Université de Montréal

Centre de santé et de services sociaux de Laval

Cité de la Santé de Laval
1755, boul. René-Laennec
Laval (Québec)
H7M 3L9

Équipe de recherche en soins de première ligne

Effectiveness of interventions to improve the detection and treatment of osteoporosis in primary care settings – A systematic review and meta-analysis

Marie-Claude Laliberté[1, 2], Sylvie Perreault[1, 3], Beverley J. Shea[4], Lyne Lalonde[1, 2, 5]

[1]Faculty of Pharmacy, University of Montreal, Quebec, Canada; [2]Research Team in Primary Care, Centre de santé et de services sociaux de Laval, Quebec, Canada; [3]Sanofi aventis Endowment Chair in Drug Utilization, Faculty of Pharmacy, University of Montreal, Quebec, Canada; [4]Community Information and Epidemiological Technologies, Institute of Population Health, Ontario, Canada; [5]Sanofi aventis Endowment Chair in Ambulatory Pharmaceutical Care, Faculty of Pharmacy, University of Montreal, Quebec, Canada

Contact person:

Marie-Claude Laliberté
University of Montreal, Faculty of Pharmacy
C.P. 6128, succursale Centre-ville
Montreal, Quebec, H3C 3J7, Canada
Telephone: (514) 343-6111, ext. 2598
Fax: (514) 343-6120
E-mail: marie-claude.laliberte@umontreal.ca

BACKGROUND

List of abbreviations	
BMD:	Bone mineral density
BSD:	Bone-specific drug
CBA:	Controlled before and after study
CCT:	Controlled clinical trial
CI:	Confidence interval
DXA:	Dual-energy x-ray absorptiometry
EPOC:	Effective Practice and Organisation of Care group
HRT:	Hormone replacement therapy
ICC:	Intra-class correlation coefficient
ITS:	Interrupted time-serie
RCT:	Randomized controlled trial
RR :	Relative risk

Osteoporosis is a major health problem affecting 75 million people in Europe, the United States and Japan [1]. In Canada and the United States, one in four women and one in eight men over the age of 50 have osteoporosis; the proportion rises to one in two for women aged 75 years and older [2, 3]. This disease is characterized by low bone mass and deterioration of bone tissue, and leads to increased bone fragility and risk of fracture, particularly of the hip, spine, and wrist [2]. In the United States and Europe alone, osteoporosis causes approximately 2.3 million fractures annually [1]. These fractures frequently result in reduced or lost mobility; decreased independence, which often leads to placement in a nursing home; and increased mortality, especially from hip fractures [4]. The annual direct costs of treating osteoporosis and its consequences are estimated at $19 billion in the United States and $1.3 billion in Canada [2, 5]. As life expectancy increases and the population demography changes, osteoporosis-related fractures are expected to double during the next half-century, at a staggering cost increment [1].

The prevention and treatment of osteoporosis through a healthy lifestyle and pharmacotherapy have proven to be efficacious, and clinical-practice guidelines are available [6-11]. Canadian and American guidelines call for all women aged 65 years and older and for men and women over 50 with at least one major risk factor for osteoporosis (previous fragility fracture, oral glucocorticoid therapy for >3 months, family history of osteoporosis, malabsorption syndrome, primary hyperparathyroidism, low bone density, hypogonadism, or early menopause) to undergo bone mineral density (BMD) testing by central dual-energy x-ray absorptiometry (DXA). Some organizations also recommend considering screening in all men 70 years or older. Pharmacotherapy is recommended for individuals at high risk of fracture, i.e. those having low BMD, those receiving or planning to receive a daily dose of prednisone at >7.5 mg or equivalent for more than three months, and those with a previous fragility fracture. Available pharmacological treatments include bisphosphonates (alendronate, risedronate, ibandronate, and zoledronic acid), raloxifene, calcitonin, and teriparatide. Bisphosphonates and teriparatide should be considered to decrease the risk of vertebral, non-vertebral and hip fractures, while raloxifene and calcitonin should be considered to decrease the risk of vertebral fractures. Hormone replacement therapy (HRT) has shown moderate effectiveness regarding the risk of vertebral, non-vertebral and hip fractures but is solely recommended to symptomatic postmenopausal women due to its risk profile. In addition to pharmacologic therapy, supplementation with calcium (1500 mg/day) and vitamin-D (800 IU/day) is recommended as mandatory adjunct therapy.

