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REVIEW

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

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Abstract This study aims to evaluate the effectiveness of primary care interventions to improve the detection and treatment of osteoporosis. Eight electronic databases and six gray literature sources were searched. Randomized controlled trials, controlled clinical trials, quasi-randomized trials, controlled before–after studies, and interrupted time series written in English or French from 1985 to 2009 were considered. Eligible studies had to include patients at risk (women ≥65 years, men ≥ 70 years, and men/women ≥50 years with at least one major risk factor for osteoporosis) or at high risk (men/women using oral glucocorticoids or with previous fragility fractures) for osteoporosis and fractures. Outcomes included bone mineral density (BMD) testing, osteoporosis treatment initiation, and fractures. Data were pooled using a random effects model when applicable. Thirteen studies were included. The majority were multifaceted and involved patient educational material, physician notification, and/or physician education. Absolute differences in the incidence of BMD testing ranged from 22% to 51% for high-risk patients only and from 4% to 18% for both at-risk and high-risk patients. Absolute differences in the incidence of osteoporosis treatment initiation ranged from 18% to 29% for high-risk patients only and from 2% to 4% for at-risk and high-risk patients. Pooling the results of six trials showed an increased incidence of osteoporosis treatment initiation (risk difference (RD)=20%; 95% CI: 7–33%) and of BMD testing and/or osteoporosis treatment initiation (RD=40%; 95% CI: 32–48%) for high-risk patients following intervention. Multifaceted interventions targeting high-risk patients and their primary care providers may improve the management of osteoporosis, but improvements are often clinically modest.

Keywords Meta-analysis · Osteoporosis · Prevention · Primary care · Systematic review

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Introduction

Despite the availability of published clinical practice guidelines and evidence of the efficacy of a healthy lifestyle and pharmacotherapy in osteoporosis prevention and treatment [1–6], studies consistently show the disease is underdetected and undertreated, even in high-risk patients [7–9].

In the effort to overcome the care gap in the detection and management of osteoporosis, many studies have used controlled study designs to evaluate interventions aimed at improving osteoporosis detection and treatment [10–26]. Results have been mixed: some studies found relatively large intervention effects [10, 14, 15, 19], some observed modest outcomes [11–13, 17, 18, 20–23], while others found no effect [16, 24–26]. A systematic review focussing on the effectiveness of these interventions may therefore provide some insights into which are the most effective strategies to adopt.

A systematic review conducted in 2008 concluded that multi-component tools targeting both physicians and patients may be effective in supporting clinical decision making in osteoporosis disease management [27]. However, the search performed for the review was limited to randomized controlled trials (RCTs) published from 1966 to 2006, and it thus excluded a substantial number of studies published from 2007 through 2009. Another recent systematic review, which was conducted by Lai et al. [28], observed that osteoporosis interventions by healthcare professionals were associated with improved quality of life, medication compliance, and calcium intake. However, the review found no effect in terms of changes in bone mineral density (BMD), medication persistence, knowledge, or other lifestyle modifications. These reviews assessed the effectiveness of the interventions for patients with established osteoporosis, though—not for people at risk for whom screening is indicated, a population for which osteoporosis interventions might best be put to use to prevent or delay the onset and consequences of the disease. An updated systematic review of interventions targeting patients at risk or at high risk for osteoporosis and fractures and candidates for osteoporosis screening or treatment thus seems to be very much in order.

The objective of this study was to assess the effectiveness of interventions aiming at improving the detection and treatment of osteoporosis in primary care regarding the incidence of BMD testing, osteoporosis treatment initiation and fractures in patients at risk and at high risk in whom osteoporosis screening or treatment is indicated under Canadian and American guidelines [1–6]. To do so, we first systematically reviewed the literature in order to identify studies that evaluate interventions designed specifically to improve osteoporosis detection and treatment in primary care and, second, we quantitatively combined their results, when applicable. More specifically, patients of interest in this review include patients in whom osteoporosis screening is indicated because of the presence of risk factors for osteoporosis and patients in whom osteoporosis treatment is recommended due to a previous fragility fracture or chronic glucocorticoid use. We expected higher incidences of BMD testing and osteoporosis treatment initiation and a lower incidence of fractures following interventions designed to improve osteoporosis detection and treatment.

Methods

Data sources

The study was based on an a priori protocol (available online at http://www.recherchepl.ca/autres-productions-scientifiques.php) which prespecified research objectives, search strategy, study eligibility criteria, and methods of data extraction and statistical analysis. The findings are reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement [29].

Studies were identified by searching 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, the Health Technology Assessment 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). We also searched the gray literature for unpublished and "in progress" studies on websites of clinical trial registries (the CenterWatch Clinical Trials Listing Service, the Current Controlled Trials International Standard Randomised Controlled Trial Number Register and metaRegister of Controlled Trials, and the World Health Organization International Clinical Trials Registry Platform Search Portal), the Turning Research Into Practice database, Digital Dissertations (ProQuest), the Canadian Institutes of Health Research website, the National Institutes of Health Research Portfolio Online Reporting Tool, and the proceedings of the International Osteoporosis Foundation World Conference on Osteoporosis from 2000 to 2008. The reference lists of the articles selected and relevant reviews [27, 30–32] were also screened for further potentially eligible studies, and the corresponding authors of the studies included were contacted.

Search strategy

Electronic databases were searched using strategies incorporating selected MeSH terms and free-text terms combined with the methodological component of the Cochrane Effective Practice and Organisation of Care (EPOC) group search strategy (available at http://epoc.cochrane.org/

specialised-register). The MEDLINE search strategy (see Appendix A) was adapted for the other databases. All search strategies were carried out with the assistance of an experienced librarian and peer reviewed by a second experienced librarian.

Study selection

Studies were included if they were RCTs (patient-randomized trials and cluster-randomized trials), controlled clinical trials or quasi-randomized trials, controlled before-after studies, or interrupted time series studies evaluating interventions aimed at improving the detection and treatment of osteoporosis. Quasi-randomized trials were defined as studies in which participants are assigned prospectively to study groups using a quasi-random allocation method, such as alternation or date of birth. Published and unpublished studies written in English or French were considered. We restricted our search to the years 1985–2009 because, since the first guidelines regarding the use of hormone replacement therapy (HRT) to prevent osteoporosis in post-menopausal women were published in 1985 [33], it is unlikely that quality improvement interventions in osteoporosis were conducted before that date. The duration of patient follow-up was limited to at least 3 months after the intervention, which corresponds to the minimum period needed to capture patients starting osteoporosis medications [18]. Abstracts of eligible studies for which no full-text report is available could also be included in the review, but, given the sparseness of data, these publications could not be considered in the principal data analysis.

Interventions of interest included those specifically designed to improve the detection and treatment of osteoporosis, such as educational lectures or meetings, training workshops, educational outreach visits, written educational material, audit and feedback, computerized decision aid support tools (such as electronic prompts or reminders), lists of at-risk patients, patient-risk assessment, and patient-mediated interventions. Furthermore, eligible interventions had to take place in a primary care setting and involve or target primary care physicians, patients, primary care nurses, community pharmacists, or a combination of these populations. In addition, eligible studies had to compare the intervention group to a comparison group receiving either the usual care or a control intervention on a topic other than osteoporosis (e.g., an educational lecture on cholesterol management). A comparison group receiving printed material on osteoporosis was considered a "usual care" group. Interventions that were a component of a general intervention for chronic diseases were excluded, as were studies evaluating the efficacy of specific medications for osteoporosis (e.g., bisphosphonates), studies on exercise and physical activity programs and studies assessing interventions to improve adherence to osteoporosis treatment. Fall-prevention interventions were also excluded, unless they included a component aimed specifically at the detection and treatment of osteoporosis. Interventions geared to specialists (e.g., rheumatologists, orthopedic surgeons) and inpatient interventions were excluded, unless a component involved primary care physicians. Interventions targeting nursing home patients were not included.

To be eligible for inclusion in the review, studies had to evaluate the intervention in a population of patients either (1) at risk for osteoporosis and fractures, including women aged 65 years or older, men aged 70 years or older, and men/women aged 50 years or older 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 no current osteoporosis treatment; or (2) at high risk for osteoporosis and fractures, including men/women of any age receiving a daily dose of at least 5 mg prednisone or equivalent for more than 3 months or with a previous fragility fracture with no current osteoporosis treatment. This population corresponds to patients for whom osteoporosis screening or treatment is indicated under published Canadian and American guidelines [1–6].

Outcomes of interest included the incidence of BMD testing; osteoporosis treatment initiation with a bisphosphonate, raloxifen, calcitonin, teriparatide, or HRT; initiation of calcium/vitamin D supplements; BMD testing and/or osteoporosis treatment initiation (composite endpoint); and fractures. These outcomes were measured at the longest follow-up time point reported.

Two investigators (MCL and GJ) independently reviewed the titles and abstracts of the studies found. The inclusion and exclusion criteria were then applied independently by six evaluators using a standardized eligibility evaluation form; each potentially relevant article was assessed by two evaluators. Eligibility criteria were assessed in the following order: type of intervention, study design, type of participants, duration of patient follow-up, and type of comparator. The first "no" response served as the primary reason for exclusion. Assessors were not blind to any information, and disagreements were resolved by discussion to reach consensus. Authors of studies for which the report was incomplete (i.e., for which information was missing) were contacted.

Data extraction and risk-of-bias assessment

Data extraction was performed by two independent investigators (MCL and GJ) using a standardized data extraction form. The following characteristics and data were extracted from each study selected: study design, unit of allocation, allocation sequence generation method, allocation sequence concealment method, country, study population, participant

inclusion and exclusion criteria, sex of included patients, description of interventions, format of interventions, duration of interventions, types of participants involved in interventions, description of the control group, duration of follow-up, data collection methods, unit of analysis, intent-to-treat analysis, total number of patients and health professionals entered in the study, randomized (if applicable), lost to follow-up (with reasons) and included in analyses in each study group, number and proportion of patients experiencing each outcome of interest in each study group, crude and adjusted risk ratios and odds ratios with confidence intervals (CIs) and/or *p* value reported for each comparison regarding outcomes of interest, reported intra-class correlation coefficients (ICC; for cluster RCTs), and source of funding. Also documented were any elements of the Chronic Care Model [34] in the intervention. The Chronic Care Model was conceptualized by Wagner. It is a multi-dimensional guide to developing effective chronic care. It centers on six key elements of care, including: (1) self-management support (e.g., self-help or peer support groups, patient education classes, self-management tools such as flowcharts on which patients record their own laboratory results, self-management plans with self-improvement goals); (2) decision support (e.g., reminders based on evidence-based guidelines, continuing medical education, academic detailing); (3) clinical information systems (e.g., creation of computerized registries to increase data accessibility, data sharing between health professionals, data sharing with patients); (4) healthcare organization (e.g., inter-professional collaboration, visit planning for continuous follow-up); (5) community resources and policies (e.g., efficient community programs, increasing collaboration between health professionals and community resources, improving the use of non-medical resources); and (6) delivery system design (e.g., creating practice teams with a clear division of labor, planned visits, training non-physician personnel to support patient self-management, arranging for routine periodic tasks). Disagreements were resolved by discussion or, if they persisted, by arbitration with a third assessor (LL or SP). Data from multiple reports of the same study were extracted on the same data extraction form.

