Osteoporosis International (2019) 30:1627–1634
https://doi.org/10.1007/s00198-019-05010-w

ORIGINAL ARTICLE

# Patients' reasons for adhering to long-term alendronate therapy

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Received: 12 February 2019 / Accepted: 7 May 2019 / Published online: 14 May 2019


## Abstract

**Summary** We aimed to determine patients' reasons for continuing alendronate therapy over 5 years by administering a questionnaire. Bone mineral density, fractures, drugs, Charlson comorbidity index, and lifestyle factors were also considered. Education and awareness of the disease appeared highly associated with good alendronate adherence while worsening health status with discontinuation.

**Introduction** Aim of this study was to investigate patients' reasons for adhering to long-term alendronate therapy (more than 5 years), as data is not available in the current literature regarding the reasons behind long-term adherence.

**Methods** We studied 204 long-term adherent alendronate users: 65 postmenopausal outpatients still adherent (group C, years on treatment = 8.70 ± 1.31) were compared to 139 age-matched patients who discontinued therapy (group S, years on treatment = 8.64 ± 1.43). We evaluated main biochemical parameters, BMD values, fractures, and Charlson comorbidity index (CCI). A questionnaire was administered to analyze the reasons for long-term adherence.

**Results** There were no significant differences between groups concerning baseline DXA values, number of fractures, and CCI. A higher education level was observed in group C (C 54% vs S 35% of patients, $p = 0.001$). At the time of interview, there was a significantly higher number of patients with a CCI of two in group S compared to the beginning of treatment (56% vs 43%, $p = 0.04$), together with a higher number of patients taking more than 3 drugs (22% vs 11%, $p = 0.01$) compared to basal evaluation. Forty-seven percent of patients reported new diseases during the treatment as the main reason for stopping alendronate. A multivariate, stepwise logistic regression analysis showed that awareness of the disease was highly associated with adherence (OR = 0.20; 95% CI 0.045–0.93, $p = 0.04$) followed by higher education (OR = 0.526, 95% CI 0.345–0.801, $p = 0.003$). Worsening of CCI was associated with discontinuation (OR = 2.75, 95% CI 1.033–7.324, $p = 0.04$).

**Conclusions** Education and disease awareness are associated with long-term alendronate adherence while competing health problems negatively impact adherence.

**Keywords** Adherence · Alendronate · Long-term therapy · Osteoporosis

## Introduction

It is well known that there is a strong association between adherence to bisphosphonate (BP) treatment and fracture risk reduction [1, 2]. The term adherence comprises both compliance and persistence to treatment. Compliance refers to how the medication is taken. Persistence is defined as the time from initiation to discontinuation of treatment.

The efficacy of BP has been extensively proven; however, several studies in real-life settings demonstrated a low adherence to this therapy [3–11]. In particular, concerning oral bisphosphonates, Karlsson and colleagues identified 40 retrospective studies reporting a pooled estimate of 12-month persistence of 45% and of 30% after 24 months [12]. Even though investigations differed for type of data source used, type of patients included, and type of oral BP prescribed, however, they all demonstrated a low adherence to therapy. In contrast, a recent study indicated a much higher persistence rate of 75% in patients with a recent fracture [13].

The majority of studies reported adherence with an observation period between 1 to a maximum of 3 years of treatment while addressing patient's reasons to persist

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[13, 14]. However, longer periods of treatment, over 5 years, were beneficial for patients who had previous vertebral fractures or in absence of fractures with a femoral T-score less than − 2.5 SD as shown by FLEX study [15].

To date, the majority of the studies explored reasons for low adherence, rather than reasons for persisting with treatment. In this context, there are no data on the reasons why patients persist in adhering to osteoporosis therapy over long periods of time.

The aim of this study was therefore to investigate, by means of a questionnaire, patients' reasons for both adhering to and for discontinuing long-term therapy (more than 5 years) with alendronate, which is the most prescribed oral bisphosphonate worldwide [16]. We also took into consideration bone mineral density, fractures, concomitant medicine use, comorbidities, lifestyle factors, and socioeconomic variables, all of which have been claimed to be important predictors of persistence for shorter periods (less than 5 years) of alendronate treatment [17, 18].