Still, Canadian [12-14] and international [15, 16] studies have consistently shown that osteoporosis is under-detected and under-treated, even for high-risk patients. A review of four Canadian studies revealed that in patients aged 40 years or older who sustained a fragility fracture, osteoporosis screening or diagnosis ranged from 1.7% to 50% of them; pharmacotherapy was prescribed to only 5.2% to 37.5% of them; and 2.8% to 61.6% took calcium/vitamin-D supplements [12]. Similar results have been found in a systematic review of 35 studies from 10 different countries performed in the same population of patients as the Canadian review, where osteoporosis screening ranged from 1% to 32%; osteoporosis diagnosis ranged from 1% to 45%; pharmacotherapy prescription varied from 1% to 65%; and 2% to 62% of patients reported calcium/vitamin-D supplements, depending on the study [15]. These findings clearly show the need for effective strategies for improving the application of osteoporosis clinical-practice guidelines.

In an attempt to overcome the care gap in the detection and management of osteoporosis, numerous randomized controlled trials (RCTs) have evaluated knowledge transfer interventions aiming at improving the detection and treatment of osteoporosis [17-26]. These interventions have included electronic reminders to physicians [17, 23], physician academic detailing [18, 20], physician audit and feedback [19], patient-specific education and mailings [21], automated phone calls to patients [20], prompts alerting physicians after fragility fractures [26], help with scheduling BMD tests [22], or combinations of these strategies [17, 18, 20, 22, 26]. Most trials have been conducted in physicians' offices [17, 19, 20, 22, 23, 26], while two were conducted in community pharmacies [24, 25]. These studies have shown mixed results: some trials found relatively large intervention effects [22, 26], some observed modest results [17, 20, 23-25], while others found no effect [18, 19, 21]. The production of a systematic review regarding the effectiveness of these interventions might therefore provide some insight on the most effective strategies to be adopted.

A systematic review on the effectiveness of clinical decision support tools for osteoporosis disease management has been previously published by Kastner and Straus in 2008 [27]. This review concluded that multi-component tools that are targeted to physicians and patients may be effective for supporting clinical decision making in osteoporosis disease management. However, the search performed in this review was limited to RCTs published from 1966 to 2006, therefore excluding a substantial number of studies on osteoporosis interventions published in 2007 through 2009. Moreover, this review assessed the effectiveness of osteoporosis management tools in men and women who had established osteoporosis (with a confirmatory diagnostic of osteoporosis or an existing or previous fragility fracture), as opposed to patients at risk for osteoporosis in whom osteoporosis screening is indicated, a population in which osteoporosis interventions may be best put to value in preventing or delaying the apparition of the disease and its consequences. For these reasons, we believe that the production of an updated systematic review targeting patients at risk or at high risk for osteoporosis and candidates for osteoporosis screening or treatment is highly relevant.

We are therefore proposing to conduct a systematic review and meta-analysis to assess the impact of interventions aiming at improving the detection and treatment of osteoporosis in primary care on the incidence of BMD testing, osteoporosis-treatment initiation and fractures in patients in whom osteoporosis screening or treatment is indicated according to published guidelines.

OBJECTIVES

Primary objectives:

1. To determine the effectiveness of interventions aiming at improving the detection and treatment of osteoporosis in primary care in patients **at risk** for osteoporosis in whom osteoporosis **screening** is indicated (women aged ≥65 years, men aged ≥70 and men/women over 50 with at least one major risk factor for osteoporosis; without previous BMD testing; and without osteoporosis treatment), regarding:
   a) the incidence of BMD testing;
   b) the incidence of osteoporosis-treatment initiation; and
   c) the incidence of fractures.