The data extraction form incorporated a risk-of-bias assessment form adapted from the Cochrane Collaboration's risk-of-bias assessment tool [35] and the Cochrane EPOC group quality checklist (available at http://epoc.cochrane.org/epoc-resources-review-authors). The risk of bias was assessed on the basis of the percentage of applicable criteria that were met and addressed allocation sequence generation, allocation sequence concealment, completeness of follow-up, blinding, baseline outcome measurements (health professional performance or patient outcomes prior to the intervention), reliability of outcome measures, possibility of contamination, possibility of unit-of-analysis error (for cluster RCTs), participants' baseline characteristics, incomplete outcome data (likelihood that missing outcome measures could bias the results), and possibility of other risks of bias. The risk-of-bias assessment was conducted at the same time and in the same way as the data extraction.

Data synthesis and analysis

Analyses were stratified according to the type of patients involved in the studies (patients at high risk for osteoporosis and fractures, namely men/women using oral glucocorticoids for ≥3 months or with a previous fragility fracture; at-risk patients, including women aged 65 years or older, men aged 70 years or older, and men/women aged 50 years or older with at least one major risk factor for osteoporosis; or both high-risk and at-risk patients) and were performed by intention to treat. If a study had more than one intervention group, we selected the one with the most intensive intervention (i.e., with the greatest number of components) in order to ensure the independence of the pooled calculations.

For each study included, the risk difference (RD) between intervention and control groups regarding each outcome of interest and the corresponding 95% CIs were computed. In studies with a cluster RCT design, adjustment was made for the design effect: the proportion of patients experiencing each outcome of interest during follow-up in each study group was divided by the design effect, which may be calculated by the formula $1+(M\text{-}1)$ ICC, where M is the average size of each cluster and ICC is the intra-class correlation coefficient [36]. If the ICC was not reported in a paper, the authors were contacted. If the ICC remained unknown, an ICC of 0.01 was assigned, and sensitivity analyses were performed to explore the impact of different values (0.05, 0.10, and 0.15). Our assumptions are reasonable, given that following an osteoporosis workshop for family physicians in a previous cluster cohort study, ICCs of 0.01 and 0.03 were observed for the incidence of BMD testing and the incidence of osteoporosis treatment initiation, respectively, in patients at-risk for osteoporosis and fractures [23].

Sources of heterogeneity were explored by examining the impact of the risk of bias in the study (studies having a proportion of applicable risk-of-bias criteria fulfilled below vs. over the median proportion of applicable criteria fulfilled in all the studies included) and study design (e.g., patient RCTs vs. cluster RCTs) on results in sub-analyses. Heterogeneity within studies targeting similar types of patients (high-risk patients vs. at-risk patients) was assessed with the chi-square (Q statistic) and quantified using the I^2 statistic, which indicates the proportion of variability across studies due to heterogeneity rather than sampling error. In groups of studies without substantial heterogeneity (with a chi-square statistic having a p value>0.10 and an I^2 statistic less than 50%), pooled RDs were calculated using a Mantel–Haenszel random effects model. Statistical analyses were performed using Cochrane

Review Manager 5 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2008).

Results

Our search identified a total of 9,545 citations. They were screened for relevance, and 91 were selected for full-text review (Fig. 1). In all, 16 reports regarding 13 different studies met the inclusion/exclusion criteria and were included in the systematic review [10–18, 37–43]. Studies were excluded for not meeting the criteria for target intervention (five studies), study design (19 studies), patients (37 studies), follow-up duration (one study), and comparator (eight studies; see Appendix B for the complete list of excluded studies with primary reasons of exclusion). A total of 19 studies (12 published and seven ongoing) were excluded because they possibly included patients who already had undergone BMD testing or were already receiving osteoporosis treatment; more specifically, five studies included patients who already had undergone BMD testing [21, 44–47], one study included patients who were already receiving osteoporosis therapy [48], seven studies included patients who already had undergone BMD testing, were already receiving osteoporosis treatment or had an osteoporosis diagnosis [25, 49–54], and six studies did not report whether patients who already had undergone BMD testing or were already receiving osteoporosis treatment were excluded or not [20, 24, 55–58]. Eligibility could not be assessed in five studies because of information missing in the reports we retrieved: for one study, the author did not respond to our messages; three studies lacked contact information for the author; and one study,

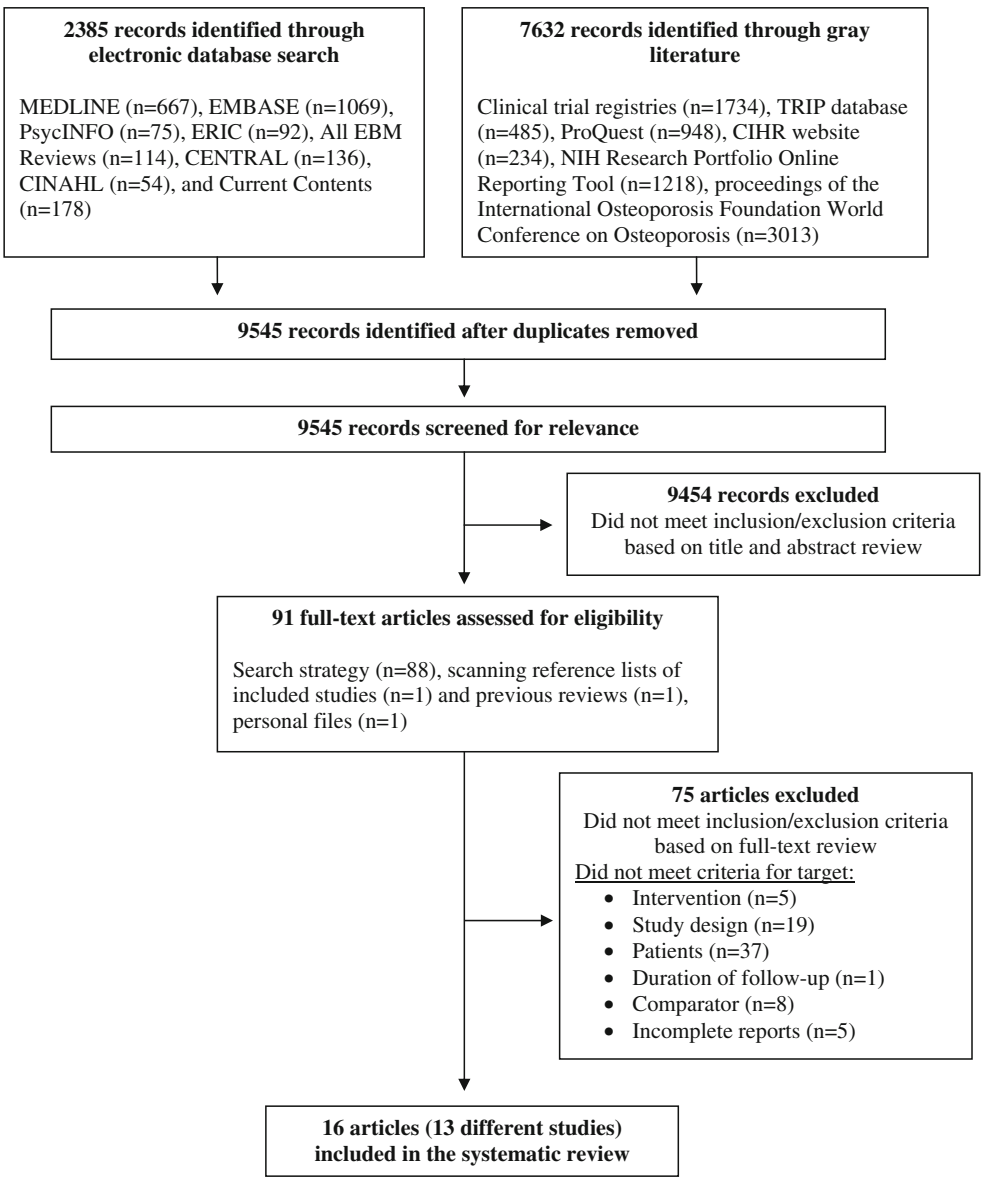


Fig. 1 Study flowchart

according to the investigator contacted, was interrupted because of problematic patient recruitment. Only one screened study was excluded because of ineligible language (Chinese); based on the information in the abstract, the study did not meet the inclusion criteria for target study design and patients.

Study characteristics

The majority of studies selected involved patients at high risk for osteoporosis and fractures (8/13 studies), and most evaluated interventions targeting primary care physicians and their at-risk patients (12/13 studies; Table 1). Three studies used a quasi-randomized design [10, 14, 41], six were patient-randomized trials [12, 15, 18, 37, 38, 42], and four were cluster-randomized trials [11, 13, 16, 17]. Two studies were ongoing [38, 41], and two others were methodological papers describing the study protocol [37, 42].

Interventions included educational material for patients (eight studies) [11–14, 16, 18, 37, 41], physician notification of patients' osteoporosis and fracture risk (eight studies) [10, 11, 14, 15, 18, 37, 38, 41], patient notification of osteoporosis and fracture risk (six studies) [10–13, 17, 41], patient counseling (four studies) [14, 15, 18, 41], electronic medical record (EMR) prompts for physicians (two studies) [12, 13], list of at-risk patients provided to physicians (two studies) [13, 17], physician education by academic detailing (two studies) [16, 17], arrangements for BMD testing and bisphosphonate prescription by the study physician (one study) [15], a risk assessment tool provided to physicians and discussion of the tool with the study coordinator before appointments with at-risk patients (one study) [42], and peripheral BMD testing by quantitative ultrasound performed by the patient's community pharmacist (one study) [18] (Table 1).

Study population also varied across studies: eight studies included both men and women [10, 14–18, 38, 41], and five involved women only [11–13, 37, 42] (Table 1). Most studies included patients with a previous fragility fracture (11 studies) [10–12, 14–18, 37, 38, 41], while others involved patients aged 65 years or older (four studies) [13, 16–18], oral glucocorticoid users (three studies) [16–18], patients with low BMD (one study) [42], a family history of osteoporosis (one study) [18], or early menopause (one study) [18]. Most studies targeted both the primary care physicians and their patients (10 studies) [11–17, 37, 38, 41]. One study involved patients, primary care physicians and community pharmacists [18], and another targeted patients, primary care physicians and orthopedic surgeons [10]. Only one study focused solely on primary care physicians [42].

In terms of the elements of the Chronic Care Model, most studies involved self-management support (10 studies) [10, 11, 13–16, 18, 37, 38, 41] and decision support (10 studies) [11–14, 16–18, 38, 41, 42] (Table 1). Other studies were related to clinical information systems (three studies) [12, 13, 17], delivery system design, and self-management support (one study) [15]. One study involved four domains: self-management support, decision support, clinical information systems, and healthcare organization [13]. Of the four cluster RCTs included in the review, none reported the value of ICCs; three authors provided these data, but one could not be contacted [11]. ICC values provided by the authors for outcomes of interest ranged from 0.02 to 0.04 [13, 16, 17].