## Methods

In January 2018, we initiated a retrospective longitudinal observational study at the Metabolic Bone Disease Unit of the University of Rome, "Sapienza" (Italy). Patients' charts were reviewed by two well-qualified physicians in order to identify consecutively new patients (age range 41–78) with an adherence to alendronate therapy of over 5 years (range of therapy 5–10 years). Patients were included if they had a period of observation of approximately 10 years recorded in their charts. From our medical database, we selected a cohort of consecutively identified new users of alendronate, who took this medication for a period of at least 5 years. Inclusion criteria were the presence of vertebral and/or hip fracture or a non-vertebral non-hip fracture with a BMD T score value less than − 3.0 at the lumbar spine or hip site, or in absence of fractures a BMD T score value less than − 3.0 at the lumbar or hip site with a comorbidity or parental history of hip fracture. These represent conditions that, in Italy, render alendronate therapy as reimbursable according to the Italian Regulatory Agency for Drugs (AIFA, Nota 79) [19]. In particular, the comorbidities included were diabetes mellitus type 1, chronic obstructive pulmonary disease, inflammatory bowel disease, severe inability to walk, rheumatoid arthritis or other connective diseases, and multiple sclerosis. The group who continued therapy for more than 5 years (group C) was compared with a group of the same sex and age range who ceased therapy (group S). When the drug was prescribed (one tablet contained 70 mg of alendronate and 5.600 IU of cholecalciferol), patients were instructed to take it once a week with a glass of water avoiding food and drink for 30 min after morning dosing and to remain upright for 30 min. When a poor calcium diet was found by questionnaire [20], they were also given an oral calcium supplementation of 1000 mg daily. Exclusion criteria were previous treatments for osteoporosis, kidney failure, peptic ulcer and, for women, being premenopausal. The study was approved by the "Polyclinic Umberto I" ethical committee. The patients who fulfilled the inclusion criteria were contacted by telephone and asked to return to the University Center.

After obtaining informed consent, patients were asked to complete a self-administered questionnaire; those who were still taking alendronate were again contacted by telephone 6 months later, to confirm that they were currently still adherent. Persistence was based on medical records and patients' information to determine if the medications were taken in a timely manner, at recommended dosages and per physicians' instructions. Subjects were invited to answer the question: "What were the reasons that made you decide to follow alendronate therapy?" by selecting ten possible items, with more than one answer being permitted. Because there was no standardized questionnaire to ascertain the reasons why patients persisted in following this therapy, we created a questionnaire which investigated areas of personal beliefs, fears, economic problems, and side effects related to alendronate therapy. The possible answers are reported in Table 1. Patients who stopped therapy were administered a second questionnaire investigating reasons for discontinuation, with only one answer allowed (Table 2).

Based on the drugs reported in the medical records, the following were considered as drugs that contribute to an increased risk of fractures: proton pump inhibitors, glucocorticoids, antiepileptics, and loop-diuretics. Comorbidity was assessed using the age-adjusted Charlson comorbidity index (CCI) [21]. All patients had the following biochemical evaluation when alendronate was initially prescribed and at the last visit: serum calcium, phosphorus, alkaline phosphatase, creatinine (with estimated creatinine clearance), and 24 h urinary calcium [22, 23]. All patients had an initial spine X-ray evaluation. All fractures reported during the follow-up were non-traumatic; we did not consider those of the skull, fingers, and toes [24]. We performed a vertebral fracture assessment (VFA) by DXA scan when the patients were recalled; during the time frame of alendronate exposure, whenever a vertebral fracture was suspected, a standardized lateral X-ray of the thoracic and lumbar spine was also performed in addition to VFA [25]. Bone mineral density (BMD) of the lumbar spine (L1–L4) in the anterior–posterior projection and of the hip (femoral neck and total hip) was measured in each patient with DXA at the beginning and at 18–24-month interval (Hologic QDR 4500, Hologic Inc., Waltham, MA, USA) [26].

