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Can Educational Interventions Improve Osteoporotic Women's Adherence to Treatment?

A Literature Review

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Poor adherence to medication and an unhealthy lifestyle increase risk of fracture, hospitalization, and medical costs in osteoporotic individuals. Therefore, a literature review was conducted using PubMed, CINAHL, Cochrane Library, and Scopus databases to identify educational interventions that improve adherence to medications and healthy lifestyles in osteoporotic women. The search was limited to the articles published between January 2002 and January 2015, and they were selected only if they were interventional studies. Twelve studies were included, in which 7 studies were focused on interventions to improve medication adherence, 4 studies on improving adherence to healthy lifestyles, and 1 study was focused on both. Educational interventions, such as tailored interventions with counseling sessions, were effective in improving adherence to medications and healthy lifestyles; however, educational materials such as leaflets did not improve adherence. Further studies are needed to investigate adherence to healthy lifestyles because this is poorly described in the literature.

Introduction

Osteoporosis is a global health issue and the leading cause of morbidity and mortality in industrialized countries (Duquet, 2014; Rousiere, 2011). The prevalence of osteoporosis has risen to 27.5 million people in Europe and 10 million aged older than 50 years in the United States (Dempster, 2011; Hernlund et al., 2013). The individuals most affected by osteoporosis are postmenopausal women (Cotte & De Pouvourville, 2011), with progressively increasing prevalence with age, moving from a 5% prevalence at 50 years of age to 50% at 85 years of age (World Health Organization [WHO], 2003b). Osteoporosis is characterized by a reduction in bone mineral density, leading to an increased risk of fragility fractures (Lee, Lee, Jang, & Ryu, 2013). In the United States, 30% of older women and 19% of older men are at risk for fragility fractures (Dawson-Hughes et al., 2012), which are a major cause of morbidity, particularly in osteoporotic women (Adachi et al., 2010). In Italy during the last decade, about 75,000 hospital admissions due to femoral neck fractures occurred each year in women, causing significant morbidity in osteoporotic individuals (Piscitelli et al., 2014; Tarantino, Feola, Piccirilli, Marziali, & Rao, 2014).

Long-term antifracture efficacy and safety are the two main goals of any osteoporosis therapy, and several medications currently exist, with different mechanisms of action and modalities of administration. These

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substances have all demonstrated their usefulness in preventing vertebral fractures and, to a lesser degree, nonvertebral fractures, including (but not limited to) hip fractures. A patient's failure to adhere to treatment compromises overall efficacy of any management strategy. As such, evidence from randomized controlled trials (RCTs) indicates that osteoporosis therapy is associated with varying degrees of efficacy in adherent patients, with risk reductions of between 30% and 70% for vertebral fractures, 15% and 20% for nonvertebral fractures, and up to 40% for hip fractures (Boonen et al., 2009). Huybrechts, Ishak, and Caro (2006) indicated a graded relationship between adherence and total rates of fracture, with the lowest rates of compliance (medication possession ratio <50%) associated with a 21% increase in the fracture rate when compared with the patients with the highest levels of compliance (medication possession ratio ≥90%) ($p < .0001$). Moreover, improving the patients' persistence by 20% was found to have the same clinical impact as a 20% increase in clinical efficacy.

The WHO defines adherence as "the extent to which a person's behavior, such as taking medication, following a diet, and executing lifestyle changes like exercising, corresponds with agreed recommendations from a health care provider" (WHO, 2003a, p. …). Suboptimal adherence to the prescribed medication is a common and well-recognized problem with regard to long-term therapy for chronic diseases, and osteoporosis therapy is no exception. In osteoporotic patients, an adherence to pharmacological and healthy lifestyle treatments plays a fundamental role in reducing morbidity, and those patients who adhere to these treatments have a 30%–70% reduction in fractures (Burrell, Frame, Ganguli, Iles, & Khan, 2013; Gold, 2011; Huas et al., 2010; van Boven, de Boer, Postma, & Vegter, 2013). However, patients with osteoporosis often show poor adherence to treatment (Gold, 2011; Hiligsmann, McGowan, Bennett, Barry, & Reginster, 2012), and 50%–75% abandon their medication within 1 year of starting drug therapy (Hiligsmann et al., 2013). This lack of adherence to osteoporosis therapy results in an increased risk of fracture, higher medical costs, increased hospitalization, and greater use of healthcare resources (Cotte & De Pouvourville, 2011; Modi, Sajjan, & Gandhi, 2014).

Poor adherence and persistence can result from forgetfulness, the inability to pay, or other nonintentional factors. In addition, the degree of intentional adherence has been associated with the balance between patients' beliefs about the necessity of taking their medication and their concerns about the safety and side effects of medications. Therefore, the information that patients receive regarding the necessity and safety of their treatment is critical. In this, the prescriber plays a central role, especially orthopaedic surgeons, who are often the first practitioners who diagnose bone fragility when faced with fractures (Tarantino et al., 2011). However, orthopaedic surgeons often fail to prescribe adequate osteoporosis therapy after fragility fractures. In a multinational survey, Dreinhofer et al. (2005) reported that many orthopaedic surgeons neglected to identify, evaluate, and treat patients with fragility fractures for osteoporosis.

