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# Improving drug adherence in osteoporosis: an update on more recent studies

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***Abstract:*** Similar to other chronic diseases such as diabetes and hypertension, osteoporosis has struggled with suboptimal medication adherence, resulting in an increased risk of fractures and all-cause mortality. The goal of this narrative review was to summarize interventions to improve medication adherence in osteoporosis. Because past reviews of this topic covered published literature through 2013, we conducted our literature search to include the period between January 2012 and November 2017. We identified 10 studies evaluating healthcare system and patient interventions aimed at improving osteoporosis treatment adherence, including three fracture liaison service (FLS) programs, one pharmacist-delivered counseling program, and six patient-directed interventions consisting of three coaching or counseling programs and three interventions using reminder prompts. Four out of the six patient-directed interventions did not lead to significant improvements in outcomes, suggesting that patient-directed interventions may have limited success in this setting. The healthcare system interventions that evaluated FLS programs and pharmacist-directed tailored counseling were effective at improving medication adherence; however, the studies were not randomized, they were costly, resource intensive and effective in countries with more centralized healthcare, possibly limiting their generalizability. In conclusion, while healthcare system interventions such as FLS, and pharmacist-delivered counseling appeared to be successful in improving osteoporosis medication adherence in some settings, behavioral interventions including patient counseling and reminder prompts for medication utilization were not, perhaps due to patient perceptions regarding osteoporosis consequences and need for treatment. Thus, these patient attributes may define patients 'at high risk' for poor adherence and developing intervention approaches to enhance patient knowledge and understanding of osteoporosis and its consequences may improve the perception of the need for treatment, optimize osteoporosis care and thereby improve overall outcomes of patients with osteoporosis. We hope that the knowledge gained through our review will help inform the design of further programs aimed at optimizing osteoporosis care.

***Keywords:*** fracture liaison service, medication adherence, osteoporosis treatment interventions

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Osteoporosis medications, such as bisphosphonates, have well established efficacy in decreasing fracture risk through increasing bone mineral density (BMD) and normalizing bone turnover in both postmenopausal and glucocorticoid-induced osteoporosis.[1,2] Clinicians tend to overestimate their patients' adherence to osteoporosis medications, with physicians believing that 69.2% of their patients are adherent while only 48.7% of patients were actually adherent based on claims data.[3] Furthermore, current estimates suggest that approximately 50–70% of the patients discontinue their osteoporosis medications within the first year of initiation.[4] This suboptimal adherence leads to increased fracture risk,[5,6] which results in increased morbidity and mortality.[7]

Management of osteoporosis is challenging since patients with osteoporosis, unlike those with diabetes or congestive heart failure, may be completely asymptomatic until they experience a fracture. In an effort to improve medication adherence, it is

essential to understand the patient-, physician-, and healthcare-related factors that influence medication adherence.[8] Because the Aday-Andersen behavioral model for health services utilization is a conceptual framework for how contextual (e.g. health system, clinics) and individual characteristics influence patient health behaviors and outcomes,[8] this model has been used as the theoretical framework guiding the development of many interventions to improve medication adherence in chronic conditions such as hypertension[9] and osteoporosis.[9,10] According to this behavioral model, the utilization of health services is determined by the interaction between predisposing factors (e.g. race, age, and health beliefs), enabling factors (e.g. social support, access to health services), and the perceived and actual need for healthcare services.[11] Hence, based on the Aday-Andersen behavioral model, patient perceptions of osteoporosis as a disease entity, perceived risks, benefits and disadvantages of medications, self-efficacy, and readiness for behavioral change about osteoporosis treatment are domains that can be targeted to improve outcomes in patients with osteoporosis. For example, patients' perceived need for osteoporosis treatment and understanding of osteoporosis improved initiation of osteoporosis medication,[12] while experiencing a consequence of inadequate treatment (fracture) or having a relevant clinical test (BMD measurement) were associated with restarting osteoporosis therapy.[13] In addition, patients' education levels, socioeconomic status, and cultural differences also contributed to their receptiveness to obtain health-related information/counseling provided by medical professionals.[12]

The purpose of our narrative review was to summarize recent interventions developed to improve medication adherence in osteoporosis. We divided these interventions into patient and healthcare system directed interventions and aimed to understand which approaches worked and which were less successful, with the goal to inform the design of future osteoporosis interventions.