**Table 1** Number of patients who answered yes to the following question: What were the reasons that made you decide to follow alendronate therapy? Multiple choices were permitted

| | Group S ($n = 139$) | Group C ($n = 65$) |
|---|---|---|
| 1. I understood the seriousness of the disease. | 122 (88%) | 63 (97%) * |
| 2. I suffered from one or more fractures. | 62 (45%) | 29 (45%) |
| 3. The therapy was easy to take. | 98 (71%) | 52 (80%) |
| 4. I trusted the Polyclinic specialized center and the suggested therapy. | 116 (83%) | 59 (91%) |
| 5. I never had any adverse events. | 90 (65%) | 36 (55%) |
| 6. My family doctor also agreed with the therapy. | 77 (55%) | 36 (55%) |
| 7. I often fell down so that I was afraid of fractures. | 120 (86%) | 60 (92%) |
| 8. My mother had a hip fracture and I was afraid that this could happen also to me. | 50 (36%) | 22 (34%) |
| 9. I believed the therapy would decrease my bone pain. | 74 (53%) | 33 (51%) |
| 10. I observed improvements in my densitometric values. | 109 (78%) | 50 (77%) |

*$p \leq 0.05$

## Statistical analysis

All statistical analyses were performed using SPSS for Windows version 13 (SPSS Inc., Chicago, IL, USA). Categorical variables are described with numbers and percentages. Continuous variables are expressed as mean value ± SD. Differences between groups were assessed with Student's *t* test for continuous variables and chi-squared test for categorical variables. A model of multivariate, stepwise logistic regression analysis was carried out considering alendronate discontinuation as the dependent variable and considering as independent variables those variables that resulted statistically different between patients who stopped alendronate therapy compared to those who continued alendronate. A $p$ value < 0.05 was considered statistically significant.

## Results

A group of 65 consecutive patients (group C), who were currently taking alendronate therapy for at least 5 years, were evaluated and compared to 149 patients (group S), with the same sex and within the same age range, who stopped alendronate after the same period of time. Ten patients in group S refused to return to our center to complete the questionnaire. Mean years since the beginning of alendronate therapy did not differ between groups (group S 8.64 ± 1.43 vs group C 8.70 ± 1.31 years, $p = 0.77$). The main reason for starting alendronate therapy was represented by fragility fractures (in group S 91% vs 86% of patients in group C, $p = 0.34$).

There was no difference between the two groups, concerning the well-known risk factors for osteoporosis, when alendronate treatment was initially prescribed (Table 3). The only difference at baseline between groups S and C was a significantly higher number of patients in group C who had achieved a higher level of education (patients who attended high school only and patients who attended high school plus university). Indeed, in group C, 54% of the patients had attended high school and/or university compared with 35% of patients in group S (Table 3, $p = 0.001$). Age-adjusted Charlson comorbidity index was similar in the two groups at baseline, as well as current medication and number of patients with secondary osteoporosis (group S 13% vs group C 14% of patients, $p = 0.82$) (Table 4). Glucocorticoid-induced osteoporosis was the most common secondary form of osteoporosis reported. The biochemical parameters, lumbar and femoral BMD, and the number of patients with fractures were not

**Table 2** Reason for discontinuation in group S

| | Group S ($n = 139$) |
|---|---|
| 1. Gastrointestinal side effects | 22 |
| 2. New fractures during alendronate therapy | 10 |
| 3. Economic problems (not drug related) | 18 |
| 4. Fear of possible side effects due to dental surgery | 19 |
| 5. Not convinced of the effectiveness of the therapy | 21 |
| 6. Onset of new diseases | 31 |
| 7. Difficulty in correctly taking the prescribed therapy | 18 |

**Table 3** Initial anthropometric parameters in patients still long-term adherent (group C) and those that discontinued (group S)

| | Group S ($n = 139$) | Group C ($n = 65$) |
|---|---|---|
| Anthropometric parameters | | |
| Age (years) | 62.1 ± 7.2 | 63.9 ± 7.6 |
| F/M | 132/7 | 52/8 |
| Age at menopause | 48.3 ± 5.1 | 48.8 ± 3.9 |
| Body mass index (kg/m$^2$) | 24.1 ± 2.5 | 23.7 ± 3.2 |
| Education (number of patients) | | |
| Elementary school | 40 (29%) | 12 (18%) |
| Secondary school | 50 (36%) | 18 (28%) |
| High school | 32 (23%) | 23 (35%) |
| University | 17 (12%) | 12 (18%) |
| High school only+ (high school+ university) | 49 (35%) | 35 (54%)* |
| Occupation (number of patients) | | |
| Retired | 24 (17%) | 6 (9%) |
| Employee | 40 (29%) | 20 (31%) |
| Housekeeper | 54 (39%) | 23 (35%) |
| Unemployed | 15 (11%) | 10 (15%) |
| Other activities | 6 (4%) | 6 (9%) |
| Risk factors for osteoporosis (number of patients) | | |
| Parental history of hip fractures | 51 (37%) | 24 (37%) |
| Alcohol (more than 3 units per day) | 11 (8%) | 10 (15%) |
| Smoking (more than 5 cigarettes per day) | 39 (28%) | 24 (37%) |

Results are presented as mean ± 1 SD, or number of patients

*$p \leq 0.05$

statistically different between groups at baseline (Table 5). In particular, the majority of patients had at least one vertebral fracture (group S 60% vs group C 54% of patients, $p = 0.45$).