Poor adherence has been associated with the failure to perceive an increased risk of fractures and dissatisfaction with treatment. A lack of persistence with the treatment or suboptimal adherence can cause side effects, including gastrointestinal problems. Moreover, osteoporotic patients are often older than 80 years, and these patients have comorbidities associated with multiple medications. Polypharmacy increases the possibility of side effects and can reduce adherence to medications. Other causes of the suboptimal adherence of elderly patients include dementia, Parkinson's disease, and a lack of social support (Modi et al., 2014).

Once practitioners decide to begin therapy in patients with fragility fractures or osteoporosis, these healthcare professionals must provide patient education with regard to osteoporosis and risk of fracture (Modi et al., 2014; Olsen & Bergland, 2014). Patients' beliefs about these risks and their need for therapy are influenced by the perceived support and attitudes of their physicians and other healthcare providers (Jin, Sklar, Min Sen Oh, & Chuen Li, 2008; Martin, Williams, Haskard, & Dimatteo, 2005). Therapies that are viewed as safe and effective by both patients and physicians, as well as convenient for the patients, should be developed. Among these patients, postmenopausal women constitute the largest population requiring effective strategies to promote adherence and persistence to osteoporosis therapy (Rabenda, Hiligsmann, & Reginster, 2009).

In the literature, interventions have been tested to evaluate their effectiveness in improving adherence in osteoporotic individuals. Educational interventions carried out by healthcare providers, such as orthopaedic nurses, surgeons, and physicians, are considered to be crucial to increase adherence in osteoporotic patients (Gold, 2011). Patients who achieve an understanding of their condition through these educational interventions are then motivated to enjoy healthy lifestyles and to adhere to ongoing therapy despite concerns about side effects (Chan & Ko, 2006; Gold, 2011; Jaarsma, Nikolova-Simons, & van der Wal, 2012). Nonetheless, a recent literature review investigated the most effective interventions for improving adherence to osteoporosis medication, and this review indicated that the efficacy of educational interventions was variable across studies (Hiligsmann et al., 2013). These results were, however, based on a mixed population of men and women. Several other studies have shown that adherence to treatment in individuals with chronic diseases, such as osteoporosis, varies by gender (Chiu, Kuo, Yu, Su, & Cheng, 2013; Gadkari & McHorney, 2012). Therefore, the goal of this literature review, specifically, was to identify educational interventions that improve osteoporotic women's adherence to medications and healthy lifestyles.

Methods

A literature review was conducted to find published studies on healthy lifestyles and pharmacological educational interventions by healthcare professionals to improve adherence in osteoporotic women. A search was

conducted, using the PubMed, CINAHL, Cochrane Library, and Scopus databases, of English and Italian language articles published from January 2002 to January 2015. The following Medical Subject Headings (MeSH terms) were used to identify relevant studies: "osteoporosis," "woman," "postmenopausal," "adherence," and "education." These key words were separated by the Boolean operators "AND" and "OR" (see Figure 1).

All RCTs and experimental/interventional studies related to the area of study were included because they provided the best evidence to assess the effectiveness of interventions to improve adherence and reported quantitative measures of adherence. Studies not written in English or Italian, observational studies, and studies in which the adherence results were not differentiated by gender were excluded. Each article was reviewed independently by three investigators, and disagreements were resolved by consensus.

A modified Delphi list was used to evaluate the quality of each study. This list was used in another literature review (Hiligsmann et al., 2013) and was considered to be adequate for the purpose of this study because the modified Delphi list made it possible to evaluate the RCTs and interventional behavioral studies as well. The list consisted of 14 domains: ethics, results, confounders, comparators, study questions, populations, sample sizes, interventions, outcome measures, follow-up, blinding processes, treatment allocations, external validity, and statistical analyses. Each domain includes several questions, and each question was assigned a score of "1" if it was clearly defined or "0" if not. The maximum score for each study that included all the information was 30 (see Table 1). The consistency of the quality score was obtained by at least two reviewers assigning a score to each study independently. If differences appeared, these were resolved by consensus.

Results

The literature search revealed 200 studies, and after reviewing the titles and abstracts, 12 studies met the inclusion criteria as shown in Figure 1. Ten RCTs were

