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Adherence to osteoporosis pharmacotherapy one year after osteoporotic fracture – a Swiss trauma centre secondary prevention project

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Summary

AIMS OF THE STUDY: According to current evidence, one out of ten fracture patients with osteoporosis does not sustain another fracture if he or she is on adequate medication. However, epidemiological surveys show that only about 15 to 30% of affected patients avail themselves of the treatments. This cohort study investigated how many fracture patients with a recommendation for antiosteoporotic therapy effectively received treatment and the possible reasons why the treatment was not implemented.

METHODS: As part of a quality improvement programme in a Swiss trauma centre, fracture patients were actively checked for osteoporosis in accordance with a standardised outpatient programme. The results, together with detailed therapy recommendations, were transmitted to each patient's general practitioner (GP). A prospective questionnaire survey evaluated all patients with a diagnosis of osteoporosis for subsequent realisation of therapy 1 year after the fracture (mean ± standard deviation; chi-square; analysis of variance; significance level $p < 0.05$).

RESULTS: A total of 305 patients received a recommendation for antiosteoporotic therapy, of whom 18 (5.9%) died before 1 year. The questionnaire was completed for 255 out of 287 patients (follow-up 88.9%; 73.8±11.5 years old at the time of survey; 77.7% female). Of these, 117 patients (45.9%) sustained a fracture of the lower extremities and 105 patients (41.1%) a fracture of the upper extremities; 33 patients (13%) had other or multiple fractures. Fifty-two cases (20.4%) had pre-existing osteoporosis at the time of fracture. At the 1-year follow-up, 132 (52%) patients were receiving prescribed drugs. The most frequent patient explanation for not taking treatment (n = 123) was, in 47.2% of cases (n = 58), that none had been prescribed; 30.1% of patients were not interested. Multivariate analysis of verifiable factors of influence confirmed that fracture patients were treated significantly more reliably with antiosteoporotic therapy if osteoporosis was diagnosed with dual energy x-ray absorptiometry alone in patients with fewer comorbidities, and that fracture patients persisted significantly more reliably with antiosteoporotic therapies when pre-existing osteoporosis was present (R^2 0.17; $p < 0.001$).

CONCLUSIONS: Following a standardised diagnostic work up for osteoporosis as part of fracture treatment, and including the communication of recommendations for antiosteoporotic therapy to the GP, only every second patient actually received the proposed treatment. This appears to be better than described in the literature but still calls for improvement. Two different solutions appear to be possible based on these findings: to endeavour to better inform and convince GPs about the need for treatment and/or for the diagnosing team to initiate antiosteoporotic therapy where indicated rather than just recommending it.

Key words: osteoporosis, fragility, fracture, therapy, adherence, secondary prevention, compliance, follow-up, quality control, survey

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Introduction

Osteoporosis is a systemic bone disease resulting in an increased risk of fracture due to reduced bone mineral density and microarchitecture [1]. The probability of sustaining an osteoporotic fracture at the age of 50 years in Switzerland is reported to be 51% for women and 20% for men [2]. The occurrence of an osteoporotic fracture is not only associated with the risk of further fractures [3], but also with increased morbidity and mortality of the affected patients. Randomised controlled trials have demonstrated that treatment of osteoporosis in patients with fragility fractures can reduce the risk of subsequent fractures by up to 50% and mortality rates by up to 30% [4–6]. Although fragility fractures are associated with considerable healthcare costs and dramatic consequences, most cohort and epidemiological studies continue to report low implementation rates for antiosteoporotic therapy of about 15 to 30% following osteoporotic or fragility fractures [7–12]. This impressive underuse of therapy is even more astonishing in the light of the fact that studies such as the one published by Kanis et al. from the UK [13] demonstrated that pharmacological therapy (generic alendronate) was

cost-effective in the prevention and treatment of fractures, with a 10-year probability for a major fracture that exceeded 7% in women. German insurance evaluations in almost 270 000 patients [14] found that, depending on the medicaments, 17 to 66% of patients regularly took prescribed bisphosphonates 1 to 2 years after their fracture. Just 2 years after regular intake of antiosteoporotic medicaments the affected women showed a significantly decreased rate of subsequent fractures in comparison with women who did not take their medication in a reliable way. In multivariate testing, reliable intake was the only variable to significantly decrease the risk of subsequent fractures [15]. It is known that interventions such as sending therapy recommendations or reminder e-mails to the attending general practitioner (GP) or patient can increase the number of patients undergoing diagnostic procedures or receiving therapy for osteoporosis [16–18]. It has been proven that such interventions are cost effective and that the effect may actually last for the longer term [19].

Rosenwasser et al. underlined that after a fracture the treating orthopaedic surgeon has the full attention of the injured patient and therefore plays a major role in steering patients into osteoporosis screening programmes and subsequent treatment [20]. Studies from Germany [21] and Canada [20], for example, have shown that if the surgeon initiates the process by ordering a bone densitometry examination, the patient is more likely to get treatment for their underlying disease than if it is just suggested that the patient see their medical doctor at some future date. Several years ago in Geneva, a clinical osteoporosis pathway for the management of patients with low trauma fracture in a selected population of 384 patients recruited over 3 years achieved the result that about two thirds of patients who received specific antiosteoporotic therapy were still on therapy 6 months later [22]. But even after more than a decade of national and international efforts and many articles demonstrating the need to take secondary fracture prevention seriously, recent reports indicate that the treatment gap for patients presenting with a fragility fracture may even have worsened [23].