## Methods

We performed an extensive literature search in PubMed to identify relevant studies published from January 2012 until November 2017, which were designed to test interventions aimed at improving osteoporosis medication adherence. The search was carried out on 3 November 2017. We used the following keywords: 'intervention', 'osteoporosis', 'drug', 'medication', 'adherence' combined with 'January 2012 to present' and limited our search to English language publications. We limited our search to this time period because a recent systematic review of the literature on osteoporosis medication adherence was published in 2013 and included studies published between January 1999 and 30 June 2012.[14] In addition, we performed a manual search through the references to ensure that all relevant studies evaluating interventions for osteoporosis medication adherence were included. We screened the publications specifically for osteoporosis medication interventions and excluded those that did not test interventions or were review articles. We identified a total of 13 studies, seven of which resulted from the public database search, and six additional studies were identified during a manual search through the manuscript reference lists.

## Discussion

Our literature search resulted in a total of 13 studies. We excluded two studies because they were not in English and one because it was a review of another study that was published before January 2012. Of the remaining 10 studies, 2 were conducted in the US, and 1 in each of the following countries: Australia, The Netherlands, Poland, Italy, France, Korea, Canada, and Turkey. The size of the study populations ranged from 100 to 4000 participants. Five of the 10 interventions were evaluated in randomized controlled clinical trials (RCTs), two in non-RCTs and three in open-label clinical trials. We summarize our results in Table 1, categorizing the interventions into healthcare system and patient interventions.

### *Healthcare system interventions*

Healthcare system interventions to improve osteoporosis medication adherence are interventions that focus on modifying the healthcare environment in order to facilitate adoption of optimal behaviors and are used to improve osteoporosis care.[11] Two specific types of healthcare system interventions are pharmacist-directed tailored counseling and the fracture liaison service (FLS).

*Pharmacist-directed interventions.* Pharmacist-directed interventions for improving osteoporosis care have included screening for risk of osteoporosis and facilitating osteoporosis diagnosis using BMD testing,[25] as well as tailored counseling

**Table 1.** Healthcare System and Patient Interventions to Improve Adherence to Osteoporosis Medications.

| Reference | Study Design | Country | Population | Intervention | Sample size by Intervention / Control | Measurement for Adherence | Results |
|---|---|---|---|---|---|---|---|
| Stuurman-Bieze et al. 2014<br><br>PMID: 24570297 | Open-label Clinical Trial with Historical Controls | Holland | Patients starting osteoporosis medications | MeMO program: pharmacist-delivered medication monitoring and counseling | Intervention (N = 495)<br>Historical control (N = 442) | Therapy discontinuation and adherence at 12 months | Intervention: 19.0% discontinued medications or were non-adherent<br><br>Control: 32.8% discontinued medications or were non-adherent; ($p<0.001$) |
| Ganda et al. 2014<br><br>PMID: 24445732 | Randomized Controlled Clinical Trial | Australia | Patients over age 45 with symptomatic fragility fractures | "Type A" FLS program in Group A Intervention (6 visits with FLS); | Intervention (N = 49)<br>Control (N = 53) | Medication possession ratio (MPR) at 24 months | Intervention: MPR = 0.78 (IQR, 0.50–0.93)<br><br>Control: MRP = 0.79 (IQR, 0.48– 0.96); (p=0.68) |
| Dehamchia-Rehailia et al. 2014<br><br>PMID: 24980182 | Open-label Clinical Trial | France | Patients with low-trauma fractures | "Type A" FLS program | Intervention (N = 335) | Self-reported medication adherence at 12 and 18 months | Intervention: 74.1% adherent at 12 months; 67.4% adherent at 18 months |
| Majumdar et al. 2017<br><br>PMID: 28275838 | Open-label Clinical Trial with a Simulated Control Group | Canada | Patients with low trauma non-hip fractures in the previous 6 weeks | Catch-a-Break: "Type C" FLS program | Intervention (N = 4633)<br>Simulated control (N = 2690) | Bisphosphonate use at 12 months | Intervention: 17.5% (95% CI 15.6–19.4) treated with bisphosphonates<br><br>Simulated Control: 13.2% (95% CI 12.4–14.0) treated with bisphosphonates; ($p < 0.001$) |
| Sewerynek et al. 2013<br><br>PMID: 23671440 | Non-randomized Controlled Clinical Trial | Poland | Postmenopausal osteoporosis patients on alendronate | Osteoporosis education (Counseling group); patient notification of laboratory results (Biochemical group); phone call to remind about medication (Nurse-assisted group) | Counseling group (N = 29)<br>Biochemical group (N = 31)<br>Nurse-assisted group (N = 31)<br>Control group (N = 32) | Medication Compliance (MPR ≥ 80%) at 12 months | Counseling group: 65.52 ± 9.0%<br>Biochemical group: 64.51 ± 8.7%<br>Nurse-assisted group: 61.29 ± 9.0%<br>Control group: 37.5 ± 8.7% |