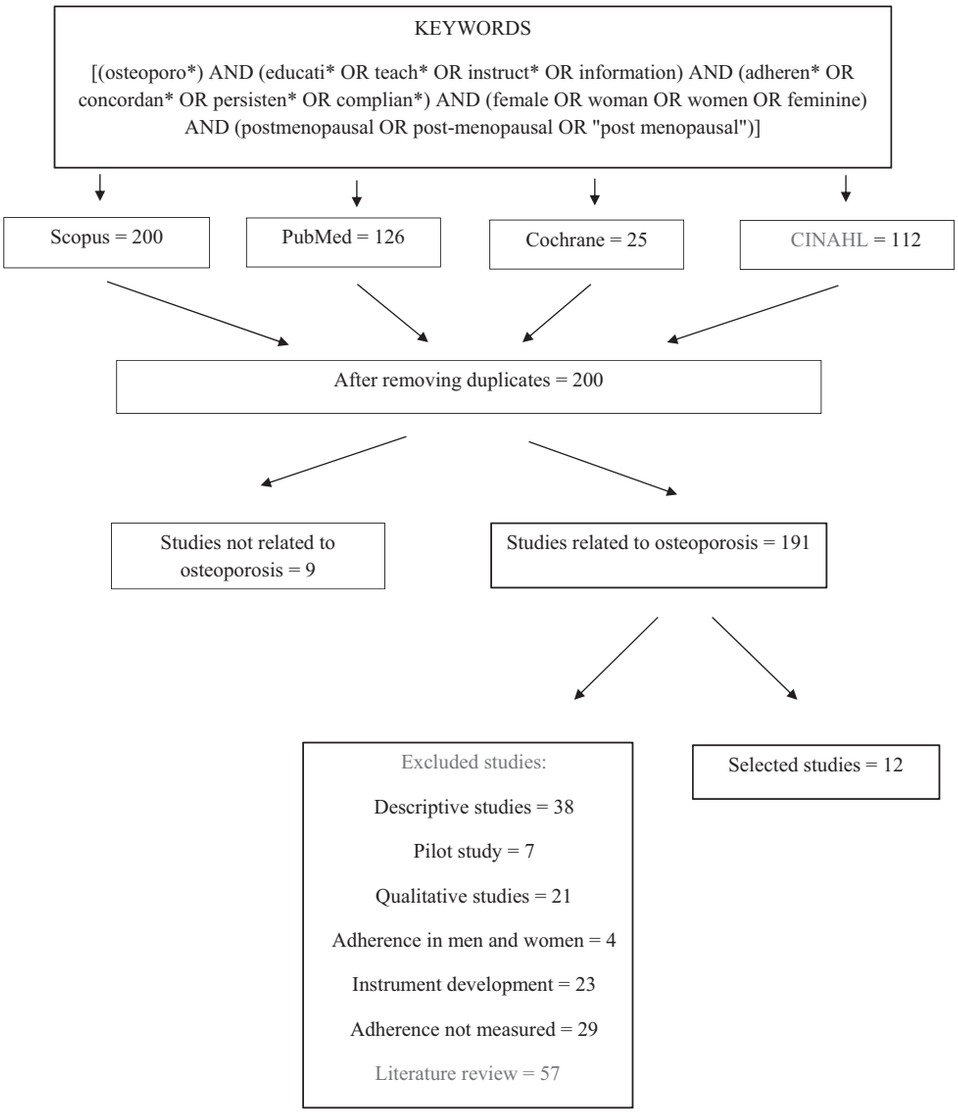

FIGURE 1. Database search strategy and the number of studies identified.

Table 1. Modified Version of the Delphi List

Domains	Modified List
1. Study question	Was the research question/objective/hypothesis or aim clearly described?
	Yes (1)/No (0)
2. Population	Were the inclusion criteria clearly described?
	Yes (1)/No (0)
	Were the exclusion criteria clearly described?
	Yes (1)/No (0)
3. Sample size and power calculations a priori	Was the sample size and power calculated a priori?
	Yes (1)/No (0)
	Were the total number of individuals, the total number of participants in the study group, and the total number of patients in the control group clearly specified?
	Yes (3, 1 each)/No (0)
4. Treatment allocation	Was randomization used in the study?
	Yes (1)/No (0)
5. Confounders	Were the potential confounders clearly described?
	Yes (1)/No (0)
6. Ethics	Was the protocol approved by the ethics committee and/or did the patients sign informed consent?
	Yes (1)/No (0)
7. Intervention	Was intervention clearly defined?
	Yes (1)/No (0)
	Was the intervention clearly described (who did what, to whom, where, and how often)?
	Yes (1)/No (0)
8. Comparator	Was a comparator included in the study?
	Yes (1)/No (0)
	Was the comparator clearly described?
	Yes (1)/No (0)
9. Outcome measures	Was (were) the measure (s) of adherence defined?
	Yes (1)/No (0)
	Was (were) the measure (s) of adherence clearly described in the study?
	Yes (1)/No (0)
	Were the clinical outcomes included in the study?
	Yes (1)/No (0)
10. Follow-up/withdrawals	Was the follow-up time specified in the study?
	Yes (1)/No (0)
11. Blinding	Was the study:
	(a) Double blind?
	Yes (2)/No (0)
	(b) Single blind?
	Yes (1)/No (0)
12. Analysis	Was the statistical method appropriate?
	Yes (1)/No (0)
	Was the analysis adjusted by confounders?
	Yes (1)/No (0)
	Were the losses of the patients to follow-up taken into account?
	Yes (1)/No (0)
	Were the characteristics of the patients lost to follow-up clearly described?
	Yes (1)/No (0)
13. Results	Were the adherence results clearly presented (e.g., baseline, interim, and at the end of the study)?
	Yes (3)/No (0)
	Were the clinical results clearly presented (e.g., baseline, interim, and at the end of the study)?
	Yes (1)/No (0)
	Were the results adjusted by confounders?
	Yes (1)/No (0)
14. External validity	Was the included population representative of the study population?
	Yes (1)/No (0)
Total	30 (100% quality score)

found, along with one prospective study and one observational study. All of the studies compared an intervention group with a control group (see Table 2), and according to the modified Delphi list, the studies' quality scores ranged from 18 to 24. In this literature review, we found several interventions that improved osteoporotic women's adherence to medication and healthy lifestyles.

