifene: o Past/present venous thromboembolic events o Hepatic impairment o Cholestasis o Severe renal impairment (CrCl < 10 mL/min) o Endometrial cancer o Uterine bleeding o Pregnancy and breast feeding Strontium Ranelate: o Pregnancy and breast feeding o Hypersensitivity Calcitonin:	**Use** form 'Query maker' in Microsoft Access® **Select** ➔ 'Contraindication to bisphosphonates' for criterion 1 ➔ 'Contraindication to strontium ranelate' for criterion 2 ➔ 'Contraindication to raloxifene' for criterion 3 ➔ 'Contraindication to calcitonin' for criterion 4

	o Hypocalcaemia o Hypersensitivity	
Step 3	Identify patients with IDS results	**Use** form 'Query maker' in Microsoft Access® **Select** ➔ 'Contraindication to bisphosphonates IDS' for criterion 1 ➔ 'Contraindication to strontium ranelate IDS' for criterion 2 ➔ 'Contraindication to raloxifene IDS' for criterion 3 ➔ 'Contraindication to calcitonin IDS' for criterion 4

CRITERION 7

Patient prescribed supplementary calcium

Is prescribed a daily dose of 500-1500 mg calcium

Step	What?	How?
Step 1	Identify patients prescribed supplementary calcium	**Use** form 'Query maker' in Microsoft Access® **Select** in 'Drug' field/ 'group': • 'supplement' for criterion 1 **Press** 'view' **Create** new query by using 'design view' **Select** 'tbl_temp' **Apply** 'patientKey', c1, d1[not like "0"], c2, d2, c3 **Run** query 1
Step 2	Identify number of Yes, No(J), No(U),	**Export** results of 'step 1' to Microsoft Excel® **Inspect** on the results ➔ Patient prescribed a daily dose of 500-

	IDS	1500 mg calcium= Yes ➔ Patient not prescribed a daily dose of 500-1500 mg calcium= No(U) ➔ documentation concerning dose, preparation and frequency not clear= IDS

CRITERION 8

Patient prescribed vitamin D

Is prescribed a daily dose of 10 – 20 microgram (400 – 800 IU) vitamin D

Step	What?	How?
Step 1	Identify patients who are prescribed vitamin D	**Use** Microsoft Access® **Create** new query by using 'design view' **Select** table: 'Patients: Drug History_tbl' **Apply** 'drug name': [like *Adcal D3* or like *Calceos* or like *Calcichew D_3* or like *Cacit D_3* or like *Calfovit D_3* or like *colecalciferol* or like *vitamin d*] Also show dose and frequency. **Run** query 1 **Export** results to Microsoft Excel®
Step 2	Identify patients who are prescribed a daily dose of 10 – 20 microgram (400 – 800 IU) vitamin D (Standard) Possible drugs containing 10 micrograms (400 units) colecalciferol are the	**Check manually** if patients are receiving the appropriate dose regimen (especially focus on Calcichew D3, it is necessary to take it twice a day!)

	following: Adcal D_3®, Calceos®, Calcichew D_3® forte Possible drugs containing 11 micrograms (500 units) colecalciferol are the following: Cacit D_3® Possible drugs containing 5 micrograms (200 units) colecalciferol are the following: Calcichew D_3® Possible drugs containing 20 micrograms (800 units) colecalciferol are the following: Calfovit®	

CRITERION 9 SEARCH 1 (excluding ibandronic acid and zoledronic acid, because they are not included in the guidelines)

A patient with osteoporosis and NOT prescribed any of the following: bisphosphonates, raloxifene, strontium ranelate or calcitonin

Isprescribed ≥ 1000 mg calcium plus 800 IU vitamin D per day.

Step	**What?**	**How?**
Step 1	Identify patients with osteoporosis and NOT prescribed bisphosphonates, raloxifene, strontium ranelate or calcitonin	**Use** form 'Query maker' in Microsoft Access® **Select** in 'Read Code' field: ➔ 'Osteoporosis' for criterion 1 ➔ 'Bisphosphonate' for criterion 2 ➔ 'strontium ranelate' for criterion 3 ➔ 'raloxifene' for criterion 4 ➔ 'calcitonin' for criterion 5 **Press** 'view' **Create** new query by using 'design view' **Select** 'tbl_temp' **Apply** 'patientKey', c1 [1], c2 [0], c3 [0], c4 [0], c5 [0] **Run** query 1
Step 2	*Preparation* for step 3	**Export** results to Microsoft Excel® **Select** 'File', 'Export' and follow the process. **Name** document 'Patient OS no (BP_ ralox_ stront_ calc)'
Step 3	Create a table in Microsoft Access® containing data exported in step 2	**Use** Microsoft Access® **Select** 'Tables', 'New', 'Import Table' **Import** Microsoft Excel®document 'Patient OS no (BP_ ralox_ stront_ calc)'and rename field c1 to 'osteoporosis', c2 to 'bp (ex ibandro)', c3 to 'strontium', c4 to 'raloxi' and c5 to 'calcito' (table 'Criterion 9 search excluding ibandronic acid')

Step 4	Identify osteoporotic patients who are prescribed calcium and/ or vitamin D	**Use** form 'Query maker' in Microsoft Access® **Select** in 'Drug' field/ 'group': • 'supplement' for criterion 1 **Press** 'view' **Create** new query by using 'design view' **Select** 'tbl_temp' and table 'CLY OS' (was created in Criterion 3, Step 2) **Link** tables via 'patientKey' **Apply** 'patientKey', osteoporosis [1] (Table 'CLY OS') and d1 [not like "0"] ('tbl_temp') **Run** query 2 (query 'CLY OS on supplement')
Step 5	Identify patients with a diagnosis of osteoporosis and not treated bisphosphonates, raloxifene, strontium ranelate or calcitonin who are prescribed >=1000 mg calcium 800 IU vitamin D per day	**Create** new query by using 'design view' **Select** table 'Criterion 9 search excluding ibandronic acid' and query 'CLY OS on supplement' **Link** tables via 'patientKey' **Apply** 'patientKey' (table 'Criterion 9 search excluding ibandronic acid') and d1, c2, c3, d2 **Run** query 3 (query 'Criterion 9 Yes Results') **Export** data to Microsoft Excel® and **check manually** if the correct dose is prescribed. ➔ only calcium is prescribed or only vitamin d is prescribed or the wrong dose is prescribed= No(U) ➔ the correct dose is prescribed= Yes ➔ documented date is not clear concerning dose, preparation, frequency= IDS
Step 6	Identify patients with a diagnosis of osteoporosis and not treated bisphosphonates, raloxifene, strontium ranelate or calcitonin who are not prescribed >=1000 mg calcium 800 IU vitamin d per day	**Create** new query by using 'Find Unmatched Query Wizard' **Select** table 'Criterion 9 Search excluding ibandronic acid' **Press** 'next' **Select** queries/ query 'Criterion 9 Yes Results' **Press** 'next' **Link** tables via 'patientKey' **Press** 'next' **Select** 'patientKey' **Press** 'next' ➔ Number additional No results= No(U) as there is no justification for not prescribing calcium and or vitamin d in this case or prescribing it in another dose

CRITERION 9- SEARCH 2 (including ibandronic acid and zoledronic acid because they are authorized by BNF but not by the guidelines)

A patient with osteoporosis and NOT prescribed any of the following: bisphosphonates, raloxifene, strontium ranelate or calcitonin

Is prescribed ≥ 1000 mg calcium plus 800 IU vitamin D per day.