Based on the responses to the questionnaire, the majority of patients indicated that the awareness of the disease was the reason for adhering to the prescribed therapy (Table 1). However, the number of patients who understood the seriousness of the disease was higher in group C than in group S (group C 97% vs group S 88% of patients, $p = 0.03$). The second reason for adhering, in both groups, was the fear of falling down and having a new fracture. Also of interest was the high number of patients who indicated the absence of side effects and an improvement in the densitometric values as reasons for persisting. However, the number of patients who expressed these reasons for alendronate adherence was not statistically different in the two groups (Table 1).

The main reason for stopping alendronate therapy in group S was related to the appearance of new diseases during the treatment (47% of patients), which discouraged them from taking this drug (Table 2). The second reason among those who discontinued treatment was gastrointestinal side effects.

We considered clinical, biochemical, and DXA values when the alendronate treatment was stopped in the group S. For the group who continued (group C), we referred to DXA, clinical and biochemical data for the same period of time, which was approximately after 8 years of treatment. Considering biochemical changes over the entire period of observation, there were no significant changes in both groups (data not shown). The only change, among the biochemical parameters studied, was a reduction of alkaline phosphatase which was significantly different from values at the beginning of the therapy in both groups ($p < 0.05$) (Table 5). After 8 years, group C had a significantly lower value compared to group S at the end of the period studied (group C 85.38 ± 33.68 vs Group S 98.96 ± 47.12 IU/L, $p = 0.03$).

Both groups C and S showed significant improvement of lumbar BMD values after alendronate prescription, but group C had a higher final value of BMD compared to group S (group C 0.847 ± 0.121 vs group S 0.788 ± 0.141 g/cm$^2$, $p = 0.004$) and had a higher final lumbar BMD T-score (group C − 1.88 ± 1.09 vs group S − 2.33 ± 1.28 SD, $p = 0.01$). Regarding total femoral BMD and corresponding T-score, both groups had a statistically significant improvement without significant differences between groups. In particular in group S, the total femoral BMD at the beginning of the therapy was 0.716 ± 0.170 and at the end 0.759 ± 0.141 g/cm$^2$ ($p = 0.02$), while total femoral T-score was − 1.80 ± 0.76 and − 1.55 ± 0.82 SD ($p = 0.008$), respectively. In group C, we

**Table 4** Initial comorbidities and therapy in patients still long-term adherent (group C) and those that discontinued (group S)

| | Group S ($n = 139$) | Group C ($n = 65$) |
|---|---|---|
| Comorbidities | | |
| Charlson comorbidity index (CCI) | | |
| Number of patients with CCI 0 | 9 (6%) | 3 (5%) |
| CCI 1 | 48 (35%) | 15 (23%) |
| CCI 2 | 60 (43%) | 34 (52%) |
| CCI 3 | 18 (13%) | 12 (18%) |
| CCI 4 | 2 (1%) | 1 (2%) |
| CCI 5 | 2 (1%) | 0 (0%) |
| Secondary osteoporosis | 18 (13%) | 9 (14%) |
| Number of patients taking therapy | | |
| No therapy | 37(27%) | 13(20%) |
| 1 drug | 22 (16%) | 11 (17%) |
| 2 drugs | 18 (13%) | 8 (12%) |
| 3 drugs | 16 (12%) | 7 (11%) |
| 4 drugs | 12 (9%) | 6 (9%) |
| 5 drugs | 14 (10%) | 7 (11%) |
| More than 5 drugs | 20 (14%) | 13 (20%) |
| Drugs that may raise fracture risk* | 40 (29%) | 16 (25%) |
| Calcium supplements (1000 mg/day) | 112 (81%) | 48 (74%) |
| Duration of alendronate therapy (years) | 8.64 ± 1.43 | 8.70 ± 1.31 |

Results are presented as mean ± 1 SD, or number of patients

*Including proton pump inhibitors and/or glucocorticoids and/or antiepileptic and/or loop-diuretics

found the total femoral BMD at the beginning of the therapy to be 0.743 ± 0.09 and at the end 0.779 ± 0.103 g/cm$^2$ ($p$ = 0.03). The total femoral T-score was − 1.66 ± 0.64 at the beginning of the therapy and − 1.4 ± 0.79 SD ($p$ = 0.04) at the end. Few new fractures occurred during alendronate treatment; there was no differences in the number of patients who experienced new peripheral fractures in group S, compared to group C (10 vs 6 patients, $p$ = 0.58). Considering morphometric vertebral fractures, we found 3 new fractures in group S and none in group C ($p$ = 0.55).