Interventions to Improve Medication Adherence

Seven studies focused on promoting interventions to improve adherence to medication. For example, in the study conducted by Montori et al. (2011), a decision aid was used to improve medication adherence. A decision aid is an evidence-based tool that facilitates decision making to improve adherence to medication, and this intervention was effective in improving the medication adherence at 6 months of follow-up.

Clowes, Peel, and Eastell (2004) evaluated the efficacy of monitoring by the nursing staff to improve medication adherence. The monitoring provided by healthcare professionals is a simple clinical tool that consists of one-on-one interactions with their patients to improve the treatment response. A monitoring schedule improved medication adherence at 12 months of follow-up.

Pharmaceutical care with a counseling package was implemented in the study conducted by Lai, Chua, Chew, and Chan (2011). This intervention included a counseling package with an osteoporosis booklet as educational reinforcement, focused on medication adherence, lifestyle modifications, and osteoporosis risk factors. Pharmaceutical care with the counseling package was effective in improving the medication adherence at 6 and 12 months of follow-up.

In the study conducted by Sewerynek et al. (2013), three kinds of interventions were tested to improve medication adherence in three different groups of patients. In the first group, a nursing care intervention with additional follow-up telephone calls conducted by nurses was used. The follow-up telephone calls were made after 3 and 9 months of treatment to monitor and remind the patient to take their medications. In the second group, a counselling approach was used, which included a 30-minute educational session regarding osteoporosis, diagnostic methods, treatment, and preventive behaviors. In the third group, biochemical tests were used to inform the patients of their serum levels of calcium, phosphorus, alkaline phosphatase, urinary calcium, and phosphorus. A nursing care intervention, with additional follow-up telephone calls, counseling, and biochemical tests, was effective in improving medication adherence at 3, 6, 9, and 12 months of follow-up.

In two studies, educational materials, such as information leaflets on osteoporosis and the efficacy of healthy lifestyles and medication adherence, were provided to the patients to improve their adherence to medication (Guilera, Fuentes, Grifols, Ferrer, & Badia, 2006; Silverman, Nasser, Nattrass, & Drinkwater, 2012). However, these interventions did not improve their medication adherence.

In the study conducted by Tüzün et al. (2013), a starter training kit was used, including a bisphosphonate usage guide and an osteoporosis training booklet. In addition, the training package included four telephone calls and four interactive educational meetings to improve medication adherence. During the telephone calls, the patients were reminded to read the booklets, informed of the topic to be covered in the next educational meeting, and invited to that meeting. The training booklet and training package were not effective in improving the medication adherence because there were no differences between the intervention and control groups.

Overall, all interventions (Clowes et al., 2004; Lai et al., 2011; Montori et al., 2011; Sewerynek et al., 2013), with the exception of the information leaflets (Guilera et al., 2006; Silverman et al., 2012), training booklet, and standard training package (Tüzün et al., 2013), were effective in improving medication adherence.

Interventions to Improve Adherence to Healthy Lifestyles

Four studies focused on interventions to improve the adherence to healthy lifestyles. For example, Oh et al. (2014) evaluated an integrated therapeutic lifestyle modification with individualized counseling sessions focused on improving adherence to healthy lifestyles, such as exercise, good nutrition, adequate calcium, and adequate vitamin D. This therapeutic lifestyle modification intervention was effective in improving nutrition and exercise at 3 months of follow-up.

In the study conducted by Blalock et al. (2002), a tailored intervention with written material about the diet, exercise, and counseling sessions was used to improve the adherence to adequate calcium intakes and exercise levels. This tailored intervention with written materials and counseling sessions improved the calcium intake and exercise levels at 3, 6 and 12 months of follow-up.

In addition, an Iranian study described an exercise educational program based on the transtheoretical change model being used to improve the adherence to exercise; fortunately, this program was an effective intervention to improve exercise levels at 3 months of follow-up (Shirazi et al., 2007).

The research conducted by Di Monaco et al. (2015) found that a multidisciplinary intervention, focused on making targeted recommendations about risk factors and behavioral changes to prevent falls, can be used to improve the adherence to healthy behaviors. However, this intervention did not improve the adherence to healthy lifestyles, such as modifications to environmental hazards at home and behavioral changes to prevent falls, at 6 months of follow-up.

Overall, all interventions (Blalock et al., 2002; Oh et al., 2014; Shirazi et al., 2007), except the multidisciplinary intervention utilized in the study conducted by Di Monaco et al. (2015), were effective in improving adherence to a healthy lifestyle.