Step	**What?**	**How?**
Step 1	Identify patients with osteoporosis and NOT prescribed bisphosphonates, raloxifene, strontium ranelate or calcitonin	**Use** form 'Query maker' in Microsoft Access® **Select** in 'Read Code' field: ➔ 'Osteoporosis' for criterion 1 ➔ 'Bisphosphonate' for criterion 2 ➔ 'Ibandro + Zoledro' for criterion 3 ➔ 'strontium ranelate' for criterion 4 ➔ 'raloxifene' for criterion 5 ➔ 'calcitonin' for criterion 6 **Press** 'view' **Create** new query by using 'design view' **Select** 'tbl_temp' **Apply** 'patientKey', c1 [1], c2 [0], c3 [0], c4 [0], c5 [0] **Run** query 1
Step 2	Preparation for step 3	**Export** results to Microsoft Excel® **Select '**File', 'Export' and follow the process. **Name** document 'Patient OS no (BP_ ralox_ stront_ calc)'
Step 3	Create a table in Microsoft Access® containing data exported in step 2	**Use** Microsoft Access®

Step 4	Identify osteoporotic patients who are prescribed calcium and/ or vitamin D	**Use** form 'Query maker' in Microsoft Access® **Select** in 'Drug' field/ 'group': • 'supplement' for criterion 1 **Press** 'view' **Create** new query by using 'design view' **Select** 'tbl_temp' and table 'CLY OS' (was created in Criterion 3, Step 2) **Link** tables via 'patientKey' **Apply** 'patientKey', osteoporosis [1] (Table 'CLY OS') and d1 [not like "0"] ('tbl_temp') **Run** query 2 (query 'CLY OS on supplement')
Step 5	Identify patients with a diagnosis of osteoporosis and not treated bisphosphonates, raloxifene, strontium ranelate or calcitonin who are prescribed >=1000 mg calcium 800 IU vitamin D per day	**Create** new query by using 'design view' **Select** table 'Criterion 9 search including ibandronic acid' and query 'CLY OS on supplement' **Link** tables via 'patientKey' **Apply** 'patientKey' (table 'Criterion 9 search including ibandronic acid') and d1, c2, c3, d2 **Run** query 3 (query 'Criterion 9 Yes Results') **Export** data to Microsoft Excel® and **check manually** if the correct dose is prescribed. ➔ only calcium is prescribed or only vitamin d is prescribed or the wrong dose is prescribed= No(U) ➔ the correct dose is prescribed= Yes ➔ documented date is not clear concerning dose, preparation, frequency= IDS
Step 6	Identify patients with a diagnosis of osteoporosis and not treated bisphosphonates, raloxifene, strontium ranelate or calcitonin who are not prescribed >=1000 mg calcium 800 IU vitamin d per day	**Create** new query by using 'Find Unmatched Query Wizard' **Select** table 'Criterion 9 Search including ibandronic acid' **Press** 'next' **Select** queries/ query 'Criterion 9 Yes Results' **Press** 'next' **Link** tables via 'patientKey' **Press** 'next' **Select** 'patientKey' **Press** 'next' ➔ Number additional No results= No(U) as there is no justification for not prescribing calcium and or vitamin d in this case or prescribing it in another dose

CRITERION 10-SEARCH 1 (excluding ibandronic acid and zoledronic acid because they are not included in the guidelines)

Patient with a recorded diagnosis of osteoporosis

Is prescribed an oral bisphosphonate as first-line therapy

Step	**What?**	**How?**
Step 1	Identify patients with a diagnosis of osteoporosis who are prescribed an oral bisphosphonate (alendronic acid, disodium etidronate, risedronate sodium) as first-line therapy Drugs containing oral bisphosphonates are the following: Alendronic acid (Fosamax®, Fosavance®), disodium etidronate (Didronel PMO®), risedronate sodium (Actonel®)	**Use** form 'Query maker' in Microsoft Access® **Select** ➔ 'Bisphosphonate' for criterion 1 ➔ **'**Osteoporosis' for criterion 2 ➔ 'raloxifene' for criterion 3 ➔ 'strontium ranelate' for criterion 4 ➔ 'calcitonin' for criterion 5 ➔ 'teriparatide' for criterion 6 **Sort** patients by 'osteoporosis' **Delete patients** who are not osteoporotic (0) **Sort** patients by each treatment **Delete** patients who are not receiving any treatment (0) **Export** results to Microsoft Excel® **Inspect** on results, focus on the date:identify patients who were prescribed a bisphosphonate <u>at first</u>

CRITERION 10-SEARCH 2 (including ibandronic acid and zoledronic acid because they are authorized by BNF but not by the guidelines)

Patient with a recorded diagnosis of osteoporosis

Is prescribed an oral bisphosphonate as first-line therapy

Step	**What?**	**How?**
Step 1	Identify patients with a diagnosis of osteoporosis who are prescribed an oral bisphosphonate (alendronic acid, disodium etidronate, risedronate sodium) as first-line therapy Drugs containing oral bisphosphonates are the following: Alendronic acid (Fosamax®, Fosavance®), disodium etidronate (Didronel PMO®), risedronate sodium (Actonel®)	**Use** form 'Query maker' in Microsoft Access® **Select** ➔ 'ibandro+zoledro' for criterion 1 ➔ **'**Osteoporosis' for criterion 2 ➔ 'raloxifene' for criterion 3 ➔ 'strontium ranelate' for criterion 4 ➔ 'calcitonin' for criterion 5 ➔ 'teriparatide' for criterion 6 **Sort** patients by 'osteoporosis' **Delete patients** who are not osteoporotic (0) **Sort** patients by each treatment **Delete** patients who are not receiving any treatment (0) **Export** results to Microsoft Excel® **Inspect** on results, focus on the date:identify patients who were prescribed a bisphosphonate <u>at first</u>

		Add results from search 1 **Change** number of applicable patients

CRITERION 11- SEARCH 1 (excluding ibandronic acid and zoledronic acid because they are not included in the guidelines)

Patient with a recorded diagnosis of osteopenia

Is prescribed an oral bisphosphonate as first-line therapy

Step	**What?**	**How?**
Step 1	Identify patients with a diagnosis of osteopenia who are prescribed an oral bisphosphonate (alendronic acid, disodium etidronate, risedronate sodium) as first-line therapy Drugs containing oral bisphosphonates are the following: Alendronic acid (Fosamax®, Fosavance®), disodium etidronate (Didronel PMO®), risedronate sodium (Actonel®)	**Use** form 'Query maker' in Microsoft Access® **Select** ➔ 'Bisphosphonate' for criterion 1 ➔ 'Osteopenia' for criterion 2 ➔ 'raloxifene' for criterion 3 ➔ 'strontium ranelate' for criterion 4 ➔ 'calcitonin' for criterion 5 ➔ 'teriparatide' for criterion 6 **Sort** patients by 'osteopenia' **Delete patients** who are not osteopenic (0) **Sort** patients by each treatment **Delete** patients who are not

		receiving any treatment (0) **Export** results to Microsoft Excel® **Inspect** on results, focus on the date:identify patients who were prescribed a bisphosphonate <u>at first</u>

CRITERION 11- SEARCH 2 (including ibandronic acid and zoledronic acid because they are authorized by BNF but not by the guidelines)

Patient with a recorded diagnosis of osteopenia

Is prescribed an oral bisphosphonate as first-line therapy

Step	**What?**	**How?**
Step 1	Identify patients with a diagnosis of osteopenia who are prescribed an oral bisphosphonate (alendronic acid, disodium etidronate, risedronate sodium) as first-line therapy Drugs containing oral bisphosphonates are the following: Alendronic acid (Fosamax®, Fosavance®), disodium etidronate (Didronel PMO®), risedronate sodium (Actonel®)	**Use** form 'Query maker' in Microsoft Access® **Select** ➔ ibandro+zoledro' for criterion 1 ➔ 'Osteopenia' for criterion 2 ➔ 'raloxifene' for criterion 3 ➔ 'strontium ranelate' for criterion 4 ➔ 'calcitonin' for criterion 5 ➔ 'teriparatide' for criterion 6 **Sort** patients by 'osteopenia' **Delete patients** who are not osteopenic (0) **Sort** patients by each treatment