Risk-of-bias assessment

Reported study quality was generally good; the median proportion of applicable criteria fulfilled was 73% (range from 30% to 90%), excluding ongoing studies [38, 41] for which much information was missing, and protocol description studies with no follow-up of patients [37, 42] (Tables 2, 3 and 4). None of the studies included in the review compared health professional performance or patient outcomes prior to the intervention (baseline outcome measurements).

Outcomes of interest

Eight studies provided data on outcomes of interest [11–18] (Table 5). Follow-up durations ranged from 4 to 16 months. In seven out of eight studies, the incidence of BMD testing was higher in the intervention group than in the control group; absolute differences ranged from 22% to 51% in studies targeting high-risk patients [11, 12, 14, 15], equalled 18% in the one study involving at-risk patients [13], and varied from 4% to 12% in studies targeting both at-risk and high-risk patients [17, 18]. In five studies, the incidence of osteoporosis treatment initiation was higher in the intervention group than in the usual-care group; absolute differences ranged from 18% to 29% in studies targeting high-risk patients [11, 14, 15] and equalled 4% in the one study involving at-risk patients [13] and 2% in a study targeting both at-risk and high-risk patients [17]. Four studies showed a statistically significant higher incidence of the composite endpoint (undergoing BMD testing and/or initiating osteoporosis treatment following the intervention) as compared to the control group; absolute differences ranged from 37% to 41% in studies targeting high-risk patients [12, 15] and from 4% to 11% in studies targeting at-risk and high-risk patients [17, 18]. Two studies reported statistically non-significant differences for initiation of calcium/vitamin D supplements [11] and fracture incidence [15].

The study showing the highest incidence of osteoporosis-related preventive practices was very intensive, and included arrangements for outpatient BMD tests and a bisphosphonate prescription written by a study physician and dispensed by the local community pharmacy [15]. The observed absolute between-group difference was 51% for BMD testing (80% in the intervention group vs. 29% in the control group; 95% CI: 39–61%), 29% for osteoporosis treatment initiation (51%

Table 1 Characteristics of studies included in the review

Study, country	Study design	Patients	Intervention/control	Components of intervention	Target(s)	Element(s) of the Chronic Care Model involved
Ashe 2004 [10], Canada	Quasi-randomized trial	Men and women aged >50 years with a low-trauma wrist fracture, with no osteoporosis diagnosis and no current osteoporosis treatment (high-risk patients)	Intervention Letter to patients indicating risk of osteoporosis Request to patients to take a letter from the orthopedic surgeon to the family physician alerting him/her to the recent low-trauma fracture Letter faxed to the family physician referring patient back for assessment and management of osteoporosis Follow-up telephone call at 4–6 weeks to remind the patient to visit his/her family physician Control: usual care (no intervention)	Patient notification Physician notification	Primary care physicians, patients, and orthopedic surgeons	Self-management support
Bessette 2008 [37], Canada	Patient RCT	Women aged ≥50 years with a fragility fracture, with no osteoporosis diagnosis and no current osteoporosis treatment (high-risk patients)	Intervention Written educational material on osteoporosis mailed to patients Short letter sent to physicians asking them to consider supplementary investigation and appropriate treatment 15-min educational video on osteoporosis mailed to patients Control: usual care (no intervention)	Physician notification Educational material for patients	Primary care physicians and patients	Self-management support
Cranney 2008 [11], Canada	Cluster RCT (randomization of practices)	Postmenopausal women with a wrist fracture confirmed by X-ray, with no current osteoporosis treatment (except HRT) (high-risk patients)	Intervention Letter mailed to the primary care physician to notify him/her of patient's recent wrist fracture and providing recommendations regarding assessment for osteoporosis treatment Two-page educational tool including a summary of recommended osteoporosis therapies and a treatment algorithm for patients with fragility fractures Reminder letter mailed to patients recommending they schedule a follow-up visit with their primary care physician to discuss osteoporosis One-page checklist of risk factors for fractures to discuss with their physician and educational booklet mailed to patients Control: usual care (no intervention)	Patient notification Physician notification Educational material for patients	Primary care physicians and patients	Self-management support Decision support

Table 1 (continued)

Study, country	Study design	Patients	Intervention/control	Components of intervention	Target(s)	Element(s) of the Chronic Care Model involved
Feldstein 2006 [12], USA	Patient RCT	Women aged 50–89 years with a fracture in 1999, with no BMD testing and no medication for osteoporosis in the 12 months preceding the start of the study (high-risk patients)	Intervention Patient-specific EMR in-basket messages were sent to the primary care provider informing him/her of the patient's risk of osteoporosis, stating the need for evaluation and treatment and listing internal and external guideline resources; a second patient-specific message was sent to primary care providers who had not ordered a BMD or pharmacological osteoporosis treatment for enrolled patients 3 months after the first message; and a copy of the letter sent to the patient was provided to the physician Advisory letter identifying the patient's risk, discussing clinical guideline recommendations and requesting that the patient discuss management options with the provider and educational material sent to patients Control: usual care (no intervention)	Patient notification Educational material for patients EMR prompts for physicians	Primary care physicians and patients	Decision support Clinical information systems
Lafata 2007 [13], USA	Cluster RCT (randomization of primary care clinics)	Women aged 65–89 years, without previous osteoporosis diagnosis, without previous BMD testing and without previous dispensing for an osteoporosis-specific medication (at-risk patients)	Intervention 3 Patient mailings recommending scheduling a visit with their doctor to discuss BMD screening results; each mailing included a letter from the individual's physician and educational information Prompt appearing in the EMR of eligible women Biweekly mailing to physicians sent to coincide with the patient mailings, listing the physician's patients with a T-score ≤−2.0 and indicating that osteoporosis treatment should be considered Control: usual care (no intervention)	Patient notification Educational material for patients EMR prompts for physicians List of at-risk patients for physicians	Primary care physicians and patients Healthcare organization	Self-management support Decision support Clinical information systems
Leslie (ongoing) [38], Canada	Patient RCT	Men and women aged ≥50 years with a hip, spine, humerus, or Colles' fracture, with no BMD testing in the 3 years preceding the start of the study and with no current osteoporosis treatment (high-risk patients)	Intervention Physician and patient notification providing a general recommendation for osteoporosis assessment Control: usual care (no intervention)	Patient notification Physician notification	Primary care physicians and patients	Self-management support Decision support

Majumdar 2004 [14] and Majumdar 2007a [39], Canada	Quasi-randomized trial (allocation by emergency departments)	Men and women aged ≥50 years with a wrist fracture, with no current osteoporosis treatment (high-risk patients)	Intervention Reminder generated for each patient faxed to the primary care physician of record to notify him/her that patient had recently been seen and treated in the emergency department for a wrist fracture and providing evidence-based treatment recommendations endorsed by opinion leaders Tailored, single-page summary of osteoporosis information provided to patients Telephone counseling session with patients within 1 week of the fracture Control: usual care+educational material and telephone counseling regarding fall prevention and home safety	Physician notification Educational material for patients Patient counseling	Primary care physicians and patients	Self-management support Decision support
Majumdar 2007b [15] and Morrish 2009 [40], Canada	Patient RCT	Men and women aged ≥50 years with a hip fracture, with no current osteoporosis treatment (high-risk patients)	Intervention One-on-one counseling provided to patients by the study case manager about the importance of BMD testing and the ability of bisphosphonate therapy and other treatments to reduce the risk of future fractures Outpatient BMD test arrangements by the study case manager Arrangements for local community pharmacies to dispense prescriptions written by a study physician for alendronate (70 mg/week) or risedronate (35 mg/week) for patients with low bone mass who wanted to start pharmacotherapy Results and treatment plans communicated to the primary care physician of record Control: usual care+counseling about fall prevention and the need for additional intake of calcium and vitamin D+educational material about osteoporosis+patients were asked to discuss with their primary care physician	Physician notification Patient counseling Arrangements for BMD testing Arrangements for bisphosphonate prescription	Primary care physicians and patients	Self-management support Delivery system design
Majumdar (ongoing) [41], Canada	Quasi-randomized trial (allocation by emergency departments)	Men and women aged ≥60 years with a chest radiograph reporting the presence of a vertebral fracture and discharged home, with no current osteoporosis treatment (high-risk patients)	Intervention Reminders and opinion-leader-generated guidelines provided to family physicians when a chest X-ray reporting the presence of a vertebral fracture is performed in the emergency department Educational leaflets and counseling provided to patients Control: usual care (no intervention)	Physician notification Educational material for patients Patient counseling	Primary care physicians and patients	Self-management support Decision support

Table 1 (continued)

Study, country	Study design	Patients	Intervention/control	Components of intervention	Target(s)	Element(s) of the Chronic Care Model involved
Pencille 2009 [42], USA	Patient RCT	Postmenopausal women aged ≥50 years with BMD levels consistent with a diagnosis of osteopenia or osteoporosis, whom their clinician finds eligible for bisphosphonate therapy, with no current osteoporosis treatment (at-risk patients)	Intervention "Osteoporosis Choice" decision-aid tool, a one-page decision aid providing the patient's individualized 10-year-risk estimate of having a major osteoporotic fracture and describing the pros and cons of treatment, one for each of 3 categories of estimated 10-year risks of fracture (<10%, 10-30%, and >30%) provided to the clinician with the aim it be reviewed by the clinician and his/her patient in the context of their clinical encounter A study coordinator reviews with the clinician the patient's tailored "Osteoporosis Choice" decision-aid tool immediately prior to the clinician's visit with that patient Control: usual care+educational booklet on osteoporosis	Risk-assessment tool for physicians and discussion with study coordinator before appointments	Primary care physicians	Decision support
Solomon 2007a [16] and Solomon 2005 [43], USA	Cluster RCT (randomization of primary care physicians)	Women aged ≥65 years and men and women aged ≥65 years with a prior fracture or using oral glucocorticoids for ≥30 days, with no BMD testing and no medication for osteoporosis in the 12 months preceding the start of the study (at-risk and high-risk patients)	Intervention Letters mailed to patients containing vignettes of patients with osteoporosis; cards with questions for the patient to ask his/her primary care physician regarding osteoporosis and space allowing a patient to list his/her current medications; and a toll-free number to discuss issues related to osteoporosis and brochures regarding fall prevention and the importance of calcium/vitamin D Physician education by an academic-detailing approach delivered by trained pharmacists and nurses Information sheets regarding medications and treatments for osteoporosis, BMD testing and interpretation, and fall prevention, patient scenarios, osteoporosis treatment algorithm, reminder flags for patient charts, and behavioral prescription pads provided to physicians Control: usual care (no intervention)	Educational material for patients Physician education by academic detailing	Primary care physicians and patients	Self-management support Decision support