*(Continued)*

**Table 1.** (Continued)

| Reference | Study Design | Country | Population | Intervention | Sample size by Intervention / Control | Measurement for Adherence | Results |
|---|---|---|---|---|---|---|---|
| Tüzün et al. 2013<br><br>PMID: 24324365 | Randomized Controlled Clinical Trial | Turkey | Postmenopausal women with osteoporosis | Telephone calls, interactive educational sessions, informational booklets | Intervention (N = 226)<br>Control (N = 222) | Self-reported persistence and compliance at 12 months | Intervention: Self-reported persistence and compliance = 152 (50.5)<br><br>Control: Self-reported persistence and compliance = 149 (49.5); (p = 0.862) |
| Solomon et al. 2012<br><br>PMID: 22371876 | Randomized Controlled Clinical Trial | U.S. | Patients starting osteoporosis medications | Telephone-based counseling program by a health educator | Intervention (N = 1046)<br>Control (N = 1041) | Medication possession ratio (MPR) at 12 months | Intervention: MPR = 49% (IQR 7, 88)<br><br>Control: MPR = 41% (IQR 1.5, 86.0); (p = 0.074) |
| Nho et al. 2016<br><br>PMID: 27294076 | Non-randomized Controlled Clinical Trial | Korea | Patients with osteoporosis | Alarm clock | Intervention (N = 50)<br>Control (N = 50) | Medication possession ratio (MPR) at 12 months | Intervention: MPR = 0.80 ± 0.33<br>Control: MPR = 0.56 ± 0.34; (P<0.001) |
| Cizmic et al. 2015<br><br>PMID: 25956282 | Randomized Controlled Clinical Trial | U.S. | Adults with osteoporosis / osteopenia | Interactive voice response phone call followed by a reminder letter to prompt | Intervention (N = 126)<br>Control (N = 118) | Proportion of patients who purchased oral bisphosphonates within 25 days of randomization | Intervention: 48.8% patients purchased their oral bisphosphonates<br><br>Control: 30.5% patients purchased their oral bisphosphonate |
| Bianchi et al. 2015<br><br>PMID: 25619634 | Randomized Controlled Clinical Trial | Italy | Postmenopausal women starting osteoporosis treatment | Educational booklets, calendar, alarm clock (Group 2) Phone call reminders and the materials for Group 2 (Group 3) | Group 2 (N = 110)<br>Group 3 (N = 111)<br>Control (N = 113) | Proportion of patients persistent to treatment (taking the drug for ≥80% of time) at 12 months | Group 2: 90.1% persistent<br>Group 3: 84.6% persistent<br><br>Control: 92.0% persistent; (p=0.288) |

MeMO, Medication Monitoring and Optimization program; MPR, Medication Possession Ratio; PCP, Primary Care Physician.
Patient-directed interventions: Behavioral Interventions using Counseling/Coaching, Interventions using medication reminder prompts
Healthcare system interventions: Pharmacist-directed and Fracture Liaison Service

approaches focusing on medication adherence, lifestyle modifications, and mitigating osteoporosis risk factors.[26] These approaches have shown mixed results, with pharmacist screening for osteoporosis risk not improving the rate of osteoporosis diagnosis, while pharmacist-based medication counseling resulted in improved medication adherence at 6- and 12-month intervals.