		Delete patients who are not receiving any treatment (0) **Export** results to Microsoft Excel® **Inspect** on results, focus on the date:identify patients who were prescribed a bisphosphonate <u>at first</u> **Add** results from search 1 **Change** number of applicable patients

CRITERION 12- SEARCH 1 (excluding ibandronic acid and zoledronic acid because they are not included in the guidelines)

Patient who is prescribed a bisphosphonate

has no reason on record to avoid bisphosphonate

Step	**What?**	**How?**
Step 1	Identify patients who are prescribed bisphosphonates (alendronic acid, disodium etidronate, risedronate sodium) Drugs containing bisphosphonates are the following: Alendronic acid (Fosamax®, Fosavance®), disodium etidronate (Didronel PMO®), risedronate sodium (Actonel®)	**Use** form 'Query maker' in Microsoft Access® **Select** ➔ 'Bisphosphonates' for criterion 1 ➔ 'Contraindication to bisphosphonates' for criterion 2 ➔ 'inab to compl with instr bp' for criterion 3 ➔ 'unsatisfact response to bp' for criterion 4 ➔ 'intol to bp' for criterion 5

Step 2	Identify patients with reasons to avoid bisphosphonates Reasons to avoid bisphosphonates: o contraindication to bisphosphonate (see 10) ➢ Oesophageal strictures and achalasia ➢ Inability to remain upright for > 30 min after ingestion ➢ Hypocalcaemia ➢ Osteomalacia (etidronate) ➢ Moderate renal impairment (CrCl < 35 mL/min) ➢ Pregnancy and breast feeding o inability to comply with the instruction for use of bisphosphonates: (see 17) ➢ ingestion on an empty stomach ➢ washing the medication down with 250 ml water ➢ avoidance of food for 30 min ➢ avoidance of lying flat within 30 min of ingestion o unsatisfactory response to bisphosphonates (another fracture occurs, decrease in BMD despite adherence to treatment) intolerance to bisphosphonates (oesophageal ulceration, erosion or stricture, severe lower GI symptoms)	**Sort** by 'Bisphosphonates' **Delete** patients who do not receive bisphosphonate(0) **Exclude** patients with reasons to avoid bisphosphonates (Mauck and Clarke 2006)!

CRITERION 12- SEARCH 2 (including ibandronic acid and zoledronic acid because they are authorized by BNF but not by the guidelines)

Patient who is prescribed a bisphosphonate

has no reason on record to avoid bisphosphonate

Step	**What?**	**How?**
Step 1	Identify patients who are prescribed bisphosphonates (alendronic acid, disodium etidronate, risedronate sodium) Drugs containing bisphosphonates are the following: Alendronic acid (Fosamax®, Fosavance®), disodium etidronate (Didronel PMO®), risedronate sodium (Actonel®)	**Use** form 'Query maker' in Microsoft Access® **Select** ➔ 'Ibandro+ Zoledro' for criterion 1 ➔ 'Contraindication to bisphosphonates' for criterion 2 ➔ 'inab to compl with instr bp' for criterion 3 ➔ 'unsatisfact response to bp' for criterion 4 ➔ 'intol to bp' for criterion 5
Step 2	Identify patients with reasons to avoid bisphosphonates <u>Reasons to avoid bisphosphonates:</u> o contraindication to bisphosphonate (see 10) ➢ Oesophageal strictures and achalasia ➢ Inability to remain upright for > 30 min after ingestion ➢ Hypocalcaemia ➢ Osteomalacia (etidronate) ➢ Moderate renal impairment (CrCl < 35 mL/min) ➢ Pregnancy and breast feeding o inability to comply with the instruction for use of bisphosphonates: (see 17) ➢ ingestion on an empty stomach ➢ washing the medication down with 250 ml water	**Sort** by 'Ibandro+ Zoledro' **Delete** patients who do not receiveibandronic acid or zoledronic acid (0) **Exclude** patients with reasons to avoid bisphosphonates (Mauck and Clarke 2006)! **Add** results from search 1 **Change** number of applicable patients

	➢ avoidance of food for 30 min ➢ avoidance of lying flat within 30 min of ingestion o unsatisfactory response to bisphosphonates (another fracture occurs, decrease in BMD despite adherence to treatment) intolerance to bisphosphonates (oesophageal ulceration, erosion or stricture, severe lower GI symptoms)	

CRITERION 13

A patient receiving treatment for osteoporosis/ osteopenia

is prescribed a standard dose regimen

Step	**What?**	**How?**
Step 1	Prepare for identifying main patient groups (female+ osteoporosis, postmenopausal+ osteoporosis, postmenopausal+ osteopenia, male+ osteoporosis)	**Use** form 'Query maker' in Microsoft Access® **Select** in 'Read Code' field: ➔ 'Postmenopausal' for criterion 1 ➔ 'Osteoporosis' for criterion 2 ➔ 'Osteopenia' for criterion 3 ➔ 'Female' for criterion 4 ➔ 'Male' for criterion 5 **Press** 'view'
Step 2	Identify female patients with a diagnosis of osteoporosis and create a table in Microsof Access® containing these patients	**Create** new query by using 'design view' **Select** 'tbl_temp' **Apply** 'patientKey', c4 [1], c2 [1] **Run** and save query 1 ('Female Osteoporosis') **Select '**File', 'Export' to Microsoft Excel® by following the process. Name document 'Female OS' **Select '**Tables', 'New', 'Import Table' **Import** Microsoft Excel®document 'Female OS'and rename field c4 to 'female' and c2 to 'Osteoporosis' (table 'Female Osteoporosis')

Step 3	Identify postmenopausal patients with a diagnosis of osteoporosis and create a table in Microsoft Access® containing these patients	**Create** new query by using 'design view' **Select** 'tbl_temp' **Apply** 'patientKey', c1 [1], c2 [1] **Run** and save query 2 ('postmenopausal osteoporosis') **Select '**File', 'Export' to Microsoft Excel® by following the process. Name document 'Postmenopausal OS' **Select '**Tables', 'New', 'Import Table' **Import** Microsoft Excel®document 'Postmenopausal OS'and rename field c1 to 'postmenopausal' and c2 to 'Osteoporosis' (table 'Postmenopausal Osteoporosis')
Step 4	Identify postmenopausal patients with a diagnosis of osteopenia and create a table in Microsoft Access® containing these patients	**Create** new query by using 'design view' **Select** 'tbl_temp' **Apply** 'patientKey', c1 [1], c3 [1] **Run** and save query 3 ('Postmenopausal Osteopenia') **Select '**File', 'Export' to Microsoft Excel® by following the process. **Name** document 'Postmenopausal ON' **Select '**Tables', 'New', 'Import Table' **Import** Microsoft Excel®document 'Postmenopausal ON' and rename field c1 to 'postmenopausal' and c3 to 'osteopenia' (table 'Postmenopausal Osteopenia')
Step 5	Identify male patients with a diagnosis of osteoporosis and create a table in Microsof Access® containing these patients	**Create** new query by using 'design view' **Select** 'tbl_temp' **Apply** 'patientKey', c5 [1], c2 [1] **Run** and save query 4 ('male osteoporosis') **Select '**File', 'Export' to Microsoft Excel® by following the process. **Name** document 'Male OS' **Select '**Tables', 'New', 'Import Table' **Import** Microsoft Excel® document 'Male OS' and rename field c5 to 'Male' and c2 to 'Osteoporosis' (table 'Male Osteoporosis')
Step 6	Identify patients prescribed daily 2g PO strontium ranelate	**Use** form 'Query maker' in Microsoft Access® **Select** in 'drug' field/ 'group': ➔ 'Strontium ranelate' for criterion 1 **Press** 'view'