Only in group S there was a significantly higher number of patients with a CCI of two at the end of the alendronate treatment compared to initial treatment (43% vs 56% of patients, $p$ = 0.04), while in group C, the increase was not statistically significant (52% vs 60%, $p$ = 0.4).

In both groups, during the entire period of observation, we found a higher number of patients with new diseases together with a decreased number of patients not taking any drug daily. However, the reduction of the number of patients not taking any drug daily was significant only in group S (37 vs 22 patients, $p$ = 0.01; group C 13 vs 10 patients, $p$ = 0.66). In both groups, there was an increased number of patients taking more than 3 drugs, but this was only statistically significant in group S (31 vs 16 patients, $p$ = 0.01; group C 7 vs 10 patients, $p$ = 0.61). Calcium supplements were taken independently of alendronate by a lower number of patients 8 years after initial alendronate prescription in both groups. Approximately 11% of patients stopped these supplements; this percentage was not statistically significant neither as regard the patients starting date of therapy nor between groups at the end of the study period.

Considering the variables that were significantly different between group S and C (which were a higher awareness of the disease and a higher level of education in group C, and in group S a worst CCI and a higher number of drugs taken, after 8 years of treatment), a model of multivariate stepwise logistic regression was carried out, considering discontinuation of the alendronate treatment as a dependent variable (Table 6). The awareness of the disease was highly associated with alendronate adherence with an odds ratio (OR) equal to 0.20 (95% CI 0.045–0.93, $p$ = 0.04) followed by a higher level of education (OR = 0.526, 95% CI 0.345–0.801, $p$ = 0.003). Worsening health status (as shown by the significant difference between CCI at the beginning and the end of the study period compared to those with a stabile burden) was associated with discontinuation (OR = 2.75, 95% CI 1.033–7.324, $p$ = 0.04). The difference in the amount of drugs taken by patients at the end of therapy compared to the beginning was not statistically significant in a stepwise regression analysis ($p$ = 0.08).

**Table 5** Initial biochemical evaluation, bone density values, and number of fractures in patients still long-term adherent (group C) and those that discontinued (group S)

| | Group S ($n = 139$) | Group C ($n = 65$) |
|---|---|---|
| Biochemical parameters | | |
| Creatinine clearance (ml/min × 1.73 $m^2$) | 79.1 ± 15.6 | 76 ± 18.4 |
| Calcium (mg/dL) | 9.5 ± 0.5 | 9.6 ± 0.4 |
| Phosphorus (mg/dL) | 3.6 ± 0.5 | 3.6 ± 0.7 |
| Alkaline phosphatase (IU/L) | 115.4 ± 49.3 | 126.6 ± 45.1 |
| 24 h urinary calcium (mg/24 h) | 175.2 ± 84.9 | 184.1 ± 87.5 |
| Fractures | | |
| Subjects with fractures | 126 (91%) | 56 (86%) |
| Subjects with vertebral fractures | 83 (60%) | 35 (54%) |
| Subjects with > 1 vertebral fracture | 19 (14%) | 8 (12%) |
| Subjects with hip fracture | 5 (4%) | 1 (2%) |
| Subjects with non-vertebral, non-hip fracture | 38 (27%) | 20 (31%) |
| Subjects with > 1 non-vertebral non-hip fracture | 37 (27%) | 19 (29%) |
| Bone mineral density (BMD) | | |
| BMD L1–L4 (g/$cm^2$) | 0.749 ± 0.11 | 0.774 ± 0.08 |
| T-score L1–L4 | − 2.73 ± 1.04 | − 2.53 ± 0.85 |
| BMD femoral neck (g/$cm^2$) | 0.616 ± 0.08 | 0.619 ± 0.06 |
| T-score femoral neck | − 2.14 ± 0.74 | − 2.22 ± 0.59 |
| BMD total hip (g/$cm^2$) | 0.716 ± 0.10 | 0.743 ± 0.09 |
| T-score total hip | − 1.86 ± 0.76 | − 1.66 ± 0.64 |