Solomon 2007b [17], USA	Cluster RCT (randomization of primary care physicians)	Women aged ≥65 years, women aged ≥45 years with a prior fracture of the hip, spine, forearm or humerus, and women and men aged ≥45 years who had used oral glucocorticoids for ≥90 days, with no BMD testing and no medication for osteoporosis in the 26 months preceding the start of the study (at-risk and high-risk patients)	Intervention One-on-one educational visits (academic detailing) with primary care physicians conducted by trained pharmacists on osteoporosis epidemiology, diagnosis and treatment Algorithm for diagnosis and treatment of osteoporosis and guide to osteoporosis pharmacotherapy provided to physicians; and tear sheets for patients with check boxes for recommendations regarding fall prevention, calcium/vitamin D use, BMD testing, and treatment provided to physicians and their staff List of at-risk patients provided to physicians Letter and automated telephone call to patients inviting them to undergo BMD testing with possibility of transfer to a centralized radiology service to schedule a BMD test Control: usual care (no intervention)	Patient notification List of at-risk patients for physicians Physician education by academic detailing	Primary care physicians and patients	Decision support Clinical information systems
Yuksel 2010 [18], Canada	Patient RCT	Men and women aged ≥65 years or aged 50-64 years with at least one major risk factor (previous fracture, family history of osteoporosis, systemic glucocorticoids for >3 months, or early menopause), with no BMD testing in the 2 years preceding the start of the study and with no current osteoporosis treatment (at-risk and high-risk patients)	Intervention 30-Min appointment for patients with their community pharmacist who provided tailored education on osteoporosis, printed osteoporosis educational material, performed a heel QUS measurement and discussed interpretation of the results with the patient; patients were encouraged to follow-up with their primary care physician for further management Study details sent to the primary care physician, including information that his/her patient was eligible for BMD testing and the QUS results with clinical interpretation Follow-up phone calls to patients at 2 and 8 weeks Control: usual care+printed educational material on osteoporosis	Physician notification Educational material for patients Heel QUS by community pharmacist Patient counseling	Community pharmacists, primary care physicians and patients	Self-management support Decision support

BMD bone mineral density, *EMR* electronic medical record, *HRT* hormone replacement therapy, *QUS* quantitative ultrasound, *RCT* randomized controlled trial

When two included reports regarding the same study are listed, the first report listed represents the main source of data

Table 2 Risk of bias in studies included in the review—randomization, blinding, and possibility of unit-of-analysis error

Study	Was the allocation sequence adequately generated?	Was the allocation adequately concealed?	Was the study adequately protected against contamination?	Were outcomes assessed blindly?	For clustered designs: Were data analyzed using a statistical method taking the clustering into account?
Ashe 2004 [10]	No (non-random method)	No (unsealed procedure)	No	Unclear	Not applicable
Bessette 2008 [37]	Yes	Yes	Yes	Unclear	Not applicable
Cranney 2008 [11]	Yes	Yes	Yes	Yes	Yes
Feldstein 2006 [12]	Yes	Yes	No	Yes	Not applicable
Lafata 2007 [13]	Yes	Unclear	Yes	Unclear	Yes
Leslie (ongoing) [38]	Unclear	Unclear	Unclear	Unclear	Not applicable
Majumdar 2004 [14] and Majumdar 2007a [39]	No (non-random method)	No (unsealed procedure)	Yes	Yes	Yes
Majumdar 2007b [15] and Morrish 2009 [40]	Unclear	Unclear	Yes	Yes	Not applicable
Majumdar (ongoing) [41]	No (non-random method)	No (unsealed procedure)	Unclear	Yes	Unclear
Pencille 2009 [42]	Yes	Yes	No	Yes	Not applicable
Solomon 2007a [16] and Solomon 2005 [43]	Yes	Yes	Yes	Unclear	Yes
Solomon 2007b [17]	Unclear	Unclear	Yes	Unclear	Yes
Yuksel 2010 [18]	Yes	Yes	Yes	Yes	Not applicable

Yes low risk of bias, *No* high risk of bias, *Unclear* unknown risk of bias

When two included reports regarding the same study are listed, the first report listed represents the main source of data

Table 3 Risk of bias in studies included in the review—completeness of follow-up, comparability of study groups, reliability of outcome measures, and other risks of bias

Study	Were outcome measures obtained for at least 80% of participants?	Were incomplete outcome data adequately addressed?	Were patients or health professionals' baseline characteristics similar?	Were baseline outcome measurements similar?	Were outcome measures reliable?	Was the study free from other risks of bias?
Ashe 2004 [10]	Yes	Yes	No	Unclear	Unclear	Yes
Bessette 2008 [37]	Not applicable	Not applicable	Not applicable	Not applicable	Unclear	Not applicable
Cranney 2008 [11]	Yes	Yes	Yes	Unclear	Unclear	Yes
Feldstein 2006 [12]	Yes	Yes	Yes	Unclear	Yes	Yes
Lafata 2007 [13]	Yes	Unclear	Yes	Unclear	Yes	No[a]
Leslie (ongoing) [38]	Not applicable	Not applicable	Not applicable	Not applicable	Yes	Not applicable
Majumdar 2004 [14] and Majumdar 2007a [39]	Yes	Yes	Yes	Unclear	Yes	Yes
Majumdar 2007b [15] and Morrish 2009 [40]	Yes	Yes	Yes	Unclear	Unclear	Yes
Majumdar (ongoing) [41]	Not applicable	Not applicable	Not applicable	Not applicable	Unclear	Not applicable
Pencille 2009 [42]	Not applicable	Not applicable	Not applicable	Not applicable	Yes	Not applicable
Solomon 2007a [16] and Solomon 2005 [43]	No	Yes	Yes	Unclear	Yes	Yes
Solomon 2007b [17]	Yes	Unclear	Yes	Unclear	Yes	Yes
Yuksel 2010 [18]	Yes	Yes	Yes	Unclear	Yes	Yes

Yes low risk of bias, *No* high risk of bias, *Unclear* unknown risk of bias

When two included reports regarding the same study are listed, the first report listed represents the main source of data

[a] Participating patients insured by the study's affiliated health plan were different from participants otherwise insured, and only patients insured by the study's affiliated health plan were considered for the assessment of the outcome regarding osteoporosis treatment initiation

Table 4 Overall risk of bias in studies included in the review

Study	Applicable risk-of-bias criteria fulfilled Number (proportion; %)	Notes
Ashe 2004 [10]	3/10 (30)	
Bessette 2008 [37]	3/5 (60)	Protocol description
Cranney 2008 [11]	9/11 (82)	
Feldstein 2006 [12]	8/10 (80)	
Lafata 2007 [13]	6/11 (55)	
Leslie (ongoing) [38]	1/5 (20)	Ongoing study
Majumdar 2004 [14] and Majumdar 2007a [39]	8/11 (73)	
Majumdar 2007b [15] and Morrish 2009 [40]	6/10 (60)	
Majumdar (2011) [41]	1/6 (17)	Ongoing study
Pencille 2009 [42]	4/5 (80)	Protocol description
Solomon 2007a [16] and Solomon 2005 [43]	8/11 (73)	
Solomon 2007b [17]	6/11 (55)	
Yuksel 2010 [18]	9/10 (90)	

When two included reports regarding the same study are listed, the first report listed represents the main source of data

vs. 22%; 95% CI: 17–41%) and 41% for the composite endpoint of undergoing BMD testing and/or initiating osteoporosis treatment (67% vs. 26%; 95% CI: 28–53%).

Stratification for the sex of study patients in the studies included in the meta-analysis revealed that interventions targeting both men and women produced results similar to those of interventions targeting women only. In studies with both men and women, absolute between-group differences ranged from 4% to 51% for BMD testing, from 3% to 29% for osteoporosis treatment initiation, and from 4% to 41% for the composite endpoint of undergoing BMD testing and/or initiating osteoporosis treatment [14, 15, 17, 18]. In studies with women only, absolute differences ranged from 18% to 28% for BMD testing and equalled 18% for osteoporosis treatment initiation and 37% for the composite endpoint [11–13].

In terms of the number of components in the intervention, one study of a two-component intervention reported no statistically significant differences in outcomes of interest [16]. In interventions with three components, absolute differences ranged from 4% to 45% for BMD testing [11, 12, 14, 17], 3% to 29% for treatment initiation [11, 14, 17], and 4% to 37% for the composite endpoint [12, 17]. Similar results emerged for interventions with four components: absolute differences ranged from 12% to 51% for BMD testing [13, 15, 18], equalled 29% for treatment initiation [15], and ranged from 11% to 41% for the composite endpoint [15, 18].

Meta-analysis

Substantial observed heterogeneity precluded a meta-analysis of the incidence of BMD testing following the intervention (Table 6). However, a meta-analysis was possible for the incidence of osteoporosis treatment initiation, which showed a significant 20% increase following intervention for high-risk patients (95% CI: 7–33%; Fig. 2a). Results were unchanged when the very intensive study by Majumdar et al. [15] was excluded (Fig. 2b). Moreover, data could be pooled regarding the incidence of the composite endpoint of undergoing BMD testing and/or initiating osteoporosis treatment, which showed a significant 40% increase following intervention in high-risk patients (95% CI: 32–48%; Fig. 3).

Sub-analyses

Sub-analyses to explore heterogeneity in relation to the risk of bias in the studies included in the meta-analysis (studies with a low risk of bias fulfilling at least 73% of their applicable criteria, vs. studies with a higher risk of bias fulfilling less than 73% of their applicable criteria; 73% corresponds to the median proportion of applicable criteria fulfilled in the studies included in our review) and regarding study designs did not change the results (Table 6). Sensitivity analyses performed for the missing ICC values in one study [11] did not change the results (Table 6).

Discussion

Our systematic review included 13 studies evaluating primary care interventions designed to improve the detection and treatment of osteoporosis in patients at risk or at high risk for osteoporosis and fractures in whom osteoporosis screening or treatment is indicated. Most of the interventions included in our study were multifaceted, targeted both primary care physicians