		Create new query by using 'design view' **Select** 'tbl_temp' **Apply** 'patientKey', c1 [not like "0"], d1, c2, d2, c3 **Run** query 5 (query 'Patient prescribed strontium ranelate') **Export** data to Microsoft Excel®and check manually if they are prescribed 2g PO daily. **Create** new query by using design view **Select** table 'Postmenopausal Osteoporosis' and query 'Patient prescribed strontium ranelate' **Link** tables via 'patientKeys' **Apply** patient keys **Run** query 6 **Apply** 'patientKey' ➔ prescribed 2g PO daily and postmenopausal woman with osteoporosis= Yes ➔ not prescribed 2g PO daily or not postmenopausal woman with osteoporosis= No(U) ➔ recorded data not clear=IDS ➔ No(J)=0… there is no justification for prescribing another dose or prescribing to another patient group
Step 7	Identify patients prescribed daily 60mg PO raloxifene	**Use** form 'Query maker' in Microsoft Access® **Select** in 'drug' field/ 'group': ➔ 'Raloxifene' for criterion 1 **Press** 'view' **Create** new query by using 'design view' **Select** 'tbl_temp' **Apply** 'patientKey', c1 [not like "0"], d1, c2, d2, c3 **Run** query 7 (query 'Patient prescribed raloxifene') **Export** data to Microsoft Excel®and check manually if they are prescribed 60mg PO daily. **Create** new query by using 'design view' **Select** table 'Postmenopausal Osteoporosis' and query 'Patient prescribed raloxifene' **Link** tables via 'patientKey' **Apply** 'patientKey' **Run** query 8 ➔ prescribed 60mg PO daily and postmenopausal woman with

		osteoporosis= Yes ➔ not prescribed 60mg PO daily or not postmenopausal woman with osteoporosis= No(U) ➔ recorded data not clear=IDS
Step 8	Identify patients prescribed teriparatide (20 micrograms daily, for a maximum duration of treatment of 18 months)	**Use** form 'Query maker' in Microsoft Access® **Select** in 'drug' field/ 'group': ➔ 'Teriparatide' for criterion 1 **Press** 'view' **Create** new query by using 'design view' **Select** tbl_temp **Apply** 'patientKey', c1 [not like "0"], d1, c2, d2, c3 **Run** Query 9 (Query 'Patient prescribed teriparatide') Export data to Microsoft Excel®and check manually if they are prescribed 20 micrograms daily, for a maximum duration of treatment of 18 months. **Create** new query by using design view **Select** Table 'Patients: NHS Read codes_QOF and MAT data items_tbl' and Query 'Patient prescribed teriparatide' **Link** tables via patient keys **Apply** 'patient keys' and 'mat data item' [male] **Run** Query 10 ➔ prescribed 20 micrograms daily, for a maximum duration of treatment of 18 months and not male = Yes ➔ not prescribed 20 micrograms daily, for a maximum duration of treatment of 18 months or male= No(U) ➔ recorded data not clear=IDS
Step 9	Identify patients prescribed calcitonin (200 units daily intranasally)	**Use** form 'Query maker' in Microsoft Access® **Select** in drug field/ group: ➔ Calcitonin for criterion 1 **Press** 'view' **Create** new query by using 'design view' **Select** 'tbl_temp' **Apply** 'patientKey', c1 [not like "0"], d1, c2, d2, c3 **Run** query 11 (query 'Patient prescribed calcitonin') Export data to Microsoft Excel®and check manually if they are prescribed 200 units intranasally.

		Create new query by using 'design view' **Select** table 'Postmenopausal Osteoporosis' and query 'Patient prescribed calcitonin' **Link** tables via 'patientKey' **Apply** 'patientKey' **Run** query 12 ➔ prescribed 200 units intranasally and postmenopausal woman with osteoporosis= Yes ➔ not prescribed 200 units intranasally or not postmenopausal woman with osteoporosis= No(U) ➔ recorded data not clear=IDS
Step 10	Identify patients prescribed a standard dose regimen for bisphophonates	**Use** form 'Query maker' in Microsoft Access® **Select** in 'drug' field/ 'group': ➔ BP **Press** 'view' **Create** new query by using 'design view' **Select** 'tbl_temp' and 'Patients: NHS Read codes_QOF and MAT data items_tbl' **Apply** 'patientKey', c1, c2, c3,d3 ('tbl_temp') and mat data item [male] (table 'Patients: NHS Read codes_QOF and MAT data items_tbl') **Run** query 13 **Export** results to Microsoft Excel® and check manually if patients are prescribed the correct dose regimen: ➔ Alendronic acid: 10mg po. Justification for not being prescribed 10mg:glucocorticoid induced osteoporosis and prescribed 5mg po ➔ Disodium etidronate: 400mg for 14 days PO, 1.25g calcium carbonate for 76 days PO (only if glucocorticoid induced osteoporosis) ➔ Risedronate sodium 5mg daily PO (only if glucocorticoid induced osteoporosis) **Create** new query by using 'design view' **Select** 'tbl_temp' and 'Patients: NHS Read codes_QOF and MAT data items_tbl' **Apply** 'patientKey', c1, c2, c3,d3 ('tbl_temp') and mat data item [female] (table 'Patients: NHS Read codes_QOF and MAT data items_tbl') **Run** query 14 **Export** results to Microsoft Excel® and check manually if patients are prescribed the correct dose regimen:

		➔ Alendronic acid: 10mg po daily, or 70 mg one weekly PO. Justification for not being prescribed 10mg or 70 mg once weekly PO: glucocorticoid induced osteoporosis or osteopenia and prescribed 5mg PO. ➔ Disodium etidronate: 400mg for 14 days PO, 1.25g calcium carbonate for 76 days PO ➔ Risedronate sodium 5mg daily PO or 35 mg weekly PO (only if osteoporosis) **Count** only one result per patient. Delete results for ibandronic acid.

CRITERION 14- SEARCH 1 (excluding ibandronic acid and zoledronic acid because they are not included in the guidelines)

Patient when started on bisphosphonate therapy

Was initiated on alendronate

Step	**What?**	**How?**
Step 1	Drugs containing bisphosphonates are the following: Alendronic acid (Fosamax®, Fosavance®), disodium etidronate (Didronel PMO®), risedronate sodium (Actonel®)	**Use** form 'Query maker' in Microsoft Access® **Select** in 'Read Code' field ➔ 'Bisphosphonate' for criterion 1 ➔ 'BP (A)' for criterion 2 **Press** 'view' **Delete** patients who are not prescribed a bisphosphonate (0) **Sort** patients by alendronate **Export** results to Excel®

CRITERION 14- SEARCH 2 (including ibandronic acid and zoledronic acid because they are authorized by BNF but not by the guidelines)

A patient with osteoporosis and NOT prescribed any of the following: bisphosphonates, raloxifene, strontium ranelate or calcitonin

has a recorded contraindication to each agent (see below)

Step	**What?**	**How?**
Step 1	Drugs containing bisphosphonates are the following: Alendronic acid (Fosamax®, Fosavance®), disodium etidronate (Didronel PMO®), risedronate sodium (Actonel®)	**Use** form 'Query maker' in Microsoft Access® **Select** in 'Read Code' field ➔ 'Bisphosphonate' for criterion 1 ➔ 'BP (I)' for criterion 2 ➔ 'BP (A) for criterion 3 **Press** 'view' **Delete** patients who are not prescribed a bisphosphonate (0) **Sort** patients by alendronate **Export** results to Excel®

CRITERION 15

A postmenopausal woman diagnosed with osteoporosis/osteopenia and not treated with alendronate