Interventions to Improve Adherence to Medication and a Healthy Lifestyle

One study was focused on interventions to improve adherence to both medication and a healthy lifestyle. Education and follow-up telephone calls were used to improve the adherence to medication, calcium intake, and frequency of exercise. A nurse educator performed

Table 2. Characteristics of the Identified Studies That Investigated the Interventions to Improve Osteoporotic Women's Adherence to Medication and Healthy Lifestyles

References	Country	Setting	Design	Sample	Intervention	Instruments to Measure Adherence	Clinicians	Results
Use of a decision aid to improve treatment decisions in osteoporosis: the osteoporosis choice randomized trial Montori et al., 2011	US	Primary care practices	Randomized control trial	100 patients 52 interventions 48 controls	Decision aid: an evidence-based tool that facilitates decision making	Haynes' single-item adherence question (medication adherence) Carbonell Abella et al., 2011	Physicians	The decision aid improved medication adherence by more than 80% in the intervention group vs. the control group at 6 months of follow-up
Impact of bone turnover markers and/or educational information on persistence in oral bisphosphonate therapy: a community setting-based trial Silverman et al., 2012	US	Community centers	Randomized control trial	239 patients 60 bone marker results at baseline, 3, and 12 months 60 educational materials every month and a membership in the National Osteoporosis Foundation 60 bone markers and educational information 59 control	Educational information including educational materials about osteoporosis given to women monthly	Track prescription refills (medication adherence) Farmer, 1999; Osterberg & Blaschke, 2005	Physicians	The bone markers and educational information did not improve medication adherence among the study groups at 12 months of follow-up
Effects of pharmaceutical care on adherence and persistence to bisphosphonates in postmenopausal osteoporotic women Lai et al., 2011	Malaysia	Hospitals	Randomized control trial	198 patients 100 interventions 98 controls	Pharmaceutical care with counseling package consisting of a counseling intervention focused on medication adherence, lifestyle modifications, and osteoporosis risk factors	Pill counts, direct reporting, and self-recording (medication adherence) Farmer, 1999; Osterberg & Blaschke, 2005	Pharmacists	The pharmaceutical care with counseling package improved medication adherence at 6 and 12 months of follow-up in the intervention group compared with the control group
Does an educational leaflet improve self-reported adherence to the therapy in osteoporosis? The OPTIMA study Guilera et al., 2006	Spain	Primary care practices	Observational study	745 patients 366 interventions 379 currently practicing	Educational leaflet focused on general information about osteoporosis, on the efficacy of global diets, on lifestyle measures, and on the importance of medication adherence	Morisky questionnaire (medication adherence) Carbonell Abella et al., 2011; Morisky et al., 1986; Val Jimenez et al., 1992	Physicians	The educational leaflet did not improve medication adherence because no differences appeared between the intervention and control groups at 12 months of follow-up

(*continues*)

Table 2. Characteristics of the Identified Studies That Investigated the Interventions to Improve Osteoporotic Women's Adherence to Medication and Healthy Lifestyle (Continued)

References	Country	Setting	Design	Sample	Intervention	Instruments to Measure Adherence	Clinicians	Results
The impact of monitoring on adherence and persistence with antiresorptive treatment of postmenopausal osteoporosis: a randomized controlled trial Clowes et al., 2004	UK	Hospitals	Randomized control trial	73 patients 25 nurse monitoring 24 marker monitoring 24 controls	Monitoring schedule consisting of one-on-one interactions with patients and healthcare professionals	Electronic monitoring devices (medication adherence) Choo et al., 1999	Nurses	The monitoring of patients improved medication adherence by 57% in the intervention group when compared with the control group at 12 months of follow-up
Impact of the training on the compliance and persistence of weekly bisphosphonate treatment in postmenopausal osteoporosis: a randomized controlled study Tüzün et al., 2013	Turkey	Primary care practices	Randomized control trial	448 patients 226 interventions 222 controls	Training booklets including information about osteoporosis and a standard training package including four telephone calls and four interactive educational meetings	Self-reporting (medication adherence) Farmer, 1999; Osterberg & Blaschke, 2005	Physicians	There are no differences between active training and passive training in terms of persistence and compliance to weekly bisphosphonate treatments
The role of counseling and other factors in compliance of postmenopausal osteoporotic patients to alendronate 70 therapy Sewerynek et al., 2013	Poland	Primary care practices	Prospective study	123 patients 29 counseled group 31 biochemical group 31 nurse-assisted group 32 controls	Nursing care intervention with additional follow-up phone calls to monitor and remind the patient to take medication; counseling approach including a 30-minute education session regarding osteoporosis; biochemical tests to inform patients about the serum levels of several electrolytes and urinary calcium	Medication possession ratio (medication adherence)	Nurses and physicians	In the intervention groups, such as the nurse-assisted group, the counseled group, and the biochemical group, adherence was better than the control group
Effects of a 3-month therapeutic lifestyle modification program to improve bone health in postmenopausal Korean women in a rural community: a randomized controlled trial Oh et al., 2014	Korea	Community centers	Randomized control trial	41 patients 21 interventions 20 controls	Therapeutic lifestyle modification intervention with individualized counseling sessions: a comprehensive approach regarding nutrition, supplementation with calcium and vitamin D, and exercise	Participants' food diaries, structured food frequency questionnaires, and a single question about exercise (adherence to healthy lifestyles) Blalock et al., 1998	Nurses	The therapeutic lifestyle modification intervention with individualized counseling sessions improved adherence to healthy lifestyles related to nutrition, calcium and vitamin D intake, and exercise at 3 months of follow-up

(*continues*)

Table 2. Characteristics of the Identified Studies That Investigated the Interventions to Improve Osteoporotic Women's Adherence to Medication and Healthy Lifestyle (Continued)