2. To determine the effectiveness of interventions aiming at improving the detection and treatment of osteoporosis in primary care in patients **at high risk** for osteoporosis in whom osteoporosis **treatment** is indicated (men/women of any age with a previous fragility fracture or with oral glucocorticoid therapy for >3 months; and without osteoporosis treatment), regarding:

a) the incidence of BMD testing;

b) the incidence of osteoporosis-treatment initiation; and

c) the incidence of fractures.

Secondary objective:

Identify the characteristics of interventions aiming at improving the detection and treatment of osteoporosis (e.g. population(s) targeted by the intervention, intensity of the intervention) associated with a higher risk of:

a) BMD testing; and

b) osteoporosis-treatment initiation.

METHODS

Criteria for considering studies for this review

Types of studies

Randomized controlled trials (RCTs) (patient-randomized trials and cluster-randomized trials), controlled clinical trials (CCTs) or quasi-randomized trials, controlled before and after studies (CBAs), and interrupted time-series (ITS) studies will be considered for this review. According to the Cochrane Effective Practice and Organisation of Care (EPOC) Group definition of study designs (see http://www.epoc.cochrane.org/en/handsearchers.html), RCTs are defined as trials in which the participants (or other units) are assigned prospectively to study groups using a process of random allocation (e.g. random number generation, coin flip). CCTs are defined as trials in which participants (or other units) are either (1) assigned prospectively to study groups using a quasi-random allocation method (e.g. alternation, date of birth, patient identifier) (also called quasi-randomized trials) or (2) *possibly* assigned prospectively using a process of random or quasi-random allocation. CBA studies are defined as studies in which observations are made before and after the implementation of an intervention, both in a group that receives the intervention and in a comparable control group that does not [28]. ITS studies are defined as studies reporting outcomes in at least 3 time points in the pre-intervention period and in at least 3 time points in the post-intervention period [28].

Types of participants

To be eligible for inclusion in the review, studies will have to evaluate an intervention aiming at improving the detection and treatment of osteoporosis on a population of patients:

1) **at risk** for osteoporosis, including:
   - women aged ≥65 years; or
   - men aged ≥70 years; or
   - men or women aged ≥50 years with at least one major risk factor for osteoporosis (family history of osteoporosis, malabsorption syndrome, primary hyperparathyroidism, hypogonadism, or early menopause);
   - with no previous BMD testing; and
   - with no current osteoporosis treatment

2) or **at high risk** for osteoporosis, including:
   - men or women of any age receiving a daily dose of >7.5 mg prednisone or equivalent for more than 3 months; or
   - men or women of any age with a previous fragility fracture;
   - with no current osteoporosis treatment.

The population of patients of interest corresponds to patients at risk for osteoporosis in whom osteoporosis screening or treatment is indicated according to published guidelines [6-11].

Moreover, interventions of interest will have to take place in a primary care setting, and must therefore involve or target either primary care physicians, at-risk or high-risk patients, primary care nurses, community pharmacists, or a combination of these types of populations. Interventions targeting specialists (e.g. rheumatologists, orthopedic surgeons) and inpatient interventions will not be included, unless a component of the intervention involves primary care physicians. Interventions targeting nursing home patients will not be included.

Types of interventions

Interventions of interest are interventions aiming at improving the detection and treatment of osteoporosis. Examples of such interventions include educational lectures or meetings, training workshops, educational outreach visits, written educational material, peer education, audit and feedback, telephone calls, computer aided decision support (such as electronic prompts or reminders), web-based educational programs (e-learning), list of at-risk patients, patient risk assessment, and patient mediated interventions. Interventions of interest will have to be specific to osteoporosis, and not be a component of a general intervention on chronic diseases (e.g. a general educational program on chronic diseases for patients with asthma, osteoporosis, diabetes or kidney disease). As we predict a great variation of interventions in their format (e.g. electronic-, paper-, or program-based), intensity, and duration, we do not limit any of these aspects. Studies evaluating the efficacy of specific medications for osteoporosis (e.g. bisphosphonates), studies of exercise/physical activity programs, and studies assessing interventions aiming at improving the adherence to osteoporosis treatment will be excluded. Fall prevention interventions will also be excluded, unless a component of the intervention involves the improvement of the detection and treatment of osteoporosis.