Is prescribed risedronate

Step	**What?**	**How?**
Step 1	A postmenopausal woman diagnosed with osteoporosis/osteopenia and not treated with alendronate isprescribed risedronate	**Use** form 'Query maker' in Microsoft Access® ➔ **Select** in 'Read Code' field 'postmenopausal' for criterion 1 ➔ 'Osteoporosis' for criterion 2 ➔ 'Osteopenia' for criterion 3 ➔ 'BP(A)' for criterion 4 ➔ 'BP(R)' for criterion 5 **Press** 'view' **Sort** patients by 'postmenopausal' **Delete** patients who are not postmenopausal (0) **Delete** patients who are not osteoporotic/ osteopenic (0) **Sort** patients by 'BP(A)' **Delete** patients who are receiving alendronic acid **Sort** patients by 'BP(R)' Patients receiving risedronate = YES

CRITERION 16

Postmenopausal women with ≥ 2 vertebral fractures and NOT treated with alendronate or risedronate

Are prescribed intermittent cyclical etidronate

Step	**What?**	**How?**
Step 1	Identify postmenopausal women with ≥ 2 vertebral fractures and NOT treated with alendronate or risedronateare prescribed intermittent cyclical etidronate	**Use** form 'Query maker' in Microsoft Access® **Select** in 'Read Code' field: ➔ 'postmenopausal' for criterion 1 ➔ 'vertebral fractures' for criterion 2 ➔ 'BP(A)' for criterion 3 ➔ 'BP(R)' for criterion 4 ➔ 'BP (E+ca)' for criterion 5 **Press** 'view' **Create** new query by using 'design view' **Select** 'tbl_temp' **Apply** 'patientKey', c1 [1], c2 [1], c3 [0], c4 [0], c5 **Run** query 1 **Export** results to Microsoft Excel® **Check manually**(in table 'Patients: NHS Read codes_QOF and MAT data items_tbl') if patients have records for 2 or more vertebral fractures and note those patients. **Delete** patients who have less than 2 vertebral fractures.

CRITERION 17- SEARCH 1 (excluding ibandronic acid and zoledronic acid because they are not included in the guidelines)

Patient who is on long-term glucocorticoid therapy (≥ 7.5 mg prednisolone or equivalents for ≥ 3 months)

Is prescribed a bisphosphonate

Step	**What?**	**How?**
Step 1	Identify patients who are on long-term glucocorticoid therapy and prescribed a bisphosphonate	**Use** form 'Query maker' in Microsoft Access® **Select** in 'Read Code' field: ➔ 'long-term steroid' for criterion 1 ➔ 'bisphosphonates' for criterion 2 **Press** 'view' **Sort** patients by 'long-term steroids' **Delete** patients who do not receive a long-term treatment with steroids (0) **Export** results to Microsoft Excel **Inspect** on 'Bisphosphonates' column: ➔ '1'= YES ➔ '0'= NO (possible justification: see criterion 12 'reasons to avoid bisphoshonates)

CRITERION 17- SEARCH 2 (including ibandronic acid and zoledronic acid because they are authorized by BNF but not by the guidelines)

Patient who is on long-term glucocorticoid therapy (≥ 7.5 mg prednisolone or equivalents for ≥ 3 months)

Is prescribed a bisphosphonate

Step	**What?**	**How?**
Step 1	Identify patients who are on long-term glucocorticoid therapy and prescribed a bisphosphonate	**Use** form 'Query maker' in Microsoft Access® **Select** in 'Read Code' field: ➔ 'long-term steroid' for criterion 1 ➔ 'bisphosphonates' for criterion 2 ➔ 'Ibandro + Zoledro' for criterion 3 **Press** 'view' **Sort** patients by 'long-term steroids' **Delete** patients who do not receive a long-term treatment with steroids (0) **Export** results to Microsoft Excel **Inspect** on 'Bisphosphonates' column and 'Ibandro + Zoledro' column: ➔ '1'= YES ➔ '0'= NO (possible justification: see criterion 12 'reasons to avoid bisphoshonates)

CRITERION 18

A postmenopausal woman diagnosed with osteoporosis requiring treatment for primary prevention of fractures who has an identifiable reason for not being prescribed a bisphosphonate

is prescribed strontium ranelate.

Step	**What?**	**How?**
Step 1	Identify postmenopausal women diagnosed with osteoporosis requiring treatment for primary prevention of fractures	**Use** form 'Query maker' in Microsoft Access® **Select** in 'Read Code' field: ➔ 'postmenopausal' for criterion 1 ➔ 'osteoporosis' for criterion 2 ➔ ' All fractures' for criterion 3 ➔ 'strontium ranelate' for criterion 4 **Press** 'view' **Sort** patients by 'postmenopausal' **Delete** those who are not postmenopausal (0) **Delete** patients who are not osteoporotic (0) **Delete** patients with records of fractures **Export** results to Microsoft Excel and import document again to create a table (table 'Criterion 18 step 1')
Step 2	Identify postmenopausal women diagnosed with osteoporosis requiring treatment for primary prevention of fractures who have an identifiable reason for not being prescribed a	**Use** form 'Query maker' in Microsoft Access® **Select** in 'Read Code' field: ➔ Contraindication to bisphosphonates' for criterion 1 ➔ 'inab to compl with instr bp' for criterion 2 ➔ 'intol to bp' for criterion 3 **Press** 'view' **Create** a new query by using 'design view' **Link** table 'Criterion 18 step 1' to 'tbl_temp' via 'patientKeys' **Apply** 'patientKey', c1, c2, c3 (table 'Criterion

	bisphosphonate and are prescribed strontium ranelate	18 step 1') and c1, c2 ('tbl_temp') **Run** query 1 **Sort** 'Contraindications to bisphosphonates' **Delete** patients with no contraindication (0) **Sort** by 'inab to compl with instr bp' **Delete** patients with (0) recorded **Sort** by 'intol to bp' **Delete** patients with (0) recorded **Check** if remaining patients are prescribed strontium ranelate

CRITERION 19

A postmenopausal woman diagnosed with osteoporosis with at least one osteoporotic fracture who has an identifiable reason for not being prescribed a bisphosphonate (see below)

Isprescribed strontium ranelateor raloxifene

Step	**What?**	**How?**
Step 1	Identify postmenopausal women diagnosed with osteoporosis with at least one osteoporotic fracture	**Use** form 'Query maker' in Microsoft Access® **Select** in 'Read Code' field: ➔ 'postmenopausal' for criterion 1 ➔ 'Osteoporosis' for criterion 2 ➔ 'osteoporotic fractures' for criterion 3 ➔ 'strontium ranelate' for criterion 4 ➔ 'raloxifene' for criterion 5 **Press** 'view' **Sort** patients by 'postmenopausal' **Delete** patients who are not postmenopausal (0) **Sort** patients by 'Osteoporosis'

		Delete patients who are not osteoporotic (0) **Sort** patients by 'osteoporotic fracture' **Delete** patients without an osteoporotic fracture (0) **Export** results to Microsoft Excel and import document again to create a table (table ' Criterion 19 Step 1')
Step 2	Identify postmenopausal women diagnosed with osteoporosis with at least one osteoporotic fracture	**Use** form 'Query maker' in Microsoft Access® **Select** in 'Read Code' field: ➔ **'**Contraindication to bisphosphonates' for criterion 1 ➔ 'inab to compl with instr bp' for criterion 2 ➔ 'intol to bp' for criterion 3 **Press** 'view' **Create** a new query by using 'design view' **Link** table 'Criterion 19 step 1' to 'tbl_temp' via 'patientKey' **Apply** 'patientKey', c1, c2, c3 (table 'Criterion 19 step 1') and c1, c2, c3, c4, c5 ('tbl_temp') **Run** query 1 **Sort** 'Contraindications to bisphosphonates' **Delete** patients with no contraindication (0) **Sort** by 'inab to compl with instr bp' **Delete** patients with (0) recorded **Sort** by 'intol to bp' **Delete** patients with (0) recorded **Check** if remaining patients are prescribed strontium ranelate or raloxifene