References	Country	Setting	Design	Sample	Intervention	Instruments to Measure Adherence	Clinicians	Results
A single postdischarge telephone call by an occupational therapist does not reduce the risk of falling in women with hip fracture: a randomized controlled trial Di Monaco et al., 2015	Italy	Post-acute rehabilitation hospital and community	Randomized control trial	153 patients 78 interventions 75 controls	Multidisciplinary intervention focused on making targeted recommendations about risk factors and behavioral changes to prevent falls	Checklist of 38 items (adherence to healthy lifestyles) Di Monaco et al., 2015	Occupational therapists	The multidisciplinary intervention did not improve adherence to healthy lifestyles because no difference appeared between the intervention and control groups at 6 months of follow-up
Effects of an osteoporosis prevention program incorporating tailored educational materials Blalock et al., 2002	US	Community centers	Randomized control trial	547 patients 273 interventions 274 controls	Tailored intervention with written materials about diet and exercise and counseling sessions	Abbreviated version of the Block-NCI Health Habits and History Questionnaire and a telephone interview with self-reporting (adherence to healthy lifestyles) Cummings et al., 1987	Physicians	The tailored intervention with written materials and counseling sessions improved adherence to healthy lifestyles in the intervention group vs. the control group
A home-based, transtheoretical change model design strength training intervention to increase exercise to prevent osteoporosis in Iranian women aged 40–65 years: a randomized controlled trial Shirazi et al., 2007	Iran	Community centers	Randomized control trial	116 patients 61 interventions 55 controls	An exercise education program based on the transtheoretical change model with strength and balance training recommendations at levels sufficient to prevent osteoporosis	Adapted shortened version of the International Physical Activity Questionnaire (adherence to healthy lifestyles) Chun, 2012; Craig et al., 2003; Oyeyemi et al., 2011	Physicians	The exercise education program based on the transtheoretical change model improved adherence to healthy lifestyles by 47.5% of the patients in the intervention group as compared with 20.0% of patients in the control group at 3 months of follow-up

(*continues*)

Table 2. Characteristics of the Identified Studies That Investigated the Interventions to Improve Osteoporotic Women's Adherence to Medication and Healthy Lifestyle (Continued)

References	Country	Setting	Design	Sample	Intervention	Instruments to Measure Adherence	Clinicians	Results
Education and phone follow-up in postmenopausal women at risk for osteoporosis Schousboe et al., 2005	US	Community centers	Unblinded randomized control trial	310 patients 158 interventions 152 controls	Education and follow-up telephone calls including a nurse educator performing one-on-one education sessions and a follow-up phone call to advise patients about risks of fracture, daily calcium intake, exercise, and therapy	Self-reporting (adherence to medication and healthy lifestyles) Farmer, 1999; Osterberg & Blaschke, 2005	Nurses	The nurse education failed to improve the initiation of and persistence with medication. However, women in the intervention group improved their calcium intake and their frequency of exercise compared with the control group

15-minute one-on-one education sessions and follow-up telephone calls at 3, 6, and 9 months, advising the patients with regard to the risk of fracture, daily calcium intake, importance of weight-bearing exercise, and therapy. This intervention was effective in improving the adherence to a healthy lifestyle but not in improving the adherence to medication at the 3, 6, 9, and 12 months of follow-up (Schousboe et al., 2005).

Instruments used to Measure Medication Adherence

Several instruments were used to measure medication adherence. One study used the Morisky questionnaire, which consists of four items with dichotomous answers, to classify the patients into three compliance categories: low, moderate, and high adherence (Guilera et al., 2006). In addition, Silverman et al. (2012) evaluated medication adherence by tracking pharmacy prescription refills. This study also used an interview to collect information regarding osteoporosis beliefs and the reasons for compliance and noncompliance. In the study conducted by Tüzün et al. (2013), the adherence was evaluated using a self-reporting persistence tool, consisting of four items with dichotomous answers, investigating whether the patients received a correct bisphosphonate treatment (i.e., exact day and dose). Lai et al. (2011) measured adherence using pill counts and self-recorded data, for which the patients recorded the dates they took their medication, and directly reported data, for which the participants revealed the number of doses of medication they had missed since the last time they visited the pharmacist. In a study conducted by Clowes et al. (2004), electronic monitoring devices were used to measure adherence by recording the date and frequency in which bottles of prescribed medication were opened. Montori et al. (2011) evaluated medication adherence via the Haynes' single-item adherence question, asking the patients if they missed any of their pills during the previous week. Finally, medication adherence was measured by the medication possession ratio during follow-up as the number of days with applied therapy within the 12-month follow-up period divided by the length of follow-up (Sewerynek et al., 2013).

Instruments Used to Measure Adherence to Healthy Lifestyles

Several instruments were used to measure adherence to healthy lifestyles. In one study, a structured food frequency questionnaire asked the patients, for example, how many times they drank milk during the previous 7 days. This was used to evaluate adherence to healthy behaviors related to dietary calcium and vitamin D intakes. Moreover, the frequency of regular exercise was measured using a question asking the patients how many days per week they did exercises, such as push-ups, sit-ups, or weight lifting (Oh et al., 2014). In another study, an abbreviated version of the Block-NCI Health Habits and History Questionnaire was used to assess how frequently the participants consumed 15 foods and their usual serving portions. In addition, a telephone interview was used to assess exercise levels by asking the patients how frequently they exercised, as

well as the type and duration of these activities (Blalock et al., 2002). In the study conducted by Shirazi et al. (2007), an adapted shortened version of the International Physical Activity Questionnaire was used to evaluate regular physical activities by collecting data about the time spent walking and physical activity intensity. Finally, a checklist of 38 items was used to appraise the behaviors of daily living activities and home environmental hazards related to the risk factors for falls (Di Monaco et al., 2015).