An extensive pharmacist-directed medication management program using a unified medical record system was the Medication Monitoring and Optimization (MeMO) program, which was implemented in the Netherlands.[15] The MeMO program used a pharmacist information system to store the medication history of enrolled patients and included patient-centered pharmacist-delivered counseling and medication therapy management for several chronic illnesses, including osteoporosis.[15] The MeMO intervention was implemented in two successive phases: an initiation phase and a continuous phase. In the MeMO initiation phase, upon filling their first prescription, patients were given structured counseling education focused on clinical effectiveness and the mechanism of actions of the prescribed medication. Approximately 2 weeks later when they received the next month's prescription, the pharmacist delivered counseling focused on side effects, beliefs, expectations, and discomforts associated with the medication. After the first 3 months, patients entered the 'continuous phase', during which monitoring for suboptimal adherence occurred. During this monitoring phase, patients received telephone calls to discuss medication-related issues (e.g. side effects, benefits of adherence) and to provide other lifestyle interventions (e.g. exercise and dietary advice). The outcomes of the 495 patients enrolled in the MeMO program were compared with those of a reference historical group of 442 patients who did not receive the tailored counseling and monitoring. Therapy discontinuation occurred in 19.0% in the participants in the MeMO program compared with 32.8% in the comparator group ($p$ value $<0.001$). The MeMO program was cost effective in patients initiating osteoporosis therapy, with an incremental cost-effectiveness ratio of €16,000 per quality-adjusted life year (QALY) gained.

While valuable, the MeMO intervention was not evaluated in a RCT and the use of historical controls raises the issue of selection bias that may have influenced the study findings. In addition, patient participation in an intensive program such as MeMO requires extensive system support, including pharmacist access to complete patient medication records, which is difficult in countries like the US that lack a centralized medical record system; patients need to obtain medications from a single pharmacy, and utilization of a pharmacy software system, which can be easily accessible to the pharmacists.

*Fracture liaison service.* The FLS is another example of a healthcare system intervention designed to improve osteoporosis care. FLS is a coordinator-led secondary fracture prevention service designed to improve osteoporosis treatment after fragility fractures.[27] FLS programs can be categorized based on the healthcare professionals involved in the process and the types of activities the healthcare providers perform (e.g. identification, assessment, and treatment of at-risk individuals). For example, the 'type A' FLS has a central coordinator who identifies patients at risk, and investigates and initiates treatment in those who need treatment. In the 'type B' FLS, the FLS coordinator identifies those at risk and refers them back to the primary care physician for further investigation and management. In the 'type C' FLS, the FLS coordinator identifies at-risk patients and informs both the patient and their primary physician of the need to initiate treatment, while in the 'type D' FLS, the coordinator provides patient education only.[28]

We identified three studies that evaluated the implementation of the FLS in Canada, Australia, and France.[16–18] An outpatient population-based 'type C' FLS program, termed 'Catch-a-Break', for patients with low-trauma non-hip fractures,[18] was conducted in Alberta, Canada. The central coordinator reviewed administrative claims data from emergency departments and ambulatory urgent care centers in order to identify patients with low-trauma (fragility) non-hip fractures and the patients were contacted within 6 weeks after fracture. The participants in the study completed questionnaires that included items similar to those in the Fracture Risk Assessment Tool (FRAX). Those with a high risk of fracture (10-year risk of major osteoporotic fracture $\geqslant 20\%$ or risk of hip fracture $\geqslant 3\%$) were asked to follow up with their family physician. The study team contacted high-risk participants who had not been seen by their family physician by a prespecified interval again at 3, 6, and 12 months to encourage a visit with their family physician. A total of 7323 patients were eligible to participate. Participation in the 'Catch-a-Break' program

increased osteoporosis treatment rates by 4% at a cost of about $44 per patient and $9167 per QALY gained. In the year following the fracture, 17.5% [95% confidence interval (CI) 15.6%–19.4%] of the intervention patients were treated with bisphosphonates *versus* 13.2% (95% CI 12.4%–14.0%) of those in a simulated control group who were not in the program. While the results were promising, Catch-a-Break was an open-label clinical trial, the duration of the study was short, (1 year) and long-term rates of recurrent fractures were not calculated.

In another study evaluating an FLS,[16] 102 patients with symptomatic fracture after minimal trauma (i.e. fall from standing height) were referred to the Secondary Fracture Prevention Program in Sydney, Australia. Participants were randomized in two groups: group A (intervention group) participants were managed by specialists in the secondary fracture prevention service for the entire duration of the study ('type A' FLS), while group B (control group) participants were seen in the secondary fracture prevention program twice and then followed up by their primary care physician until the final visit at 24 months. The medication possession ratio (MPR) at 24 months was similar between patients who attended the 3-month study visit compared with those who did not [MPR 0.78, interquartile range (IQR) 0.50–0.93 *versus* MPR 0.79, IQR 0.48–0.96; $p = 0.68$]. Medication persistence at 24 months was also similar in both groups (64% *versus* 61%, respectively; $p = 0.75$). While one of the strengths of this study was that it was a RCT, which showed potential for improved osteoporosis outcomes using a secondary fracture prevention program, the study population was small, with 35 and 39 people in the intervention and comparator arms, respectively. In addition, the study had a high dropout rate of 24% and it is possible that the results lack generalizability with patients who were more likely to be persistent and adherent to treatment being more likely to consent to be randomized for participation in this study.