CRITERION 20

Postmenopausal woman diagnosed with osteoporosis and at least one osteoporotic fracture

who has either

- a reason to avoid bisphosphonates
- a contraindication to strontium ranelate
  - pregnancy
  - breast feeding
- an intolerance to strontium ranelate
  - persistent nausea
  - persistent diarrhoea

and who is either

- aged ≥ 65 years with a T-Score ≤ -4 SD
- aged ≥ 65 years with a T-Score ≤ -3.5 SD and has more than two fractures
- aged 55-64 years with a T-Score ≤ -4 SD and has more than two fractures

Step	**What?**	**How?**
Step 1	Identify patients prescribed teriparatide Identify postmenopausal women diagnosed with osteoporosis with at lleastoneosteoporotic fracture among patients prescribed teriparatide Identify whether remaining patients present a reason to avoid bisphosphonates and strontium ranelate and are at the required age and present the required T-Score as indicated above	

CRITERION 21- SEARCH 1(including ibandronic acid and zoledronic acid because they are authorized by BNF but not by the guidelines)

A postmenopausal woman diagnosed with osteoporosis and with at least one vertebral fracture; NOT treated with a bisphosphonate, raloxifene, strontium ranelate or teriparatide

Is prescribed calcitonin.

Step	**What?**	**How?**
Step 1	Identify postmenopausal women with a diagnosis of osteoporosis and at least one vertebral fracture who are prescribed calcitonin	**Use** form 'Query maker' in Microsoft Access® **Select** in 'Read Code' field: ➔ 'postmenopausal' for criterion 1 ➔ 'Osteoporosis' for criterion 2 ➔ 'osteoporotic fractures' for criterion 3 ➔ 'Bisphosphonate' for criterion 4 ➔ 'strontium ranelate' for criterion 5 ➔ 'calcitonin' for criterion 6 **Press** 'view' **Delete** patients who are not postmenopausal (0) **Delete** patients who are not osteoporotic (0) **Delete** patients without fractures (0) **Delete** patients who are receiving a bisphosphonate, raloxifene, strontium ranelate or teriparatide (Mauck and Clarke 2006) **Sort** remaining patients by 'calcitonin' **Export** results to Microsoft Excel® **Use** form 'Query maker' in Microsoft Access® **Select** in 'Read Code' field: ➔ 'postmenopausal' for criterion 1

		➔ 'Osteoporosis' for criterion 2 ➔ 'osteoporotic fractures' for criterion 3 ➔ 'Bisphosphonate' for criterion 4 ➔ 'raloxifene' for criterion 5 ➔ 'teriparatide' for criterion 6 **Press** 'view' **Delete** patients who are not postmenopausal (0) **Delete** patients who are not osteoporotic (0) **Delete** patients without fractures (0) **Delete** patients who are receiving a bisphosphonate, raloxifene, strontium ranelate or teriparatide (Mauck and Clarke 2006) **Sort** remaining patients by 'calcitonin' **Export** results to Microsoft Excel®

CRITERION 21**-** SEARCH 2 (excluding ibandronic acid andzoledronicacid because they are not included in the guidelines)

A postmenopausal woman diagnosed with osteoporosis and with at least one vertebral fracture; NOT treated with a bisphosphonate, raloxifene, strontium ranelate or teriparatide

Is prescribed calcitonin.

Step	**What?**	**How?**
Step 1	Identify postmenopausal women with a diagnosis of osteoporosis and at least one vertebralfracture who are prescribed calcitonin	**Use** form 'Query maker' in Microsoft Access® **Select** in 'Read Code' field: ➔ 'postmenopausal' for criterion 1 ➔ 'Osteoporosis' for criterion 2 ➔ 'osteoporotic fractures' for criterion 3 ➔ 'Bisphosphonate' for criterion 4 ➔ 'BP (I)' for criterion 5 ➔ 'strontium ranelate' for criterion 6 **Press** 'view' **Delete** patients who are not postmenopausal (0) **Delete** patients who are not osteoporotic (0) **Delete** patients without fractures (0) **Delete** patients who are receiving a bisphosphonate, raloxifene, strontium ranelate or teriparatide (Mauck and Clarke 2006) **Sort** remaining patients by 'calcitonin' **Export** results to Microsoft Excel® **Use** form 'Query maker' in Microsoft Access® **Select** in 'Read Code' field:

		➔ 'postmenopausal' for criterion 1 ➔ 'Osteoporosis' for criterion 2 ➔ 'osteoporotic fractures' for criterion 3 ➔ 'Bisphosphonate' for criterion 4 ➔ 'raloxifene' for criterion 5 ➔ 'teriparatide' for criterion 6 **Press** 'view' **Delete** patients who are not postmenopausal (0) **Delete** patients who are not osteoporotic (0) **Delete** patients without fractures (0) **Delete** patients who are receiving a bisphosphonate, raloxifene, strontium ranelate or teriparatide **Sort** remaining patients by 'calcitonin' **Export** results to Microsoft Excel®

APPENDIX 5: INTER RATER RELIABILITY TESTING PRACTICE A

Table 28 Inter-rater reliability testing Adherence

Criterion 1	Student 1	Student 2
Patient diagnosed with osteoporosis has a recorded DEXA scan.		
Not applicable	16	16
Yes	77	77
No(J)	6	6
No(U)	55	55
IDQ	0	0
IDS	0	0
Adherence%	58,33	58,33

Criterion 2	Student 1	Student 2
DXE scan is performed at two specific sites (anteroposterior spine and hip)		
Not applicable		
Yes	243	243
No(J)	0	0
No(U)	67	67
IDQ	1	1
IDS	6	6
Adherence%	76,9	76,9

Criterion 3	Student 1	Student 2
Patient with osteoporosis is prescribed calcium and vitamin D.		
Not applicable	16	16
Yes	76	76
No(J)	0	0
No(U)	62	62
IDQ	0	0
IDS	0	0
Adherence%	55,07	55,07

Criterion 4	Student 1	Student 2
Patient with osteopenia is prescribed calcium and vitamin D.		
Not applicable	138	138
Yes	9	9
No(J)	0	0
No(U)	7	7
IDQ	0	0
IDS	0	0
Adherence%	56,25	56,25

.

Criterion 5	Student 1	Student 2
Patient with vitamin D deficiency or aged over 64 is prescribed vitamin D.		
Not applicable	30	31
Yes	73	72
No(J)	0	0
No(U)	51	51
IDQ	0	0
IDS	0	0
Adherence%	58,87	58,54

Criterion 6 S1	Student 1	Student 2

Patient with osteoporosis NOT prescribed bisphosphonates, raloxifene, strontium ranelate, calcitonin or teriparatide has a contraindication to each agent.		
Not applicable	101	100
Yes	0	0
No(J)	0	0
No(U)	53	54
IDQ	0	0
IDS	0	0
Adherence%	0	0

Criterion 6 S2	**Student 1**	**Student 2**
Not applicable	101	101
Yes	0	0
No(J)	0	0
No(U)	52	53
IDQ	0	0
IDS	0	0
Adherence%	0	0

Criterion 7	**Student 1**	**Student 2**
Patient prescribed calcium is prescribed a daily dose of 500-1500 mg.		
Not applicable	69	69
Yes	84	84
No(J)	0	0
No(U)	1	1
IDQ	0	0
IDS	0	0
Adherence%	98,82	98,82