Instruments Used to Measure Adherence to Medication and a Healthy Lifestyle

In the study conducted by Schousboe et al. (2005), a questionnaire was used to investigate the calcium intake, exercise habits, and medication adherence of the patients. The questionnaire asked the patients if they had increased their use of calcium supplements or their daily intake of calcium-rich foods (with yes/no response categories), if they increased their frequency of exercise over the past year, or if they were still taking their medications.

Discussion

We reviewed the literature to investigate educational interventions seeking to improve osteoporotic women's adherence to medication and healthy lifestyles. Overall, we reviewed 10 RCTs, one prospective study, and one observational study placed in the highest levels of the evidence-based medicine pyramid (Berlin & Golub, 2014). Despite the small number of studies reviewed, all of them offered solid scientific evidence, having obtained good scores on the modified Delphi list. No study reported conducting a double-blind trial, even though this is perceived to be the most objective method to minimize bias (Moylan, Harold, O'Neill, & Kowalczuk, 2014). In addition, the absence of double-blind studies can be justified because it can be difficult, and sometimes impossible, to set up double-blind trials with the participants in educational interventions.

Several studies (Clowes et al., 2004; Lai et al., 2011; Montori et al., 2011; Sewerynek et al., 2013) showed that decision aids, a monitoring schedule with nurses, pharmaceutical care with counseling packages, nursing care interventions with additional follow-up telephone calls, a counseling approach, and biochemical interventions improved medication adherence. These are interventions that have direct relationships in common between the patients and healthcare professionals. In particular, the study conducted by Lai et al. (2011) used counseling to develop therapeutic relationships. According to two studies with mixed samples of men and women affected by osteoporosis, a telephone counseling intervention was also effective in improving medication adherence (Cook, Emiliozzi, & McCabe, 2007; Nielsen et al., 2010). In another study, a standardized educational intervention led by a nurse was useful in improving medication adherence (Robbins, Rausch, Garcia, & Prestwood, 2004). In addition, a retrospective study showed that the pharmaceutical care provided by pharmacists further improved adherence to medication (Heilmann, Friesleben, & Billups, 2012). Although our results were limited to only four studies on tailored educational interventions, we found that these were effective in improving medication adherence. This result contrasts with a previous literature review (Hiligsmann et al., 2013), which stated that the efficacy of educational interventions was variable across studies.

In the present literature review, three studies showed that educational materials, such as leaflets or training booklets and standard training packages, did not improve adherence to medication (Guilera et al., 2006; Silverman et al., 2012; Tüzün et al., 2013), which is consistent with the literature. In a study with a sample of men and women affected by osteoporosis, the educational materials provided by the clinicians through letters and automated telephone calls did not significantly improve medication adherence (Shu et al., 2009). Furthermore, in a related RCT study, the educational materials were not an effective way to improve medication adherence in a population of postmenopausal women treated for breast cancer (Neven et al., 2014).

In this literature review, we found five studies that tested several interventions to improve adherence to healthy lifestyles. Four of them (Blalock et al., 2002; Oh et al., 2014; Schousboe et al., 2005; Shirazi et al., 2007) showed that a therapeutic lifestyle modification intervention, a tailored intervention with written materials, education, and follow-up telephone calls, counseling sessions, and an exercise education program based on the transtheoretical change model improved adherence to healthy lifestyles. These interventions focused on promoting adequate nutrition and exercise levels (Blalock et al., 2002; Oh et al., 2014; Schousboe et al., 2005; Shirazi et al., 2007). In accordance with the literature, regular exercise and a balanced diet with an adequate calcium and vitamin D intake are fundamental changes in one's lifestyle that can reduce the risk of fractures (Christianson & Shen, 2013; Pearson, Burkhart, Pifalo, Palaggo-Toy, & Krohn, 2005; Rizzoli, Bischoff-Ferrari, Dawson-Hughes, & Weaver, 2014; Zhu & Prince, 2015).

In contrast, the study conducted by Di Monaco et al. (2015) showed that a multidisciplinary intervention focused on giving targeted recommendations about behavioral changes did not improve adherence to the healthy lifestyles that reduce the risk factors for falls. In this study, the absence of an improvement in adherence to healthy lifestyles may be explained by an inadequate consideration of different patients' needs and behaviors. The target recommendations were probably focused on giving standard information to all patients, instead of giving tailored information.

From the overall results of this literature review, we can deduce that the most effective educational interventions in improving adherence seem to be counseling or patient–healthcare professional relationships, rather than educational materials or standardized recommendations. Thus far, the literature reviews focused on osteoporotic individuals have only investigated interventions to improve adherence to medication (Hiligsmann et al., 2013; White et al., 2010). In our literature review, we have also considered studies seeking to investigate interventions focused on improving adherence to healthy lifestyles. Therefore, we have taken into account both aspects of adherence, which are important for

individuals with osteoporosis because drug treatments and healthy lifestyles, with a proper diet and regular exercise, promote bone health, reducing the risk of fractures (Weycker, Macarios, Edelsberg, & Oster, 2007; Zhu & Prince, 2015). However, in the studies that investigated adherence to healthy lifestyles, the concept of adherence was not clearly defined. Nonetheless, all of these studies measured the frequency of behaviors related to healthy lifestyles; therefore, they evaluated increased frequency as a measure of adherence, which is included in the WHO's (2003a) definition of adherence.