A third FLS study[17] enrolled patients with low-trauma fracture into a 'type A' FLS program. The study enrolled 335 patients who were followed for over 2 years. The FLS nurse coordinator identified the patients with minimal trauma fractures (vertebral or nonvertebral), assessed for risk factors for fractures, coordinated BMD measurement *via* dual-energy x-ray absorptiometry (DXA) and facilitated prescription of prescribed medications for osteoporosis if needed. Of those participating in this intensive FLS program, 74.1% and 67.4% were still taking osteoporosis treatment at 12 and 18 months, respectively. The main reported reason for treatment discontinuation was nonrenewal of the medication prescriptions. One of the weaknesses of the study was that this was an open-label trial and self-reported data were obtained from patient questionnaires that included some nonvalidated items, which can result in biases, missing data, and inaccurate accounts by patients. In addition, patients with cognitive impairment who did not attend the FLS were not included. The treatment adherence and drug intake were measured by self-report, which can lead to inaccurate accounts.

Taken together, these studies show the effectiveness of the FLS in the management of osteoporosis and medication adherence, but these findings are limited by the relative small sample size of each study, the potential of selection bias, the absence of a control group receiving usual care in some studies and the lack of a randomized study design for two of the three trials reviewed. Further studies involving larger and more diverse populations are needed to better establish the value and cost effectiveness of FLS models of care in the United States healthcare system.

### *Patient-directed behavioral interventions*

*Behavioral interventions using counseling or coaching sessions.* Patient counseling or coaching interventions conducted by nurses, physicians or trained counselors, used counseling approaches and educational sessions on osteoporosis, its treatment, and the importance of healthy lifestyle behaviors.

A controlled clinical trial in Poland included patients on alendronate in whom medication adherence as measured by MPR at 6-month intervals was determined.[19] The patients were divided into four groups based on the type of the intervention they received. There were a total of 32 patients in the control group, 29 in a counseling group (patients received a 30 min counseling session), 31 in a biochemical group (participants were informed about their serum calcium phosphate, alkaline phosphatase, urine calcium, and urine phosphorus levels), and 31 in a nurse-led group (at 3 and 9 months participants received a phone call during which they discussed with a nurse about medication adherence and

appropriate drug intake). In the counseling group, medication compliance (MPR) and persistence at 12 months was 65.52 ± 9.0% compared to the control group 37.5 ± 8.7%. However, this difference was not significant. The findings of this small study are limited because the participants were not randomized and selection bias may have played a role.

A multicenter RCT in Turkey included 448 postmenopausal women between 45 and 75 years of age with osteoporosis.[20] Patients were randomized into active and passive training groups and were followed four times after the initial training visit (visit 1) during 12 months of treatment. Both groups underwent standardized education using booklets providing information on osteoporosis and bisphosphonate therapy, which were included in a 'starter training kit'. The active training groups received additional telephone calls with interactive and educational objectives, and were asked to attend educational sessions. There were no significant differences in medication adherence between active and passive training groups as measured by self-reported medication persistence and compliance [active training group, 152 (50.5%) *versus* passive training group, 149 (49.5%), $p = 0.862$] at 12 months. There were also no significant differences in the Quality of Life European Foundation for Osteoporosis scores between the active and passive training groups at either visit 1 (first month of treatment) or visit 5 (12th month of treatment).

A large RCT included 2097 patients.[21] Both the intervention and the comparator arms were mailed educational materials regarding osteoporosis. Participants in the intervention arm received motivational interviewing *via* telephone from health educators, with each participant receiving about 12 telephone counseling sessions discussing osteoporosis medication, use of vitamin D and calcium supplements, and adverse effects of medication. In addition, the health educators involved in motivational interviewing aimed to understand barriers to treatment access and adherence. The primary endpoint of the study was MPR, which was 49% in the intervention group and 41% in the control group, but this numerical difference did not reach statistical significance. The strengths of this study include its randomized controlled design as well as its large sample size. However, one weakness of this study is the long lag time between enrollment and intervention exposure of 113 days, which may have limited the benefit of intervention, because many patients might have already discontinued the use of their osteoporosis medication by the time of the first study phone call.