Criterion 8	**Student 1**	**Student 2**
Patient prescribed vitamin D is prescribed a daily dose of 400-800 IU.		
Not applicable	76	76
Yes	77	77
No(J)	0	0
No(U)	1	1
IDQ	0	0
IDS	0	0
Adherence%	98,72	98,72

Criterion 9 S1	**Student 1**	**Student 2**
Patient with osteoporosis and NOT prescribed bisphosphonates, raloxifene, stronium ranelate or calcitonin is prescribed >=1000 mg calcium plus 800 IU vitamin D per day.		
Not applicable	100	100
Yes	10	11
No(J)	0	0
No(U)	43	42
IDQ	0	0
IDS	0	1
Adherence%	18,52	20,37

Criterion 9 S2	Student 1	Student 2
Not applicable	101	101
Yes	10	11
No(J)	0	0
No(U)	42	41
IDQ	0	0
IDS	1	1
Adherence%	18,87	20,75

Criterion 10 S1	Student 1	Student 2
Patient with osteoporosis is prescribed an oral bisphosphonate as first-line therapy.		
Not applicable	16	16
Yes	81	81
No(J)	0	0
No(U)	57	57
IDQ	0	0
IDS	0	0
Adherence%	58,7	58,7

Criterion 10 S2	Student 1	Student 2
Not applicable	16	16
Yes	82	82
No(J)	0	0
No(U)	56	56
IDQ	0	0
IDS	0	0
Adherence%	59,42	59,42

Criterion 11	Bergmann	Doblhammer
Patient with osteopenia is prescribed an oral bisphosphonate as first-line therapy.		
Not applicable	138	138
Yes	9	9
No(J)	0	0
No(U)	7	7
IDQ	0	0
IDS	0	0
Adherence%	56,25	56,25

Criterion 12 S1	Student 1	Student 2
Patient prescribed a bisphosphonate has no reason to avoid them.		
Not applicable	63	63
Yes	75	75
No(J)	0	0
No(U)	0	0
IDQ	0	0
IDS	16	16
Adherence%	82,42	82,42

Criterion 12 S2	Student 1	Student 2
Not applicable	62	62
Yes	75	75
No(J)	0	0

No(U)	0	0
IDQ	0	0
IDS	14	14
Adherence%	81,52	81,52

Criterion 13	**Student 1**	**Student 2**
Patient receiving osteoporosis/osteopenia treatment is prescribed a standard dose regimen.		
Not applicable	60	60
Yes	81	84
No(J)	0	0
No(U)	10	10
IDQ	0	0
IDS	3	0
Adherence%	86,17	89,36

Criterion 14 S1	**Student 1**	**Student 2**
Postmenopausal when started on bisphosphonate was initiated on alendronate.		
Not applicable	63	63
Yes	79	79
No(J)	0	0
No(U)	12	12
IDQ	0	0
IDS	0	0
Adherence%	86,81	86,81

Criterion 14 S2	**Student 1**	**Student 2**
Not applicable	62	62
Yes	79	79
No(J)	0	0
No(U)	13	13
IDQ	0	0
IDS	0	0
Adherence%	85,87	85,87

Criterion 15	**Student 1**	**Student 2**
Postmenopausal woman with osteoporosis/osteopenia and NOT treated with alendronate is prescribed risedronate.		
Not applicable	89	89
Yes	8	8
No(J)	0	0
No(U)	57	57
IDQ	0	0
IDS	0	0
Adherence%	12,31	12,31

Criterion 16	**Student 1**	**Student 2**
Postmenopausal woman with at least two vertebral fractures and NOT treated with alendronate or risedronate is prescribed intermittent cyclical etidronate.		
Not applicable	152	152
Yes	0	0
No(J)	0	0
No(U)	2	2
IDQ	0	0

IDS	0	0
Adherence%	0	0

Criterion 17	**Student 1**	**Student 2**
Patient on long-term oral steroid therapy is prescribed a bisphosphonate.		
Not applicable	no result	no result
Yes	no result	no result
No(J)	no result	no result
No(U)	no result	no result
IDQ	no result	no result
IDS	no result	no result
Adherence%	no result	no result

Criterion 18	**Student 1**	**Student 2**
Postmenopausal woman with osteoporosis with a reason for not being prescribed a bisphosphonate is prescribed strontium ranelate.		
Not applicable	153	153
Yes	0	0
No(J)	0	0
No(U)	1	1
IDQ	18	20
IDS	0	0
adherent	0	0

Criterion 19	**Student 1**	**Student 2**
Postmenopausal woman with osteoporosis with at least one vertebral fracture and a reason for not being prescribed a bisphosphonate is prescribed strontium ranelate or raloxifene.		
Not applicable	153	153
Yes	0	0
No(J)	0	0
No(U)	1	1
IDQ	5	6
IDS	0	0
Adherence%	0	0

Criterion 20	**Student 1**	**Student 2**
Postmenopausal woman with osteoporosis and at least one vertebral fracture who has either a reason to avoid BPs OR an intolerance to strontium ranelate AND who is either older than 54 with a T-Score <= -4 SD OR older than 64 with a T-Score <= - 3,5 and more than two fractures OR 55-64 years with a T-Score <= - 4 SD and more than two fractures is prescribed teriparatide.		
Not applicable	no result	no result
Yes	no result	no result
No(J)	no result	no result
No(U)	no result	no result
IDQ	no result	no result
IDS	no result	no result
Adherence%	no result	no result

Criterion 21	**Student 1**	**Student 2**
Postmenopausal woman with osteoporosis, at least one		

vertebral fracture and NOT treated with BPs, raloxifene or strontium ranelate is prescribed calcitonin.		
Not applicable	150	150
Yes	0	0
No(J)	0	0
No(U)	4	4
IDQ	0	0
IDS	0	0
Adherence%	0	0

Table 29 Inter-rater reliability testing Applicability

Criterion	Applicability 1	Applicability 2	Percentage of Discrepancy	Percentage of Agreement
1	40,2	40,2	0	100
2	30,8	27,6	10,4	89,6
3	50	50	0	100
4	56,3	56,3	0	100
5	59,1	58,8	0,5	99,5
6	0	0	0	100
7	99,2	99,2	0	100
8	98,2	97,3	0,9	99,1
9	22,6	23,5	3,8	96,2
10	56	56	0	100
11	56,3	56,3	0	100
12	85,9	85,9	0	100
13	82,1	84,1	2,4	97,6
14	86,1	86,1	0	100
15	12,4	12,4	0	100
16	nr	nr	0	100
17	nr	nr	0	100
18	0	0	0	100
19	0	0	0	100
20	nr	nr	0	100
21	0	0	0	100
		Mean%	0,86	99,14

Table 30 Inter-rater reliability testing Yes-results

Criterion	Yes 1	Yes 2	Percentage of Discrepancy	Percentage of Agreement
1	78	78	0	100
2	32	32	0	100
3	100	100	0	100
4	9	9	0	100
5	101	100	1,0	99,0
6	0	0	0	100
7	118	118	0	100
8	109	109	0	100
9	19	20	5	95
10	112	112	0	100
11	9	9	0	100
12	116	116	0	100
13	119	122	2,5	97,5
14	105	105	0	100
15	12	12	0	100

16	0	0	0	100
17	0	0	0	100
18	0	0	0	100
19	0	0	0	100
20	0	0	0	100
21	0	0	0	100
Mean%			0,4	99,6

Table 31 Inter-rater reliability testing Justified non-adherence

Criterion	No(J) 1	No(J) 2	Percentage of Discrepancy	Percentage of Agreement
1	6	6	0	100
2	0	0	0	100
3	0	0	0	100
4	0	0	0	100
5	0	0	0	100
6	0	0	0	100
7	0	0	0	100
8	0	0	0	100
9	0	0	0	100
10	0	0	0	100
11	0	0	0	100
12	0	0	0	100
13	0	0	0	100
14	0	0	0	100
15	0	0	0	100
16	0	0	0	100
17	0	0	0	100
18	0	0	0	100
19	0	0	0	100
20	0	0	0	100
21	0	0	0	100
Mean%			0	100