The comparison group may receive either usual care (or no intervention), or a control intervention on another topic than osteoporosis (e.g. educational lecture on cholesterol management). A comparison group receiving usual care as well as printed material on osteoporosis will be considered as an "usual care" group. Finally, the duration of patient's follow-up is limited to a minimum of three months following the intervention, which represents the minimal duration needed to capture patients starting osteoporosis medications [24].

Types of outcomes

Primary outcomes to be measured at the longest follow up time point are:

1. The number and proportion of individuals having received a BMD test by central DXA in each study group;
2. The number and proportion of individuals having initiated osteoporosis pharmacotherapy with a bone-specific drug (BSD, namely a bisphosphonate, raloxifen, calcitonin or teriparatide) or HRT in each study group;
3. The number and proportion of individuals having initiated calcium/vitamin-D supplements in each study group;

4. The number and proportion of individuals having received a BMD test and/or having initiated osteoporosis pharmacotherapy with a BSD or HRT (composite endpoint) in each study group, when available; and
5. The number and proportion of individuals having experienced a fragility fracture in each study group.

Because interventions of interest are not associated with any adverse effects, no such effects will be considered. Reported outcomes will not be considered as eligibility criteria for inclusion in the systematic review, i.e. a study not reporting any outcome of interest will not be excluded from the review, but will not take part in the meta-analysis.

Search methods for identification of studies

Published and unpublished studies written in English or French will be considered. Studies published (or conducted if not published) between 1985 (the year in which the first guidelines regarding the use of HRT in post-menopausal women for the prevention of osteoporosis were published [29]) and 2009 will be included. Abstracts of eligible studies for which no full-text report is available will also be included in the review, although these publications will not take part in the main data analysis because of the expected scarce data available.

Electronic searches

The following electronic databases will be searched: MEDLINE (1950-2009), EMBASE (1980-2009), PsycINFO (1967-2009), ERIC (1965-2009), All EBM Reviews (which includes the Cochrane Database of Systematic Reviews, ACP Journal Club, the Database of Abstracts of Reviews of Effects (DARE), the Health Technology Assessment (HTA) database, the National Health Service Economic Evaluation database, and the Cochrane Methodology Register database), CENTRAL (1991-2009), CINAHL (1981-2009) and Current Contents (1993-2009). These databases will be searched using a strategy incorporating selected MeSH terms and free text terms combined with the methodological component of the EPOC search strategy (see http://www.epoc.cochrane.org/en/newPage1.html). The MEDLINE search strategy (see **Appendix I**) will be translated into the other databases using the appropriate controlled vocabulary as applicable. Search strategies will be performed with the assistance of an experienced librarian and will be adapted for each database used. All search strategies will be peer-reviewed by a second experienced librarian.

Grey literature

This systematic review will not be restricted to published studies. Websites of the following clinical trial registries will be searched for relevant studies: the CenterWatch Clinical Trials Listing Service, the Current Controlled Trials International Standard Randomised Controlled Trial Number (ISRCTN) Register and *meta*Register of Controlled Trials (*m*RCT), and the World Health Organization (WHO) International Clinical Trials Registry Platform Search Portal (includes ClinicalTrials.gov, the Australian and New Zealand Clinical Trials Registry, the Chinese Clinical Trial Register, the Clinical Trials Registry – India, the German Clinical Trials Register, the Iranian Registry of Clinical Trials, the Current Controlled Trials ISRCTN register, the Japan Primary Registries Network, the Netherlands National Trial Register, the Pan African Clinical Trial Registry, and the Sri Lanka Clinical Trials Registry). The online databases Turning Research Into Practice (TRIP) database and Digital Dissertations (ProQuest) will also be searched. In addition, the Canadian Institutes of Health Research (CIHR) website and the National Institutes of Health (NIH) Research Portfolio Online Reporting Tool (RePORT) will be searched for relevant studies. Finally, proceedings of the International Osteoporosis Foundation's (IOF)

World Conference on Osteoporosis from 2000 to 2008 will be searched (as published in Osteoporosis International).