Table 5 Results of studies included in the review regarding outcomes of interest

Study	Participants (*N*)[a]	Duration of follow-up	Number of intervention components	Number of Chronic Care Model elements	Outcome(s)	Reported results (%, intervention vs. control)	Risk difference (95% CI)
Studies targeting high-risk patients							
Cranney 2008 [11]	Intervention:	6 months	3	2	BMD testing by DXA	53.3% vs. 25.5%	28% (16–39%)
	125 patients, 56 practices				Osteoporosis treatment initiation	28.0% vs. 10.3%	18% (8–27%)
	Control: 145 patients, 63 practices				Initiation of calcium/vitamin D supplements	15.0% vs. 9.2%	6% (−2 to 14%)
Feldstein 2006 [12]	Intervention:	6 months	3	2	BMD testing by DXA	22.9% vs. 0.9%	22% (15–31%)
	110 eligible patients				Osteoporosis treatment initiation	10.1% vs. 4.0%	6% (−1 to 14%)
	Control: 103 eligible patients				BMD testing by DXA and/or osteoporosis treatment initiation (composite endpoint)	43.1% vs. 5.9%	37% (27–47%)
Majumdar 2004 [14] and Majumdar 2007a [39]	Intervention: 55 patients	6 months	3	2	BMD testing by DXA	62.0% vs. 17.0%	45% (27–60%)
	Control: 47 patients				Osteoporosis treatment initiation	40.0% vs. 10.6%	29% (13–45%)
Majumdar 2007b [15] and Morrish 2009 [40]	Intervention: 110 patients	6 months	4	2	BMD testing by DXA	80.0% vs. 29.0%	51% (39–61%)
	Control: 110 patients				Osteoporosis treatment initiation	51.0% vs. 22.0%	29% (17–41%)
					BMD testing by DXA and/or osteoporosis treatment initiation (composite endpoint)	67.2% vs. 26.0%	41% (28–53%)
					Fragility fractures	2.0% vs. 2.0%	0% (−5% to 5%)
Study targeting at-risk patients							
Lafata 2007 [13]	Intervention: 4086 patients, 5 primary care clinics	12 months	4	4	BMD testing by DXA	28.9% vs. 10.8%	18% (16–20%)
	Control: 2901 patients, 5 primary care clinics				Osteoporosis treatment initiation	9.1% vs. 5.2%	4% (2–6%)
Studies targeting both at-risk and high-risk patients							
Solomon 2007a [16] and Solomon 2005 [43]	Intervention: 3339 patients, 207 primary care physicians	11–16 months	2	2	BMD testing by DXA	6.7% vs. 6.9%	0% (−1% to 1%)
	Control: 3268 patients, 207 primary care physicians				Osteoporosis treatment initiation	7.1% vs. 7.1%	0% (−1% to 1%)
					BMD testing by DXA and/or osteoporosis treatment initiation (composite endpoint)	10.9% vs. 10.9%	0% (−1% to 2%)
Solomon 2007b [17]	Intervention: 997 patients, 222 primary care physicians	7–10 months	3	2	BMD testing by DXA	12.6% vs. 8.8%	4% (1–7%)
	Control: 976 patients, 212 primary care physicians				Osteoporosis treatment initiation	6.0% vs. 3.7%	2% (0–4%)
					BMD testing by DXA and/or osteoporosis treatment initiation (composite endpoint)	14.4% vs. 10.0%	4% (2–7%)
Yuksel 2010 [18]	Intervention: 129 patients	4 months (16 weeks)	4	2	BMD testing by DXA	22.0% vs. 10.0%	12% (3–21%)
	Control: 133 patients				Osteoporosis treatment initiation	5.0% vs. 2.0%	3% (−2 to 8%)
					BMD testing by DXA and/or osteoporosis treatment initiation (composite endpoint)	22.0% vs. 11.0%	11% (2–20%)

BMD bone mineral density, *CI* confidence interval, *DXA* dual-energy X-ray absorptiometry

When two included reports regarding the same study are listed, the first report listed represents the main source of data

[a] Number of patients and clusters (if applicable) assigned to each study group

Table 6 Results of heterogeneity tests in primary and sub-analyses

Outcome	Analysis	Included studies	Results of heterogeneity tests	Pooled risk difference (95% CI)[a]
Primary analyses				
BMD testing by DXA	High-risk patients	Cranney 2008 [11] Feldstein 2006 [12] Majumdar 2007b [15] Majumdar 2004 [14]	χ^2=21.03, *df*=3 (*p*=0.0001); I^2=86%	
	Non-high-risk patients	Lafata 2007 [13] Solomon 2007a [16] Solomon 2007b [17] Yuksel 2010 [18]	χ^2=37.16, *df*=3 (*p*<0.0001); I^2=92%	
Osteoporosis treatment initiation	High-risk patients	Cranney 2008 [11] Feldstein 2006 [12] Majumdar 2007b [15] Majumdar 2004 [14]	χ^2=4.41, *df*=3 (*p*=0.22); I^2=32%	20% (7–33%)
	Non-high-risk patients	Lafata 2007 [13] Solomon 2007a [16] Solomon 2007b [17] Yuksel 2010 [18]	χ^2=18.92, *df*=3 (*p*=0.0003); I^2=84%	
BMD testing by DXA and/or osteoporosis treatment initiation	High-risk patients	Feldstein 2006 [12] Majumdar 2007b [15]	χ^2=0.73, *df*=1 (*p*=0.39); I^2=0%	40% (32–48%)
	Non-high-risk patients	Solomon 2007a [16] Solomon 2007b [17] Yuksel 2010 [18]	χ^2=10.66, *df*=2 (*p*=0.005); I^2=81%	
Sub-analyses				
BMD testing by DXA	High-risk patients–higher quality studies	Cranney 2008 [11] Feldstein 2006 [12] Majumdar 2004 [14]	χ^2=6.20, *df*=2 (*p*=0.05); I^2=68%	
	Non-high-risk patients–higher quality studies	Solomon 2007a [16] Yuksel 2010 [18]	χ^2=7.42, *df*=1 (*p*=0.006); I^2=87%	
	High-risk patients-patient-randomized trials	Feldstein 2006 [12] Majumdar 2007b [15]	χ^2=19.17, *df*=1 (*p*<0.001); I^2=95%	
	Non-high-risk patients–cluster-randomized trials	Lafata 2007 [13] Solomon 2007a [16] Solomon 2007b [17]	χ^2=30.95, *df*=2 (*p*<0.001); I^2=94%	
Osteoporosis treatment initiation	Non-high-risk patients–higher quality studies	Solomon 2007a [16] Yuksel 2010 [18]	χ^2=2.73, *df*=1 (*p*=0.10); I^2=63%	
	High-risk patients–patient-randomized trials	Feldstein 2006 [12] Majumdar 2007b [15]	χ^2=4.03, *df*=1 (*p*=0.13); I^2=33%	17% (10–44%)

Table 6 (continued)

Outcome	Analysis	Included studies	Results of heterogeneity tests	Pooled risk difference (95% CI)[a]
	Non-high-risk patients–cluster-randomized trials	Lafata 2007 [13] Solomon 2007a [16] Solomon 2007b [17]	χ^2=14.89, *df*=2 (*p*=0.0001); I^2=93%	
BMD testing by DXA and/or osteoporosis treatment initiation	Non-high-risk patients–higher quality studies	Solomon 2007a [16] Yuksel 2010 [18]	χ^2=5.92, *df*=1 (*p*=0.01); I^2=83%	
	High-risk patients–patient-randomized trials	Feldstein 2006 [12] Majumdar 2007b [15]	χ^2=0.73, *df*=1 (*p*=0.39); I^2=0%	40% (32–48%)
	Non-high-risk patients–cluster-randomized trials	Solomon 2007a [16] Solomon 2007b [17]	χ^2=5.93, *df*=1 (*p*=0.01); I^2=83%	
Sensitivity analyses				
BMD testing by DXA	High-risk patients–unknown ICC value in Cranney 2008 [11] set to 0.05	Cranney 2008 [11] Feldstein 2006 [12] Majumdar 2007b [15] Majumdar 2004 [14]	χ^2=20.96, *df*=3 (*p*=0.0001); I^2=86%	
	High-risk patients–unknown ICC value in Cranney 2008 [11] set to 0.10	Cranney 2008 [11] Feldstein 2006 [12] Majumdar 2007b [15] Majumdar 2004 [14]	χ^2=20.94, *df*=3 (*p*=0.0001); I^2=86%	
	High-risk patients–unknown ICC value in Cranney 2008 [11] set to 0.15	Cranney 2008 [11] Feldstein 2006 [12] Majumdar 2007b [15] Majumdar 2004 [14]	χ^2=20.88, *df*=3 (*p*=0.0001); I^2=86%	
Osteoporosis treatment initiation	High-risk patients–unknown ICC value in Cranney 2008 [11] set to 0.05	Cranney 2008 [11] Feldstein 2006 [12] Majumdar 2007b [15] Majumdar 2004 [14]	χ^2=4.42, *df*=3 (*p*=0.22); I^2=32%	20% (7–33%)
	High-risk patients–unknown ICC value in Cranney 2008 [11] set to 0.10	Cranney 2008 [11] Feldstein 2006 [12] Majumdar 2007b [15] Majumdar 2004 [14]	χ^2=4.41, *df*=3 (*p*=0.22); I^2=32%	20% (7–33%)
	High-risk patients–unknown ICC value in Cranney 2008 [11] set to 0.15	Cranney 2008 [11] Feldstein 2006 [12] Majumdar 2007b [15] Majumdar 2004 [14]	χ2=4.16, *df*=3 (*p*=0.22); I^2=32%	19% (6–33%)

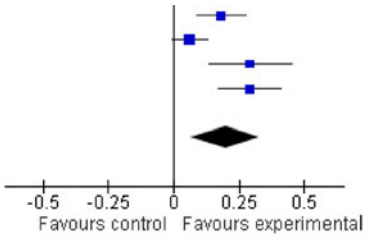
BMD bone mineral density, *CI* confidence interval, *DXA* dual-energy X-ray absorptiometry, *ICC* intra-class correlation coefficient

[a] The pooled risk difference is presented only for groups of studies without substantial heterogeneity (with a chi-square statistic having a *p* value>0.10 and an I^2 statistic less than 50%)

Fig. 2 Effect of interventions aimed at improving detection and treatment of osteoporosis in primary care on incidence of osteoporosis treatment initiation in high-risk patients including (**a**) and excluding (**b**) the very intensive study conducted by Majumdar et al. [15]

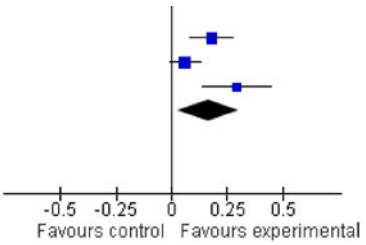
(a)

Study	Weight	Risk difference (95% CI)	Risk difference (95% CI)
Cranney 2008 [11]	26.4%	18% (9–27%)	
Feldstein 2006 [12]	28.3%	6% (-1–13%)	
Majumdar 2004 [14] and Majumdar 2007a [39]	21.1%	29% (14–45%)	
Majumdar 2007b [15] and Morrish 2009 [40]	24.2%	29% (17–41%)	
Total	**100.0%**	**20% (7–33%)**	
χ^2=4.41, *df*=3 (*p*=0.22); I^2=32%			



(b)

Study	Weight	Risk difference (95% CI)	Risk difference (95% CI)
Cranney 2008 [11]	35.0%	18% (9–27%)	
Feldstein 2006 [12]	38.2%	6% (-1–13%)	
Majumdar 2004 [14] and Majumdar 2007a [39]	26.8%	29% (14–45%)	
Total	**100.0%**	**17% (3–30%)**	
χ^2=3.86, *df*=2 (*p*=0.22); I^2=32%			



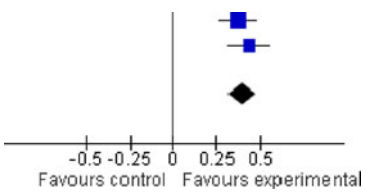
When two included reports regarding the same study are listed, the first report listed represents the main source of data

and their at-risk patients and often included educational material for patients, physician notification, and/or continuing medical education for physicians. Absolute differences in the incidence of BMD testing ranged from 22% to 51% in studies with high-risk patients and from 4% to 18% in studies involving at-risk and high-risk patients. Absolute differences in the incidence of osteoporosis treatment initiation ranged from 18% to 29% in studies with high-risk patients only and from 2% to 4% in studies involving at-risk and high-risk patients. Two studies reported statistically non-significant differences for initiation of calcium/vitamin D supplements and fracture incidence. Interventions with at least three components had a greater impact than interventions with two components on outcomes of interest. A meta-analysis pooling the results of four trials showed that the incidence of osteoporosis treatment initiation in high-risk patients increased by 20% following intervention (95% CI: 7–33%), and the combination of the data from two other studies showed that the incidence of BMD testing and/or initiating osteoporosis treatment in high-risk patients also increased by 40% with the intervention (95% CI: 32–48%). It has been observed that very costly and labor intense interventions are generally efficacious, but these interventions are not generalizable to most clinical settings.