Table 32 Inter-rater reliability testing Unjustified non-adherence

Criterion	No(U) 1	No(U) 2	Percentage of Discrepancy	Percentage of Agreement
1	109	109	0	100
2	56	56	0	100
3	100	100	0	100
4	7	7	0	100
5	70	70	0	100
6	84	85	1,2	98,8
7	1	1	0	100
8	3	3	0	100
9	65	64	1,5	98,5
10	88	88	0	100
11	7	7	0	100
12	0	0	0	100
13	15	15	0	100

14	17	17	0	100
15	85	85	0	100
16	2	2	0	100
17	0	0	0	100
18	33	33	0	100
19	1	1	0	100
20	0	0	0	100
21	9	9	0	100
Mean%			0,1	99,9

APPENDIX 6: MAT DATA ITEMS

Table 33 MAT Data items

	Data item
H/O: peptic ulcer	Contraindications to bisphosphonates
Oesophageal stricture or achalasia	Contraindications to bisphosphonates
Inability to remain upright for >30 min after ingestion	Contraindications to bisphosphonates
Hypocalcaemia	Contraindications to bisphosphonates/calcitonin
Osteomalacia (Etidronate)	Contraindications to bisphosphonates
Moderate renal impairment (CrCl < 35ml/min)	Contraindications to bisphosphonates
Pregnancy and breast feeding	Contraindications to bisphosphonates/raloxifene/strontium ranelate
DVT - Deep vein thrombosis	Contraindication to raloxifene
Liver function tests abnormal	Contraindication to raloxifene
Chronic liver disease NOS	Contraindication to raloxifene
[D]Abnormal liver function test	Contraindication to raloxifene
Dysfunctional uterine bleeding	Contraindication to raloxifene
[V] Personal history DVT- deep vein thrombosis	Contraindication to raloxifene
Chronic renal failure	Contraindication to raloxifene
Past and present venous thromboembolic events	Contraindication to raloxifene
Hepatic impairment	Contraindication to raloxifene
Cholestasis	Contraindication to raloxifene
Severe renal impairment (CrCl<10ml/min)	Contraindication to raloxifene
Endometrial cancer	Contraindication to raloxifene
Pregnancy and breast feeding	Contraindications to bisphosphonates/raloxifene/strontium ranelate
Hypersensitivity	Contraindications to strontium ranelate/calcitonin
Hypocalcaemia	Contraindications to bisphosphonates/calcitonin
DEXA - Dual energy X-ray photon absorptiometry	DEXA
Dual energy X-ray photon absorptiometry	DEXA
Hip DXA scan	DEXA
Hip DXA scan result normal	DEXA
Hip DXA scan result osteopenic	DEXA
Hip DXA scan result osteoporotic	DEXA
Lumbar DXA scan	DEXA
Lumbar DXA scan result normal	DEXA
Lumbar DXA scan result osteopenic	DEXA
Lumbar DXA scan result osteoporotic	DEXA
Lumbar spine DXA scan	DEXA
Bone density scan	DEXA IDS
Body Mass Index low K/M	Independent clinical risk factor/ indicator of low BMD
Alcohol dependence syndrom	Independent clinical risk factor/ indicator of low BMD
Alcohol intake of 4 or more units per day	Independent clinical risk factor/ indicator of low BMD
H/O: rheumatoid arthritis	Independent clinical risk factor/ indicator of low BMD
Rheumatoid Arthritis	Independent clinical risk factor/ indicator of low BMD
Rheumatoid lung	Independent clinical risk factor/ indicator of low BMD
Irritable bowel syndrome	Independent clinical risk factor/ indicator of low BMD
Crohn's disease	Independent clinical risk factor/ indicator of low BMD
BMI less than 22 kg/m^2	Independent clinical risk factor/ indicator of low BMD
Ankylosing spondylitis	Independent clinical risk factor/ indicator of low BMD
Parental history of hip fracture	Independent clinical risk factor/ indicator of low BMD
CKD follow-up	Renal impairment IDS
CKD Monitoring Defaulter	Renal impairment IDS
Chronic kidney disease stage 3	Renal impairment IDS
Serum creatinine raised	Renal impairment IDS

Renal Monitoring Defaulter	Renal impairment IDS
Vitamin D deficiency	Vitamin D deficiency
Oesophageal ulceration	Intolerance to bisphosphonates
Erosion or stricture	Intolerance to bisphosphonates
Severe lower GI symptoms	Intolerance to bisphosphonates
Persistent nausea	Intolerance to strontium ranelate
Persistent diarrhoea	Intolerance to strontium ranelate

APPENDIX 7: INTERVIEW QUESTIONS

'From a public health perspective, what are the challenges regarding osteoporosis?'

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1 Do you think that the population has sufficient knowledge about the disease and the risk factors?

Is there enough information provided about the disease?

Do you think that the community pharmacy is providing enough information? Is this done actively or passively through e.g. leaflets? Would more information encourage more people to refer themselves to a doctor for diagnosis?

For better treatment of those already diagnosed, do you think an assessment of patients' knowledge would help to improve the outcomes of treatment?

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2 Do you think that there is enough awareness of the disease in the population?

Is it already the subject of public health awareness campaigns?

What can the public do for themselves to identify their vulnerability to the disease?

Might it be worth it to mount a mass public health campaign like the one for smoking? Or to develop a special service for osteoporosis?

If yes, what do you think pharmacists have to offer in such a campaign/service?

Is there already such a service?

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3 Do you think pharmacists are aware enough of the risk of osteoporosis to e.g. advise a patient who has been prescribed long-term oral steroid therapy that he/she should be considered for bisphosphonate therapy?

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4 How are people without diagnosis diagnosed?

What do you think about the FRAX®? Do you use it? Do you think it is a helpful tool to identify candidates for primary prevention? Do you think it might be feasible to use it in community pharmacies for access to the public on a large scale?

5 Pharmacists provide dietary and smoking advice in general.

Do you think they focus sufficiently on the connection between diet, smoking, exercise etc and osteoporosis?

Do you think they currently give health education and health recommendations relevant to osteoporosis?

6 As the instructions for use of e.g. bisphosphonates are complicated but should be complied with, there is a recognised need to support medicines compliance for osteoporosis therapy.

Do you think general medical practitioners provide sufficient help to target the problem of compliance in osteoporosis treatment?

Do you think community pharmacists provide sufficient help to target the problem of compliance in osteoporosis treatment?

Do you think they are aware enough of e.g. patients not taking the prescribed calcium? If no, might it be useful and feasible to create a standard procedure for patients receiving osteoporosis treatment in order to increase the numbers of compliant patients?

7 Falls in elderly people with osteoporosis are a major health problem and the effect of

concomitant medicines taken by a patient can increase the risk of falling.

Do you think that community pharmacists can help to reduce the risk of falling by systematically reviewing a patient's medication?

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8 Do you think patients are aware of programmes such as the Home Falls Prevention Programme (HFPP) and local support groups?

Do you think pharmacists give enough information about how to access these programmes and support groups?

Do you think pharmacists themselves are sufficiently aware and active in these programmes?

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9 Is adherence to clinical guidelines in osteoporosis treatment an important problem in your view?

For patients diagnosed with osteoporosis and just started on bisphosphonate treatment

a. Is there a follow up service through community pharmacies to monitor adherence to the guidelines?

b. Is there a follow up service through community pharmacies to monitor patient compliance?

10

Do you think that there is a need for more collaboration between general practitioners and community pharmacists?

If yes, can you give any specific examples?

Do you have any further comments?

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