Reference lists

The reference lists of included articles and relevant reviews will be screened for further potentially eligible studies.

Correspondence

A comprehensive list of relevant articles along with the inclusion criteria for the review will be sent to the first authors of included studies, asking if they know of any additional studies (published or unpublished) that might be relevant for the review. Moreover, contact authors of potentially relevant studies for which no article was published will be contacted.

Data collection and analysis

Selection of studies

Titles and abstracts of all retrieved studies will be screened to remove obviously irrelevant reports by two independent assessors (MCL, Ph.D. student, and Ghaya Jouini, M.Sc. student). Thereafter, full text copies of potentially relevant studies will be similarly screened by two independent assessors (MCL and other reviewers to be determined) against the prespecified eligibility criteria using a standardized eligibility evaluation form (see **Appendix II**). Multiple reports of the same study will be identified and linked together. Eligibility criteria will be assessed in the following order: type of intervention, study design, type of participants, duration of minimal patient's follow-up, and type of comparator; the first "no" response will be used as the primary reason for exclusion of the study. To ensure that the selection criteria are applied consistently, eligibility criteria will be tested on two potentially relevant articles beforehand. Assessors will not be blind to any information included in retrieved studies and disagreements will be resolved by discussion in order to reach consensus. If the disagreement persists, arbitration will be made by either Dr. Lyne Lalonde or Dr. Sylvie Perreault (Ph.D. directors). The reason for exclusion will be documented for each excluded study. Authors of ongoing studies for which the report is incomplete (i.e. with missing information) will be contacted to know whether their study fulfills all eligibility criteria for this review.

Data extraction and management

For each included study, two independent assessors (MCL and Ghaya Jouini) will extract data independently using a standardized data extraction form based on the EPOC data collection sheet (available at http://www.epoc.cochrane.org/en/_handsearchers.html), which will be piloted on two included studies for formal use. Any disagreements will be resolved by discussion; if the disagreement persists, arbitration will be made by a third assessor (Dr. Lyne Lalonde or Dr. Sylvie Perreault).

The following characteristics and data will be extracted from each included study: study design, country where the study was done, unit of allocation, sequence generation method, allocation sequence concealment, blinding, possibility of contamination, unit of analysis, intent-to-treat analysis, possibility of unit-of-analysis error (if relevant), study population, participants' inclusion and exclusion criteria, gender of included patients, type of participants involved in interventions, duration of maximal follow-up, data collection methods, content of interventions, format/medium of interventions, duration of interventions, elements of the Chronic Care Model [30] involved in the intervention, details of control intervention (if relevant), total number of patients and professionals that entered the study, were

randomized and were included in analyses in each study group, number and proportion of patients having experienced each outcome of interest in each study group, effect sizes with confidence intervals (CIs) and/or p-value reported for each comparison regarding outcomes of interest, reported intra-class correlation coefficients (ICC) (in cluster RCTs), possibility of other risks of bias, and funding source. The data extraction form is presented in **Appendix III**.

Authors will be contacted for missing information or clarification if needed. Data from multiple reports of the same study will be extracted in one data extraction form.

Assessment of risk of bias in included studies

Data extractors will assess the risk of bias in eligible studies using the standardized form developed for data extraction (**Appendix III**), which integrates a risk of bias assessment form adapted from the Cochrane Collaboration's risk of bias assessment tool [28] and the EPOC quality checklist (available at http://www.epoc.cochrane.org/en/handsearchers.html). The domains addressed in the risk of bias assessment tool are: sequence generation, allocation concealment, completeness of follow-up, blinding, similarity of study groups regarding baseline outcome measurements, reliability of outcome measurement, possibility of contamination, possibility of unit-of-analysis error (for cluster RCTs), similarity of study participants' baseline characteristics, and incomplete outcome data. As in data extraction, inconsistencies will be resolved by discussion in order to reach consensus. If the disagreement persists, arbitration will be made by a third assessor. Assessors will not be blind to any information included in retrieved studies.