The adherence to medication can be measured using direct and indirect methods. Direct methods are those that directly observe whether the patients take their medication, whereas indirect methods are those that assume that the patients have taken their medication. In this literature review, we did not find the use of direct methods, such as the measurement of drug concentrations in the blood, measurement of biological body markers in the body, and direct observation of patients taking their medication. Instead, indirect methods, such as pill counts, patient self-reports, and the use of electronic monitoring, were widely used (Farmer, 1999; Osterberg & Blaschke, 2005). Among the instruments that measured the adherence to drug therapy, only the Morisky questionnaire (Carbonell Abella et al., 2011; Morisky, Green, & Levine, 1986; Val Jimenez, Amoros Ballestero, Martinez Visa, Fernandez Ferre, & Leon Sanroma, 1992) and the Haynes–Sackett questionnaire (Carbonell Abella et al., 2011) have been validated in populations with chronic diseases, such as hypertension, diabetes, and dyslipidemia. However, pill counts with electronic monitoring have been validated in a hypertensive population (Choo et al., 1999). Among the instruments that measured adherence to healthy lifestyles, the Structured Food Frequency Questionnaire (Blalock et al., 1998), the adapted shortened version of the International Physical Activity Questionnaire (Chun, 2012; Craig et al., 2003; Oyeyemi et al., 2011), and the abbreviated version of the Block-NCI Health Habits and History Questionnaire (Cummings, Block, McHenry, & Baron, 1987) have shown adequate psychometric properties.

The present review is limited in several aspects. Despite a methodical literature search, we may have overlooked some journal articles because of the selected search strategy or database filters. Only 12 studies were included in this literature review, and this limits the generalizability of our results. No statistical procedures were used to aggregate the data because the instruments or the focus of the interventions described in the studies reviewed differed too widely.

Moreover, among the selected studies, the longest follow-up was 12 months, meaning that the adherence measures were limited to this length of time. Therefore, it was not possible to determine the changes that adherence might undergo after this period.

Conclusions

Osteoporosis is a large and growing disease, and fragility fractures constitute a significant public health concern. Knowledge of the risk factors and an understanding of inadequate responses are important to assist clinicians both in identifying patients who require close monitoring during treatment and in determining when changes in therapy are warranted. With regard to postmenopausal osteoporosis, therapy reduces, but does not eliminate, the risk of fracture. In addition, poor adherence to osteoporosis medication plans results in around a 50% reduction in the potential benefits observed in clinical trials and a doubling of the cost per quality-adjusted life years gained from the medications (Hiligsmann et al., 2012).

The results of the economic modeling suggest that nonadherence and nonpersistence are costly and that behavioral interventions to improve therapy would be cost-effective. These results emphasize the need to address treatment adherence in order to maximize the benefits of these agents in terms of the outcome. This, therefore, would reduce the burdens that osteoporosis and associated fractures place on individuals and the healthcare system. Secondary prevention programs, including fracture liaison services, bone therapy groups, telephone calls from nurses or other healthcare providers, and regularly scheduled follow-up visits, have been shown to improve patient adherence to, and persistence with, therapy.

In summary, according to the literature, educational interventions should be conducted in this context because they are effective in improving osteoporotic women's adherence to medication plans and healthy lifestyles. On the basis of our review, we conclude that the most effective interventions have been those that use counseling or patient–healthcare professional relationships as a part of the educational interventions. Further studies should be conducted with direct and indirect methods of measurement and with a follow-up of more than 12 months to clarify the causes of nonadherence. Moreover, the concept of adherence should be investigated in more detail because, although medication adherence is clearly described in the literature, adherence to healthy lifestyles is still inadequately researched. Therefore, additional RCTs and observational studies may need to be conducted that take into account specific interventions to improve the adherence to both medication and healthy lifestyles.

Practice Implications

In clinical practice, educational interventions directed at osteoporotic women are an essential tool because they allow the improvement of the adherence to drug treatments and healthy lifestyles. Educational interventions provided by nurses allow women to improve poor behaviors, and better adherence over time helps women lower their risks of fractures and, consequently, reduce hospitalizations and healthcare costs (Celi et al., 2013). Moreover, it is important that clinical nurses know that educating patients with only written materials, without a patient–healthcare professional relationship, may not change the patient's behavior, which can be seen from this literature review.

On the basis of the results of this literature review, the Guardian Angel research project was created (www.guardian-angel.it). The aim of this multicenter longitudinal study was to improve medication adherence, healthy lifestyles, and the quality of life of

postmenopausal osteoporotic women through a tailored educational intervention conducted by nurses (Alvaro et al., 2015). In this study, both inpatients and outpatients were enrolled. A tailored educational intervention was performed at the baseline and during three follow-up telephone calls to reinforce the education.

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AUTHOR QUERIES

TITLE: Can Educational Interventions Improve Osteoporotic Women's Adherence to Treatment?: A Literature Review

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