Results are presented as mean ± 1 SD and number of subjects

## Discussion

This study investigates, for the first time, patients' reasons for long-term adherence to alendronate treatment together with reasons for discontinuation after long-term adherence. In addition to analyzing these reasons, bone mineral density, fractures, concomitant drugs taken, comorbidities, lifestyle factors, and socioeconomic variables are also reported. It should be kept in mind that in our particular population, alendronate therapy was reimbursed by the Italian National Health System, therefore excluding possible biases due to economic constraints related to drug cost.

Our results are mainly in line with the latest review article [27], which included studies with a shorter follow-up time and analyzed adherence to all drugs currently available for osteoporosis therapy. In this review, poorer medication adherence was related to older age and misconceptions about osteoporosis, higher dosing frequency, and medication side effects [27]. A previous Italian survey of osteoporotic women taking several anti-osteoporotic treatments showed that the main reasons for discontinuation were side effects and lack of motivation. In that survey, the adherence to treatment was higher in patients with severe and well-documented osteoporosis; however, the study was carried out for a short period of time [18].

We have demonstrated that, in the long-term therapy, awareness of the disease is 80% associated with adherence together with a higher education level (48% associated). A previous study showed that a self-perception of fracture risk, which captures some aspects of fracture risk not currently measured using conventional fracture prediction tools, was also associated with improved medication uptake [28]. Another point of interest in our investigation was that worsening health conditions were one of the major reasons for stopping alendronate therapy; this was not only subjectively assessed by questionnaire but also objectively ascertained by CCI. Thus, competing diseases occurring during

**Table 6** Multivariate, stepwise logistic regression analysis in all samples considering the discontinuation to alendronate therapy

| Variables | *B* | Wald | Sig. | OR | 95% CI | |
|---|---|---|---|---|---|---|
| | | | | | Inferior | Superior |
| Level of education | − 0.643 | 8.975 | 0.003 | 0.526 | 0.345 | 0.801 |
| Disease awareness | − 1.585 | 4.220 | 0.040 | 0.205 | 0.045 | 0.930 |
| CCI at the end–CCI at baseline | 1.012 | 4.097 | 0.043 | 2.750 | 1.033 | 7.324 |
| Constant | 3.525 | 15.577 | 0.000 | 33.967 | | |

*CCI* Charlson comorbidity index

osteoporosis treatment may reduce alendronate adherence. This finding should alert physicians that in a long-term treatment, worsening health conditions should deserve higher attention regarding patients' adherence to alendronate therapy.

In addition, we reported patients' concerns about safety. In particular, fear of possible osteonecrosis of the jaw during dental procedures caused some patients to stop treatment, a finding already shown by other studies [10, 29]. Correct information offered to patients may decrease the number of subjects who stop alendronate therapy. Low compliance is multifactorial, probably a consequence of fear of adverse events, together with the lack of specific symptoms associated with reduced bone mass [29].

The present study had some limitations. Due to the observational and retrospective nature of the study, we did not report the alendronate possession ratio and relied on voluntary patient information to determine if the medications were taken in a timely manner, at recommended dosages and per physicians' instructions. The finding of higher mean levels of alkaline phosphatase together with lower mean BMD values reached at the end of the observation period in patients non-adherent in respect to those that were still adherent seem to suggest a lower possession rate. These findings reinforce the concept that optimal and longer alendronate adherence translates in better biochemical and densitometric outcomes. We only relied on changes in bone densitometry results as a parameter to judge the effectiveness of therapy; however, it cannot be excluded that a measurement of specific bone resorption markers, after few months of treatment and during follow-up, might have improved adherence, as it has been shown in studies carried out for a shorter period of treatment [30].

In conclusion, our investigation demonstrates that optimal adherence to alendronate therapy is probably facilitated by the level of the patients' education. In our study, worsening health conditions are associated with almost three times more likely probability of alendronate discontinuation; this emphasizes the poor knowledge of complications of osteoporosis (i.e., fractures) in respect to other diseases. Undertreatment, in patients with fragility fractures, adversely impacts on public health outcomes and mortality, a finding already shown in community-based population [31].

## Compliance with ethical standards

**Conflicts of interest** None.

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