Assessment of reporting biases

The risk of publication bias will be explored by the production of funnel plots, plotting interventions' effect estimates from individual studies (on a logarithmic scale) against the standard error of these interventions' effect estimates, which represent a measure of studies' precision. In the absence of bias the plot should approximately resemble a symmetrical inverted funnel, and the more pronounced the asymmetry in the funnel, the more likely it is that the amount of bias will be substantial [28]. These funnel plots will integrate "contour" lines corresponding to different thresholds of statistical significance of each study results (e.g. $0.1>p>0.05$, $0.05>p>0.01$, $p<0.01$). If studies appear to be missing in areas of statistical non-significance, this will add credence to the possibility that the funnel plot's asymmetry is due to publication bias, and, conversely, if the supposed missing studies are in the areas of higher statistical significance, this would suggest the cause of the asymmetry may be more likely to be due to factors other than publication bias (e.g. inadequate analysis, heterogeneity in interventions' intensity) [28]. Such plots will be graphed in homogeneous categories of interventions (e.g interventions involving high-risk patients). Moreover, the results of published trials will be compared to those of all trials, i.e. when both published and unpublished trials are analyzed.

Data synthesis

A flow chart showing the progress of inclusion and exclusion of studies through the stages of the meta-analysis including the number of potentially relevant studies identified through electronic database searching and through other sources, the number of potentially relevant studies retrieved for more detailed evaluation and screened, the number of full-text articles assessed for eligibility, the number of studies included in the systematic review, the number of studies included in the meta-analysis, and the number of studies excluded at each stage, with reasons for exclusion, will be presented.

The primary analysis will be restricted to studies at low risk of bias, i.e. studies for which assessors have answered "Yes" to all risk of bias assessment questions. Analyses will be stratified according to type of patients (patients at high risk for osteoporosis and fractures vs. non- high-risk patients) and will be

performed by intention-to-treat, whenever possible. In studies having more than one intervention group, the one with the most intensive intervention (with the most intervention components) will be chosen in order to ensure the independency of pooled effect size estimates.

For each included study, the absolute change from baseline will be calculated with 95% confidence limits regarding outcomes of interest. The relative risk (RR) regarding the probability of each outcome of interest with the corresponding 95% CIs will also be computed in included studies. In studies with a cluster RCT design, crude data regarding each outcome will be adjusted for the design effect as assessed by the following formula: 1+(M-1)ICC, where M is the average size of each cluster and ICC is the intra-class correlation coefficient. If the ICC is not reported in the paper, authors will be contacted. In the cases where the ICC will be left unknown, an ICC of 0.01 will be used and sensitivity analyses will be performed in order to explore the impact of varying values (0.05, 0.10, 0.15 and 0.2). In a previous cluster cohort study, an ICC of 0.01 and 0.03 was observed regarding the incidence of BMD tests and the incidence of osteoporosis-treatment initiation, respectively, in patients at-risk for osteoporosis and fractures following an osteoporosis training workshop offered to family physicians [31].

The presence of heterogeneity within studies targeting similar types of patients (high-risk patients vs. non- high-risk patients) will be assessed using the Q and I^2 statistics. In groups of studies without substantial heterogeneity (with a I^2 statistic less than 50%), meta-analysis will be performed. Meta-analysis will not be done in groups of studies with substantial heterogeneity (with a I^2 statistic over 50%). Sources of heterogeneity will be explored by examining the following individual study characteristics in sub-analyses: 1) participants involved in interventions (e.g. patients only, primary care physicians and patients); 2) study design (e.g. patient RCTs vs. cluster RCTs); and 3) number of components (e.g. one component vs. multiple components). If between-study inconsistency is felt to be too great to meaningfully pool results quantitatively, the results will be reported descriptively.