A previous systematic review by Kastner and Straus [27] centering on the effectiveness of clinical decision support

Fig. 3 Effect of interventions aimed at improving detection and treatment of osteoporosis in primary care on incidence of BMD testing and/or osteoporosis-treatment initiation in high-risk patients

Study	Weight	Risk difference (95% CI)	Risk difference (95% CI)
Feldstein 2006 [12]	56.9%	37% (27–47%)	
Majumdar 2007b [15] and Morrish 2009 [40]	43.1%	44% (32–55%)	
Total	**100.0%**	**40% (32–48%)**	
χ^2=0.73, *df*=3 (*p*=0.39); I^2=0%			



tools for osteoporosis disease management was published in 2008. Study heterogeneity prevented the authors from statistically combining the results of individual studies. Still, they concluded that multi-component tools targeting both physicians and patients may be effective in supporting clinical decision making in osteoporosis disease management. The review was limited to RCTs published from 1966 to 2006, though, and so excluded many studies on osteoporosis interventions published from 2007 through 2009. (The present review included 10 studies published or conducted between 2007 and 2009). Moreover, the 2008 review assessed the effectiveness of osteoporosis management tools in men and women with established osteoporosis (i.e., with a confirmatory diagnosis of osteoporosis or an existing or previous fragility fracture), as opposed to patients at risk for osteoporosis for whom screening is indicated. Lai et al. [28] conducted a systematic review of osteoporosis interventions targeting community-dwelling postmenopausal women with osteoporosis. They observed that the interventions were associated with improved quality of life, medication compliance, and calcium intake, although no effect was observed in terms of changes in BMD, medication persistence, knowledge, and other lifestyle modifications. Again, their review targeted only women with established osteoporosis. Furthermore, it did not assess the effect of interventions on osteoporosis screening and treatment.

The small number of studies precluded the use of meta-regression models. Therefore, the differential effectiveness of the various components of the interventions could not be investigated. However, previous systematic reviews suggest that passive dissemination of information such as traditional continuing medical education seems to be generally ineffective, while the use of computerized decision support systems, educational outreach visits, audit and feedback, and patient-mediated interventions seem to improve general professional performance at a greater extent [59–64]. Furthermore, the results of the present systematic review and meta-analysis are in line with these previous reviews regarding interventions aiming at improving general professional performance; they suggest that multifaceted interventions tend to be more effective than single interventions but often lead to only modest improvements in professional practice [59–64].

In the specific area of osteoporosis, numerous barriers to the application of guidelines by primary care physicians have been identified at the patient, provider, and healthcare system levels [65]. Barriers at the patient level include denial of osteoporosis diagnosis and risk factors, lack of awareness of osteoporosis treatment and prevention therapies and their efficacy, and lack of understanding of the potential morbidity and mortality of untreated osteoporosis [65]. Barriers at the physician level include lack of recognition of fragility fracture events as osteoporosis-defining events; low prioritization of osteoporosis for patients with multiple comorbidities; resistance to change; lack of awareness of the morbidity, mortality, and healthcare costs associated with osteoporosis; uncertainty about the indications for and interpretation of BMD testing; reluctance to start a new treatment in seniors already taking many medications; lack of time; and competing demands during appointments [65, 66]. Finally, barriers at the healthcare system level include the static nature of traditional healthcare processes; lack of system-wide standard orders; insufficient coordination of care between subspecialty and primary care providers; unwillingness of physicians to assume responsibility for preventive care; and fragmented financing for preventive care [65].

In light of these findings, it can be hypothesized that the involvement of various health professionals such as community pharmacists, physician assistants, and nurse practitioners in addition to primary care physicians in future interventions might help address barriers at the patient level by educating patients about the gravity of osteoporosis, its risk factors, and its therapies. Broader professional involvement might also help in dealing with barriers at the physician level by providing physicians with guideline-based recommendations on osteoporosis screening and treatment following the assessment of patient risk factors. A recent RCT included in this review notably assessed a community–pharmacist-driven intervention in which a pharmacist evaluated patient risk factors, made recommendations regarding BMD testing and pharmacotherapy, and forwarded recommendations to the primary care physician [18]; however, the study yielded only modest improvements. Targeting community pharmacists more intensively and giving them a greater role in osteoporosis detection and management may be an interesting avenue for developing future strategies.

To reduce the probability of bias, the rigorous methodology of our systematic review restricted the selection of studies to designs with the highest internal validity (e.g., RCTs). We conducted a comprehensive search of the literature using well-defined terms and inclusion/exclusion criteria, and we had articles evaluated at each level of selection by two independent assessors using standardized forms. We also addressed potential sources of variability between studies by assessing the risk of bias and by exploring differences in the populations of patients targeted, interventions, populations involved in interventions, study designs, and outcomes.

This study has some limitations. First, since our meta-analysis relies on data from published studies only, the possibility of a publication bias cannot be ignored. In other words, other studies with statistically non-significant results may well not have been included, and the observed impact of interventions might therefore be overestimated. We decided not to draw funnel plots because the number of studies in the

review that reported each outcome of interest was low; the funnel plot method is not recommended when a meta-analysis covers fewer than 10 studies [35]. Second, only one of the studies reported data on the incidence of fractures following intervention; no conclusion can therefore be drawn for this outcome. We should not be surprised; the studies evaluating interventions designed to improve osteoporosis screening and treatment typically had a follow-up duration of 1 year or less, a period that is clearly insufficient for assessing the impact any interventions might have on the fracture rate, for it may take years until significant changes in this outcome can be detected [1]. Furthermore, the impact of intervention characteristics could not be investigated using meta-regression models because of the small number of studies included in the review. Finally, the external validity of some interventions included in this review, such as EMR prompts, may be low since these interventions require specialized resources and may therefore not be implemented in other contexts.

In summary, our results suggest that multifaceted interventions targeting high-risk patients and their primary care providers may be effective in improving the management of osteoporosis, but the improvement is often modest, particularly for non-high-risk patients. Since most interventions included in the present systematic review targeted only primary care physicians and their patients, it may therefore be worthwhile if future research dealt with developing and evaluating more intensive multidisciplinary interventions that target various health professionals such as community pharmacists, physician assistants, and nurse practitioners in addition to primary care physicians, in order to insure continuity of care.

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Conflicts of interest None.

Appendix A. MEDLINE search strategy (Ovid SP)

1. osteoporosis/or osteoporosis, postmenopausal/
2. osteoporos#s.mp.
3. 1 or 2
4. intervention$.mp.
5. education, medical/or education, medical, continuing/or education, nursing/or education, nursing, continuing/or education, pharmacy/or education, pharmacy, continuing/
6. health education/or patient education as topic/
7. health promotion/
8. education.mp.
9. ”Referral and Consultation”/
10. Reminder Systems/
11. reminder$.mp.
12. prompt$.mp.
13. academic detailing$.mp.
14. audit$.mp.
15. feedback/or feedback$.mp.
16. alert$.mp.
17. Mass Screening/or screening*.mp.
18. risk assessment/or (risk$1 adj3 assessment$).mp. or (risk$1 adj3 estimat$).mp.
19. workshop$.mp.
20. ((improv$ or increas$) and (rate$ adj4 (testing or treatment or care))).mp.
21. ((improv$ or increas$) adj5 diagnos$).mp.
22. or/4–21
23. Physician's Practice Patterns/
24. health personnel/or exp allied health personnel/or health educators/or exp nurses/or exp nursing staff/or pharmacists/or physicians/or physicians, family/or family practice.mp.
25. (physician$ or nurs$ or pharmac$ or primary care or (care adj3 provider$)).mp.
26. Patients/
27. ((patient$ or participant$ or wom#n or men or man) and educat$).mp.
28. pharmacies/or Community Pharmacy Services/
29. or/23–28
30. 3 and 22 and 29
31. limit 30 to ”middle aged (45 plus years)”
32. limit 31 to yr=”1985-Current”
33. randomized controlled trial.pt.
34. random$.tw.
35. control$.tw.
36. intervention$.tw.
37. evaluat$.tw.
38. or/33–37
39. animal/
40. human/
41. 39 not (39 and 40)
42. 38 not 41
43. 32 and 42

Appendix B. List of excluded studies

Table 7 List of excluded studies

Study	Unmet primary inclusion criteria
Ashe MC, McKay HA, Janssen P et al. (2005) Improving osteoporosis management in at-risk fracture clinic patients. J Am Geriatr Soc 53 (4):727–728	Study design
Bailey K, Combs MC, Rogers LJ et al. (2000) Measuring up. Could this simple nursing intervention help prevent osteoporosis? AWHONN Lifelines 4(2):41–44	Intervention
Barr RJ, Stewart A, Torgerson DJ et al. (2009) Population screening for osteoporosis risk: a randomised control trial of medication use and fracture risk. Osteoporos Int Jun 30 [Epub ahead of print]	Patients (patients not at risk nor at high risk)
Barr RJ, Stewart A, Torgerson DJ et al. (2005) Screening elderly women for risk of future fractures - participation rates and impact on incidence of falls and fractures. Calcif Tissue Int 76(4):243–248	Patients (includes patients who are already receiving osteoporosis treatment)
Blalock SJ (principal investigator). GIOP prevention among people with rheumatoid arthritis (ongoing study). Information retrieved from Current Controlled Trials (metaRegister). Available at: http://www.controlled-trials.com/. Project number: NCT00609830	Patients (patients not at risk nor at high risk)
Blalock SJ, Currey SS, DeVellis RF et al. (2000) Effects of educational materials concerning osteoporosis on women's knowledge, beliefs, and behavior. Am J Health Promot 14(3):161–169	Patients (patients not at risk nor at high risk)
Bliuc D, Eisman JA, Center JR (2006) A randomized study of two different information-based interventions on the management of osteoporosis in minimal and moderate trauma fractures. Osteoporos Int 17(9):1309–1317	Comparator
Boire G (principal investigator). Strategies to treat osteoporosis following a fragility fracture (ongoing study). Information retrieved from Current Controlled Trials (metaRegister), available at: http://www.controlled-trials.com/. Project number: NCT00512499	Patients (includes patients who already have undergone BMD testing, are already receiving osteoporosis treatment or have an osteoporosis diagnosis)
Brown JL, Kiernan NE (2001) Assessing the subsequent effect of a formative evaluation on a program. Eval Program Plann 24(2):129–143	Patients (patients not at risk nor at high risk)
Chan MF, Ko CY (2006) Osteoporosis prevention education programme for women. J Adv Nurs 54(2):159–170	Patients (patients not at risk nor at high risk)
Chan MF, Ko CY, Day MC (2005) The effectiveness of an osteoporosis prevention education programme for women in Hong Kong: a randomized controlled trial. J Clin Nurs 14(9):1112–1123	Patients (patients not at risk nor at high risk)
Chen Y, Liu X, Cai D (2006) Evaluation on effect of health education for middle-aged and senile patients with osteoporosis in community [Chinese]. Chinese Nursing Research 20(3A):650–652	Language and study design
Chevalley T, Hoffmeyer P, Bonjour JP et al. (2002) An osteoporosis clinical pathway for the medical management of patients with low-trauma fracture. Osteoporos Int 13(6):450–455	Study design
Ciaschini PM, Straus SE, Dolovich LR et al. (2008) Community-based randomised controlled trial evaluating falls and osteoporosis risk management strategies. Trials 9:62	Patients (includes patients who already have undergone BMD testing)
Clark EM (principal investigator). Evaluation of the impact of a case-finding strategy for vertebral fractures (ongoing study). Information retrieved from Current Controlled Trials (metaRegister), available at: http://www.controlled-trials.com/. Project number: NCT00463905	Patients (includes patients who have already undergone BMD testing or are already receiving osteoporosis treatment)
Crockett JA, Taylor SJ, McLeod LJ (2008) Patient responses to an integrated service, initiated by community pharmacists, for the prevention of osteoporosis. Int J Pharm Pract 16(2):65–72	Patients (patients not at risk nor at high risk)
Curtis JR, Westfall AO, Allison J et al. (2007) Challenges in improving the quality of osteoporosis care for long-term glucocorticoid users: a prospective randomized trial. Arch Intern Med 167(6):591–596	Patients (does not report if patients who already had undergone BMD testing or were receiving osteoporosis treatment were excluded)
Dabrera G (2007) Use of an integrated care pathway in improving secondary prevention of osteoporosis. Journal of Integrated Care Pathways 11(3):126–127	Study design
Doyle R, Rajacich D (1991) The Roy Adaptation Model. Health teaching about osteoporosis. AAOHN J 39(11):508–512	Intervention