*Behavioral interventions using prompts for taking medications.* Behavioral interventions including prompts to take medications through telephone calls, alarm clocks, calendars, and pillboxes coupled with osteoporosis educational booklets were evaluated in two RCTs and one controlled interventional trial. Of the three studies mentioned below, two of them used telephone calls or interactive voice responses as their primary means to deliver the behavioral interventions.

One RCT evaluated whether employing a telephone messaging system to provide prompts to take medications and education to patients was associated with improved medication adherence among 245 patients.[23] The participants in the intervention group received an automated voice response phone call or a voicemail, which instructed the participants about the benefits and risks of the bisphosphonate therapy. Patients could elect to be transferred to the mail order pharmacy to fill the prescription and could indicate if the prescription had already been purchased. If a participant had not filled their prescription within 7 days, a reminder call was made and a letter was sent to prompt the participant to take their osteoporosis medication. The proportion of patients who purchased a prescription within 25 days of study enrollment was significantly higher in the intervention compared with the comparator group (48.8% *versus* 30.5%). Limitations of this study are that phone calls were conducted only in English, and the short duration of follow up of approximately 1 month, which limited the period of time during which medication adherence was measured.

Similarly, another study evaluated whether an intervention prompting medication use through alarm clocks could improve adherence to weekly bisphosphonate therapy among patients with osteoporosis in a small non-RCT included 43 patients in the alarm group and 42 patients in the control group who were followed for 12 months.[22] Patients in the alarm group received an alarm clock that was set to ring on the days they were supposed to take their bisphosphonate to prompt medication-taking behavior. Medication adherence was defined as MPR of at least 0.80. In this study, the MPR (0.80 ± 0.33) in the alarm clock group was higher than

that of the control group (0.56 ± 0.34), indicating that the use of alarms was associated with improved medication adherence. However, the study was small and nonrandomized.

A RCT included 334 patients divided into three groups: a control group (group 1); a group that received educational booklets providing information on osteoporosis, and the importance of adherence to treatment as well as calendars, and an alarm clock to prompt medication administration (group 2); and a group that received all materials used by group 2, and also phone calls by trained physicians and nurses who discussed with patients a list of predefined osteoporosis topics (group 3).[24] This RCT found no significant difference in medication adherence between the three groups. At the end of the study, 90.1% and 84.6% of the participants were persistent in groups 2 and 3 respectively, compared with 92% of the control group ($p = 0.288$). Only 114 (46.1%) out of 247 women starting the trial were considered as fully adherent and persistent (all medication doses taken throughout the 12 months) to treatment. Limitations of the study include the relatively short duration of follow up (12 months), which was not long enough to assess long-term medication adherence. In a subanalysis of this study, the frequency of drug administration was significantly associated with medication adherence, with patients receiving weekly and monthly dosing having a five- and eightfold higher medication adherence, respectively, compared with those exposed to daily administration ($p < 0.0001$).

## Conclusion

Clinical trials data showed that osteoporosis medications significantly reduce the risk of both vertebral and nonvertebral fractures. However, due to suboptimal adherence to osteoporosis drug therapy, patients with osteoporosis face poor clinical and economic effects. Thus, the need to improve adherence is a critical issue in treating patients with osteoporosis. Design of future interventions to improve osteoporosis care can be informed by the experience drawn from the interventions summarized in this review. For example, most interventions included herein were evaluated in non-RCTs, which are prone to selection bias and included small samples. While establishing programs such as the MeMo program, where the intervention was directed towards the pharmacists, or FLS programs, where the interventions included care coordination for patients with fragility fractures, is attractive because these interventions were successful in non-RCTs, these programs were resource intensive and more rigorous testing is advisable before scaling up of these types of programs. Studies that included patient reminders using alarm clocks and telephone calls to promote medication-taking behavior did not improve medication adherence, perhaps due to lack of perceived need for treatment or understanding of their disease process and its relevance to their lifetime overall health status. These patient attributes may define patients 'at high risk' for poor adherence and developing interventional approaches to enhance patient knowledge and understanding of osteoporosis and its consequences may improve the perception of the need for treatment, optimize osteoporosis care, and thereby improve overall outcomes of patients with osteoporosis.

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## Conflict of interest statement

The authors declare that there is no conflict of interest.

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