In sub-groups of homogenous studies, pooled RRs regarding the probability of each outcome of interest with the corresponding 95% CIs will be computed using a random-effects model. Because of the expected diversity of the interventions, it may not be possible to pool the results of individual studies.

Finally, if enough studies are included, the impact of the following characteristics of interventions of interest on the summary estimates of effects will be investigated using meta-regression (moderator analysis): population(s) involved in the intervention (e.g. primary care physicians, patients, community pharmacists), number of components in interventions, duration of interventions, number of elements of the Chronic Care Model [30] involved in the intervention, format/medium of interventions (e.g. paper, electronic), and gender of targeted patients. This statistical method is similar to multiple regression analysis, with the outcome variable being the effect estimate and the explanatory variables being characteristics of studies that might influence the size of intervention effect. Characteristics deemed significant at $p < 0.20$ in a bivariate model will be included in a multivariate model. A backward-selection procedure will thereafter be carried out, and characteristics meeting the 0.10 significance level will be included in the final model. Because at least 10 studies are required for every moderator (intervention characteristics) in the analysis, it may not be possible to undertake meta-regression analyses.

The statistical analyses will be carried out using RevMan 5 (Cochrane software), while meta-regression analyses will be performed using SPSS.

Sensitivity analysis

In order to assess the influence of restricting the primary analysis to studies at low risk of bias, sensitivity analyses including studies at "high" or "unclear" risk of bias, i.e. studies having the answer "No" or "Unclear" in some risk of bias assessment questions, will be performed. Moreover, sensitivity analyses

will be performed with ICC values of 0.05, 0.10, 0.15 and 0.20 in the cases where the ICC will be left unknown, in order to explore the impact of the ICC value decision on the reviews' conclusions.

POTENTIAL CONFLICTS OF INTEREST

There is no conflict of interest to declare regarding this review.

REFERENCES

1. European Foundation for Osteoporosis and the National Osteoporosis Foundation. Who are candidates for prevention and treatment for osteoporosis? Osteoporos Int 1997; 7(1):1-6
2. Osteoporosis Canada. About osteoporosis: What is osteoporosis? Available from: http://www.osteoporosis.ca/english/About%20Osteoporosis/what-is/default.asp?s=1. Accessed 11 Aug 2008
3. Gordon M, Huang J (1995) Monograph Series on Aging-related Diseases: VI. Osteoporosis. Chronic Diseases in Canada 16 (1). Available from: http://www.phac-aspc.gc.ca/publicat/cdic-mcc/16-1/a_e.html. Accessed 11 Aug 2008
4. Lorrain J, Paiement G, Chevrier N et al. Population demographics and socioeconomic impact of osteoporotic fractures in Canada. Menopause 2003; 10(3):228-34
5. National Osteoporosis Foundation. Fast facts on osteoporosis. Available from: http://www.nof.org/osteoporosis/diseasefacts.htm. Accessed 11 Aug 2008
6. Brown JP, Josse RG. 2002 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada. CMAJ 2002; 167(10 Suppl):S1-34
7. Cheung AM, Feig DS, Kapral M et al. Prevention of osteoporosis and osteoporotic fractures in postmenopausal women: recommendation statement from the Canadian Task Force on Preventive Health Care. CMAJ 2004; 170(11):1665-7
8. Hodgson SF, Watts NB, Bilezikian JP et al. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the prevention and treatment of postmenopausal osteoporosis: 2001 edition, with selected updates for 2003. Endocr Pract 2003; 9(6):544-64
9. American College of Rheumatology Ad Hoc Committee on Glucocorticoid-Induced Osteoporosis. Recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis: 2001 update. Arthritis Rheum 2001; 44(7):1496-503
10. National Osteoporosis Foundation. Clinician's guide to prevention and treatment of osteoporosis. Available from: http://www.nof.org/professionals/Clinicians_Guide.htm. Accessed 8 July 2009
11. U.S. Preventive Services Task Force. Screening for osteoporosis in postmenopausal women: recommendations and rationale. Ann Intern Med 2002; 137(6):526-8
12. Papaioannou A, Giangregorio L, Kvern B et al. The osteoporosis care gap in Canada. BMC Musculoskelet Disord 2004; 5:11
13. Perreault S, Dragomir A, Desgagne A et al. Trends and determinants of antiresorptive drug use for osteoporosis among elderly women. Pharmacoepidemiol Drug Saf 2005; 14(10):685-95
14. Bessette L, Ste-Marie LG, Jean S et al. The care gap in diagnosis and treatment of women with a fragility fracture. Osteoporos Int 2008; 19(1):79-86
15. Giangregorio L, Papaioannou A, Cranney A et al. Fragility fractures and the osteoporosis care gap: an international phenomenon. Semin Arthritis Rheum 2006; 35(5):293-305
16. Elliot-Gibson V, Bogoch ER, Jamal SA et al. Practice patterns in the diagnosis and treatment of osteoporosis after a fragility fracture: a systematic review. Osteoporos Int 2004; 15(10):767-78
17. Lafata JE, Kolk D, Peterson EL et al. Improving osteoporosis screening: Results from a randomized cluster trial. J Gen Intern Med 2007; 22(3):346-51
18. Solomon DH, Katz JN, Finkelstein JS et al. Osteoporosis improvement: a large-scale randomized controlled trial of patient and primary care physician education. J Bone Miner Res 2007; 22(11):1808-15
19. Curtis JR, Westfall AO, Allison J et al. Challenges in improving the quality of osteoporosis care for long-term glucocorticoid users: a prospective randomized trial. Arch Intern Med 2007; 167(6):591-6