Table 7 (continued)

Study	Unmet primary inclusion criteria
Drummond KA. Effectiveness of learning about osteoporosis with group or impersonal delivery methods in congregate meals participants. Immaculata College, USA, 1998, 158 pages	Patients (does not report if patients who already had undergone BMD testing or were receiving osteoporosis treatment were excluded)
Edwards BJ, Bunta AD, Madison LD et al. (2005) An osteoporosis and fracture intervention program increases the diagnosis and treatment for osteoporosis for patients with minimal trauma fractures. Jt Comm J Qual Patient Saf 31(5):267–274	Study design
Eekman DA (principal investigator). Implementation of a strategy of osteoporosis screening in patients over 50 years of age with a first fracture (ongoing study). Information retrieved from Current Controlled Trials (ISRCTN Register), available at: http://www.controlled-trials.com/. Project number: ISRCTN52352361	Patients (includes patients who already have undergone BMD testing)
Elliot-Gibson V, Jain R, Jiwa F et al. Population based post-fracture osteoporosis program. Proceedings of the International Osteoporosis Foundation World Conference on Osteoporosis; December 3–7 2008, Bankok, Thailand, p.89. Available at: http://www.iofbonehealth.org/wco/2008/homepage.html	Study design
Evans KD (2004) Osteoporosis education for at-risk women. Radiol Technol 76(2):164–167	Study design
Francis H (2005) Osteoporosis screening service. Practice Nurse 29(9):23	Study design
Francis KL, Matthews BL, Van Mechelen W et al. (2009) Effectiveness of a community-based osteoporosis education and self-management course: A wait list controlled trial. Osteoporos Int 20(9):1563–1570	Patients (includes patients who have already undergone BMD testing or have an osteoporosis diagnosis)
Fraser M, McLellan AR (2004) A fracture liaison service for patients with osteoporotic fractures. Prof Nurse 19(5):286–290	Study design
Gasparotto J. Cues to action: Do they result in belief and behavioural change in women? Brock University, Canada, 2008, 149 pages	Patients (patients not at risk nor at high risk)
Grahn Kronhed AC, Blomberg C, Karlsson N et al. (2005) Impact of a community-based osteoporosis and fall prevention program on fracture incidence. Osteoporos Int 16(6):700–706	Patients (patients not at risk nor at high risk)
Grahn Kronhed AC, Blomberg C, Lofman O et al. (2006) Evaluation of an osteoporosis and fall risk intervention program for community-dwelling elderly. A quasi-experimental study of behavioral modifications. Aging Clin Exp Res 18(3):235–241	Patients (does not report if patients who already had undergone BMD testing or were receiving osteoporosis treatment were excluded)
Handley A (2009) The bone detectives. Nurs Stand 23(29):20–21	Study design
Harrington JT, Barash HL, Day S et al. (2005) Redesigning the care of fragility fracture patients to improve osteoporosis management: a health care improvement project. Arthritis Rheum 53(2):198–204	Study design
Hayter K. The effect of an osteoporosis prevention program on knowledge and self-efficacy. Grand Valley State University, USA, 1999, 99 pages	Patients (patients not at risk nor at high risk)
Indyk VM. Effect of education on osteoporosis knowledge, health beliefs, and self-care health promotion behaviors in postmenausal nulliparous Roman Catholic women religious. Wayne State University, USA, 2007, 222 pages	Patients (patients not at risk nor at high risk)
Jaglal SB, Hawker G, Bansod V et al. (2009) A demonstration project of a multi-component educational intervention to improve integrated post-fracture osteoporosis care in five rural communities in Ontario, Canada. Osteoporos Int 20(2):265–274	Study design
Jaquet A (principal investigator). Osteoporosis-school (ongoing study). Information retrieved from Current Controlled Trials (metaRegister), available at: http://www.controlled-trials.com/. Project number: NCT00224991	No author contact information
Kandel L, Kessous R, Brezis M et al. Improving the diagnosis rate of osteoporosis in women after a fracture of the distal radius. Proceedings of the International Osteoporosis Foundation World Conference on Osteoporosis; December 3–7 2008, Bankok, Thailand, p.139. Available at: http://www.iofbonehealth.org/wco/2008/homepage.html	Follow-up duration
Kilgore ML (principal investigator). Improving osteoporosis care in high-risk home health patients (ongoing study). Information retrieved from Current Controlled Trials (metaRegister), available at: http://www.controlled-trials.com/. Project number: NCT00679198	Patients (includes patients who have already undergone BMD testing, are already receiving osteoporosis treatment or have an osteoporosis diagnosis)

Table 7 (continued)

Study	Unmet primary inclusion criteria
Kloseck M, Crilly RG, Hanson H et al. Improving the diagnosis and treatment of osteoporosis using a senior-friendly peer-led community education model: a randomized controlled trial. Proceedings of the International Osteoporosis Foundation World Conference on Osteoporosis; December 3–7 2008, Bankok, Thailand, p.601. Available at: http://www.iofbonehealth.org/wco/2008/homepage.html	Patients (includes patients who have already undergone BMD testing or are already receiving osteoporosis treatment)
Klotzbach-Shimomura K (2001) Project Healthy Bones: An Osteoporosis Prevention Program for Older Adults. Journal of Extension 39(3)	Study design
Lacroix AZ, Buist DS, Brenneman SK et al. (2005) Evaluation of three population-based strategies for fracture prevention: results of the osteoporosis population-based risk assessment (OPRA) trial. Med Care 43(3):293–302	Comparator
Laslett LL (principal investigator). Education for osteoporosis in persons with existing fractures (ongoing study). Information retrieved from ClinicalTrials.gov, available at: http://clinicaltrials.gov/. Project number: NCT00575250	Comparator
Laslett LL, Whitham JN, Gibb C et al. (2007) Improving diagnosis and treatment of osteoporosis: Evaluation of a clinical pathway for low trauma fractures. Archives of Osteoporosis 2(1–2):1–6	Study design
Leslie WD (principal investigator). A randomized controlled trial of a bone density decision aide (ongoing study). Information retrieved from Current Controlled Trials (metaRegister), available at: http://www.controlled-trials.com/. Project number: NCT00285168	Study interrupted because of problematic patient recruitment
Levy BT, Hartz A, Woodworth G et al. (2009) Interventions to improving osteoporosis screening: an Iowa Research Network (IRENE) study. J Am Board Fam Med 22(4):360–367	Patients (includes patients who already have undergone BMD testing)
Liu Y, Nevins JC, Carruthers KM et al. (2007) Osteoporosis risk screening for women in a community pharmacy. J Am Pharm Assoc (2003) 47(4):521–526	Study design
Majumdar SR, Johnson JA, McAlister FA et al. (2008) Multifaceted intervention to improve diagnosis and treatment of osteoporosis in patients with recent wrist fracture: a randomized controlled trial. CMAJ 178(5):569–75	Comparator
McDonough RP, Doucette WR, Kumbera P et al. (2005) An evaluation of managing and educating patients on the risk of glucocorticoid-induced osteoporosis. Value Health 8(1):24–31	Patients (does not report if patients who already had undergone BMD testing or were receiving osteoporosis treatment were excluded)
The Medical and Health Research Council of The Netherlands, Implementation of screening and treatment of high-risk fracture patients by an osteoporosis nurse-practitioner (Project record). 2009, Issue 4, Health Technology Assessment Database	Study design
Morrison LS, Tobias JH (2005) Effect of a case-finding strategy for osteoporosis on bisphosphonate prescribing in primary care. Osteoporos Int 16(1):71–77	Comparator
Nahm ES (principal investigator). Dissemination of a theory-based bone health program in online communities (ongoing study). Information retrieved from NIH Research Portfolio Online Reporting Tool, available at: http://projectreporter.nih.gov/reporter.cfm. Project number: 1R01NR011296-01	Patients (patients not at risk nor at high risk)
Naunton M, Peterson GM, Jones G (2006) Pharmacist-provided quantitative heel ultrasound screening for rural women at risk of osteoporosis. Ann Pharmacother 40(1):38–44	Study design
Naunton M, Peterson GM, Jones G et al. (2004) Multifaceted educational program increases prescribing of preventive medication for corticosteroid induced osteoporosis.[see comment]. J Rheumatol 31(3):550–556	Patients (includes patients who are already on osteoporosis therapy or already have an osteoporosis diagnosis)
No investigator stated. Comparison of osteoporosis disease management strategies (ongoing study). Information retrieved from Current Controlled Trials (metaRegister), available at: http://www.controlled-trials.com/. Project number: NCT00145080	No author contact information
No investigator stated. Improving Care of Osteoporosis: Multi-Modal Intervention to Increase Testing and Treatment (ICOMMIITT)	Comparator

Table 7 (continued)