20. Solomon DH, Polinski JM, Stedman M et al. Improving care of patients at-risk for osteoporosis: A randomized controlled trial. J Gen Intern Med 2007; 22(3):362-7
21. Solomon DH, Finkelstein JS, Polinski JM et al. A randomized controlled trial of mailed osteoporosis education to older adults. Osteoporos Int 2006; 17(5):760-7
22. Majumdar SR, Beaupre LA, Harley CH et al. Use of a case manager to improve osteoporosis treatment after hip fracture: Results of a randomized controlled trial. Arch Intern Med 2007; 167(19):2110-5
23. Feldstein A, Elmer PJ, Smith DH et al. Electronic medical record reminder improves osteoporosis management after a fracture: A randomized, controlled trial. J Am Geriatr Soc 2006; 54(3):450-7
24. Yuksel N, Majumdar SR, Biggs C et al. Community pharmacist-initiated screening program for osteoporosis: randomized controlled trial. Osteoporos Int 2009; [Epub 2009 Jun 5]
25. McDonough RP, Doucette WR, Kumbera P et al. An evaluation of managing and educating patients on the risk of glucocorticoid-induced osteoporosis. Value Health 2005; 8(1):24-31
26. Davis JC, Guy P, Ashe MC et al. HipWatch: osteoporosis investigation and treatment after a hip fracture: a 6-month randomized controlled trial. J Gerontol A Biol Sci Med Sci 2007; 62(8):888-91
27. Kastner M, Straus SE. Clinical decision support tools for osteoporosis disease management: a systematic review of randomized controlled trials. J Gen Intern Med 2008; 23(12):2095-105
28. Higgins JPT, Green S, Cochrane Collaboration (editors). Cochrane handbook for systematic reviews of interventions. Chichester, West Sussex; Mississauga, Ontario: Wiley-Blackwell, 2008.
29. Ladewig PA. Protocol for estrogen replacement therapy in menopausal women. Nurse Pract 1985; 10(10):44-7
30. Bodenheimer T, Wagner EH, Grumbach K. Improving primary care for patients with chronic illness. Jama 2002; 288(14):1775-9
31. Laliberte MC, Perreault S, Dragomir A et al. Impact of a primary care physician workshop on osteoporosis medical practices. Osteoporos Int 2009 [Epub ahead of print]