Study	Unmet primary inclusion criteria
(ongoing study). Information retrieved from Current Controlled Trials (metaRegister), available at: http://www.controlled-trials.com/. Project number: NCT00788632	
No investigator stated. Osteoporosis disease management demonstration project (ongoing study). Information retrieved from Current Controlled Trials (metaRegister), available at: http://www.controlled-trials.com/. Project number: NCT00139425	No author contact information
No author stated (1999) Focus on caregiving. Nutrition center: nutrition screening and intervention for osteoporosis. Provider 25(8):65	Intervention
Olegario R, Park J, Kjell J (2008) Clinical pharmacists boost success of osteoporosis outreach effort. Drug Benefit Trends 20(10):391–400	Study design
Peters S, Singla D, Raney E (2006) Impact of pharmacist-provided osteoporosis education and screening in the workplace. J Am Pharm Assoc 46(2):216–218	Study design
Ribeiro V, Blakeley JA (2001) Evaluation of an osteoporosis workshop for women. Public Health Nurs 18(3):186–193	Patients (patients not at risk nor at high risk)
Rolnick SJ, Kopher R, Jackson J et al. (2001) What is the impact of osteoporosis education and bone mineral density testing for postmenopausal women in a managed care setting? Menopause 8(2):141–148	Study design
Rothert ML, Holmes-Rovner M, Rovner D et al. (1997) An educational intervention as decision support for menopausal women. Res Nurs Health 20(5):377–387	Intervention
Rozental TD, Makhni EC, Day CS et al. (2008) Improving evaluation and treatment for osteoporosis following distal radial fractures. A prospective randomized intervention. J Bone Joint Surg Am 90 (5):953–961	Comparator
Ryan P (principal investigator). Tailored computerized intervention for bihavior change (ongoing study). Information retrieved from NIH Research Portfolio Online Reporting Tool, available at: http://projectreporter.nih.gov/reporter.cfm. Project number: 1R15NR009021-01A2	Patients (patients not at risk nor at high risk)
Saag KG (principal investigator). Improving care of osteoporosis: Multimodal interventions to increase testing (ongoing study). Information retrieved from NIH Research Portfolio Online Reporting Tool, available at: http://projectreporter.nih.gov/reporter.cfm. Project number: 5P60AR048095-07	Comparator
Saver BG, Gustafson D, Taylor TR et al. (2007) A tale of two studies: the importance of setting, subjects and context in two randomized, controlled trials of a web-based decision support for perimenopausal and postmenopausal health decisions. Patient Educ Couns 66(2):211–222	Intervention
Schousboe JT, DeBold RC, Kuno LS et al. (2005) Education and phone follow-up in postmenopausal women at risk for osteoporosis: effects on calcium intake, exercise frequency, and medication use. Dis Manag Health Out 13(6):395–404	Comparator
Sedlak CA, Doheny MO, Estok PJ et al. (2005) Tailored interventions to enhance osteoporosis prevention in women. Orthop Nurs 24(4):270–276	Patients (patients not at risk nor at high risk)
Shepstone L (principal investigator). A pragmatic randomised controlled trial of the effectiveness and cost effectiveness of Screening for Osteoporosis in Older women for the Prevention of fractures (SCOOP) (ongoing study). Information retrieved from Current Controlled Trials (ISRCTN Register), available at: http://www.controlled-trials.com/. Project number: ISRCTN55814835	Patients (includes patients who already have undergone BMD testing)
Solomon DH, Finkelstein JS, Polinski JM et al. (2006) A randomized controlled trial of mailed osteoporosis education to older adults. Osteoporos Int 17(5):760–767	Patients (includes patients who have already undergone BMD testing, are already receiving osteoporosis treatment or have an osteoporosis diagnosis)
Spencer J (2005) Implementing a nurse-led fracture intervention service. Nurs Times 101(32):32–35	Study design
Tsauo JY (principal investigator). What is the best policy to prevent osteoporotic fracture? (ongoing study). Information retrieved from Current Controlled Trials (metaRegister), available at: http://www.controlled-trials.com/. Project number: NCT00173693	Patients (patients not at risk nor at high risk)

Table 7 (continued)

Study	Unmet primary inclusion criteria
Tung WC, Lee IF (2006) Effects of an osteoporosis educational programme for men. J Adv Nurs 56(1):26–34	Patients (patients not at risk nor at high risk)
Välimäki MJ (principal investigator). Effectiveness of an educational program in the prevention of osteoporosis and fractures (ongoing study). Information retrieved from Current Controlled Trials (metaRegister), available at: http://www.controlled-trials.com/. Project number: NCT00589615	Patients (missing information, no response from author)
Waalen J, Bruning AL, Peters MJ et al. (2009) A telephone-based intervention for increasing the use of osteoporosis medication: a randomized controlled trial. Am J Manag Care 15(8):e60–70	Patients (includes patients who already have undergone BMD testing)
White TL. Improving osteoporosis knowledge and healthy bone habits of rural-dwelling older adults. Texas Woman's University, USA, 2008, 226 pages	Patients (does not report if patients who already had undergone BMD testing or were receiving osteoporosis treatment were excluded)

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4. American College of Rheumatology Ad Hoc Committee on Glucocorticoid-Induced Osteoporosis (2001) Recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis: 2001 update. Arthritis Rheum 44(7):1496–503
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8. Giangregorio L, Papaioannou A, Cranney A et al (2006) Fragility fractures and the osteoporosis care gap: an international phenomenon. Semin Arthritis Rheum 35(5):293–305
9. Elliot-Gibson V, Bogoch ER, Jamal SA et al (2004) Practice patterns in the diagnosis and treatment of osteoporosis after a fragility fracture: a systematic review. Osteoporos Int 15(10):767–78
10. Ashe M, Khan K, Guy P et al (2004) Wristwatch-distal radial fracture as a marker for osteoporosis investigation: a controlled trial of patient education and a physician alerting system. J Hand Ther 17(3):324–8
11. Cranney A, Lam M, Ruhland L et al (2008) A multifaceted intervention to improve treatment of osteoporosis in postmenopausal women with wrist fractures: a cluster randomized trial. Osteoporos Int 19(12):1733–40
12. Feldstein A, Elmer PJ, Smith DH et al (2006) Electronic medical record reminder improves osteoporosis management after a fracture: a randomized, controlled trial. J Am Geriatr Soc 54 (3):450–7
13. Lafata JE, Kolk D, Peterson EL et al (2007) Improving osteoporosis screening: results from a randomized cluster trial. J Gen Intern Med 22(3):346–51
14. Majumdar SR, Rowe BH, Folk D et al (2004) A controlled trial to increase detection and treatment of osteoporosis in older patients with a wrist fracture. Ann Intern Med 141(5):366–73
15. Majumdar SR, Beaupre LA, Harley CH et al (2007) Use of a case manager to improve osteoporosis treatment after hip fracture: results of a randomized controlled trial. Arch Intern Med 167 (19):2110–5
16. Solomon DH, Katz JN, Finkelstein JS et al (2007) Osteoporosis improvement: a large-scale randomized controlled trial of patient and primary care physician education. J Bone Miner Res 22 (11):1808–15
17. Solomon DH, Polinski JM, Stedman M et al (2007) Improving care of patients at-risk for osteoporosis: a randomized controlled trial. J Gen Intern Med 22(3):362–7
18. Yuksel N, Majumdar SR, Biggs C et al (2010) Community pharmacist-initiated screening program for osteoporosis: randomized controlled trial. Osteoporos Int 21(3):391–8
19. Davis JC, Guy P, Ashe MC et al (2007) HipWatch: osteoporosis investigation and treatment after a hip fracture: a 6-month randomized controlled trial. J Gerontol A Biol Sci Med Sci 62 (8):888–91
20. McDonough RP, Doucette WR, Kumbera P et al (2005) An evaluation of managing and educating patients on the risk of glucocorticoid-induced osteoporosis. Value Health 8(1):24–31
21. Levy BT, Hartz A, Woodworth G et al (2009) Interventions to improving osteoporosis screening: an Iowa Research Network (IRENE) study. J Am Board Fam Med 22(4):360–7
22. Majumdar SR, Johnson JA, McAlister FA et al (2008) Multifaceted intervention to improve diagnosis and treatment of osteoporosis in patients with recent wrist fracture: a randomized controlled trial. CMAJ 178(5):569–75
23. Laliberté MC, Perreault S, Dragomir A et al (2010) Impact of a primary care physician workshop on osteoporosis medical practices. Osteoporos Int 21(9):1471–85
24. Curtis JR, Westfall AO, Allison J et al (2007) Challenges in improving the quality of osteoporosis care for long-term glucocorticoid users: a prospective randomized trial. Arch Intern Med 167(6):591–6
25. Solomon DH, Finkelstein JS, Polinski JM et al (2006) A randomized controlled trial of mailed osteoporosis education to older adults. Osteoporos Int 17(5):760–7

26. Solomon DH, Katz JN, La Tourette AM et al (2004) Multifaceted intervention to improve rheumatologists' management of glucocorticoid-induced osteoporosis: a randomized controlled trial. Arthritis Rheum 51(3):383–7
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31. Solomon DH, Morris C, Cheng H et al (2005) Medication use patterns for osteoporosis: an assessment of guidelines, treatment rates, and quality improvement interventions. Mayo Clin Proc 80 (2):194–202
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38. Leslie WD (principal investigator). Closing the post fracture care gap in Manitoba (ongoing study). Information retrieved from Current Controlled Trials (metaRegister), available at: http://www.controlled-trials.com/. Project number: NCT00594789
39. Majumdar SR, Johnson JA, Lier DA et al (2007) Persistence, reproducibility, and cost-effectiveness of an intervention to improve the quality of osteoporosis care after a fracture of the wrist: results of a controlled trial. Osteoporos Int 18(3):261–70
40. Morrish DW, Beaupre LA, Bell NR et al (2009) Facilitated bone mineral density testing versus hospital-based case management to improve osteoporosis treatment for hip fracture patients: additional results from a randomized trial. Arthritis Rheum 61(2):209–15
41. Majumdar SR (principal investigator). Addressing vertebral osteoporosis incidentally detected to prevent future fractures (ongoing study). Information retrieved from ClinicalTrials.gov, available at: http://clinicaltrials.gov/. Project number: NCT00388908
42. Pencille LJ, Campbell ME, Van Houten HK et al (2009) Protocol for the Osteoporosis Choice trial. A pilot randomized trial of a decision aid in primary care practice. Trials 10:113
43. Solomon DH, Brookhart MA, Polinski J et al (2005) Osteoporosis action: design of the healthy bones project trial. Contemp Clin Trials 26(1):78–94
44. Waalen J, Bruning AL, Peters MJ et al (2009) A telephone-based intervention for increasing the use of osteoporosis medication: a randomized controlled trial. Am J Manag Care 15(8):e60–70
45. Eekman DA (principal investigator). Implementation of a strategy of osteoporosis screening in patients over 50 years of age with a first fracture (ongoing study). Information retrieved from Current Controlled Trials (ISRCTN Register). Available at: http://www.controlled-trials.com/. Project number: ISRCTN52352361
46. Shepstone L (principal investigator). A pragmatic randomised controlled trial of the effectiveness and cost effectiveness of Screening for Osteoporosis in Older women for the Prevention of fractures (SCOOP) (ongoing study). Information retrieved from Current Controlled Trials (ISRCTN Register). Available at: http://www.controlled-trials.com/. Project number: ISRCTN55814835
47. Ciaschini PM, Straus SE, Dolovich LR et al (2008) Community-based randomised controlled trial evaluating falls and osteoporosis risk management strategies. Trials 9:62
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