Against this background, the aim of this 1-year follow-up quality-control study at a Swiss trauma centre was to verify the implementation and adherence rate of antiosteoporotic therapy in patients who, on sustaining a new fracture, went through standard diagnostic procedures and were given specific recommendations for antiosteoporotic therapy. Given the lack of knowledge as to why patients in effect do not take antiosteoporotic remedies even though specifically recommended, the reasons for lack of compliance were investigated in more detail in this patient survey.

Materials and methods

The prospective observational investigation was approved by the Cantonal Ethics Board, EK2013/036 (NCT 02157753).

The main goal of this quality-control study was to verify the implementation of and the adherence to specific therapy in patients who had sustained a fracture 1 year earlier and for whom the indication for antiosteoporotic therapy was assessed and the therapy accordingly recommended. In addition, for patients not taking antiosteoporotic remedies even though recommended, we wanted to identify the reasons impeding therapy: first, by analysing possible factors of influence gathered via standard data management (e.g., age of patient, status of living, trauma energy evaluated as described by patient or next of kin, type of osteoporosis diagnosis [by dual energy x-ray absorptiometry, DXA, for T-Score-values <-2.5 only versus additional use of the WHO Fracture Risk Assessment Tool, FRAX in cases with a T-score ≥-2,5], comorbidities [using the age unadjusted Charlson score [24]]) and second, by asking patients additional specific questions (prejudice, adverse events, contraindication overlooked, financial problems, etc.) using a postal questionnaire. If the information was not available directly from patients, it was taken from their GPs using the same procedure. Data collection was undertaken by a study nurse (S.M.), who additionally phoned patients or their GP to request missing data.

The investigation took place in the trauma unit of a Swiss trauma centre where about 500 fracture patients aged 50 or older are hospitalised per year. In 2012, a standard diagnostic pathway was introduced for this group of fracture patients, independent of gender or the level of causal trauma energy. It included DXA, a standard questionnaire to evaluate risk of osteoporosis, the FRAX and a focused laboratory workup. Taking all this information into account, a detailed therapy recommendation was formulated by a rheumatology specialist in the field (C.H.) in accordance with current guidelines [25] (http://www.svgo.ch) and sent to the relevant general practitioner. The study cohort under evaluation for this investigation comprised all consecutive patients for whom a recommendation for the therapy of osteoporosis was given. The main outcome measure was the percentage of persons who consistently took their antiosteoporotic remedies, based on patients' self declaration and/or the information provided by GPs.

Data are given as n (%) or mean ± standard deviation (SD) if not stated otherwise. Chi-square tests were used to compare binary variables, and analysis of variance (ANOVA) to compare mean values of continuous variables. Forward stepwise multivariate logistic regression analysis was performed to identify independent predictors on the use versus non-use of specific antiosteoporotic therapy. The significance of each variable was assessed with the likelihood ratio test; odds ratio (OR) and 95% confidence interval (CI) were calculated. All p values were two-tailed.

Results

Of the 305 cases with a recommendation for antiosteoporotic therapy in accordance with our protocol, 287 (94.1%) were still alive 1 year after they sustained their fracture. Of these, responses were received for 255 cases (88.9%) at the 1-year follow-up: in 193 cases from patients (75.7%) and in 62 cases (24.3%) from the participating GPs.

The characteristics of fracture patients who responded to the survey versus those cases where their GP responded are given in table 1. Groups were not different with regard to patients' age or gender, level of causal trauma energy, or type of indication for therapy of osteoporosis. In cases where GPs' answers were used patients had more comorbidities (Charlson) and were significantly more often living in a nursing home.

Of the 255 investigated patients, 117 (45.9%) sustained a fracture of the lower and 105 (41.1%) a fracture of the upper extremities; 33 patients (13%) had other or multiple fractures. At the 1-year follow-up, 132 (52%) of all patients with an indication for antiosteoporotic therapy actually received specific antiosteoporotic drugs. This rate did not differ whether the information was given by patients themselves (101/193; 52%) or by their GP (31/62; 50%). Of the 132 patients who received antiosteoporotic specific drugs, 85 (65%) took bisphosphonates, 32 (25%) denosumab and 13 (10%) other medication. Forty-four percent of patients (n = 57) took their remedies by themselves; in 48% (n = 62) treatment was given by GPs and in 8% (n = 11) it was given differently. Two patients took their medication on a daily basis (1.5%), 50 (38.5%) weekly, 5 (3.8%) monthly, 21 (16.2%) quarterly, 32 (24.6%) twice a year and 9 (8.5%) once a year. In 13 cases there were different combinations or the information was not complete. Overall, 188 patients (74.6%) took calcium and 194 (77%) vitamin D.

In univariate analysis, the subgroup of patients who did not take specific antiosteoporotic remedies were found to be more ill according to the Charlson Score (p <0.001) and osteoporosis was diagnosed more often on the basis of pathological osteodensitometry (DXA) only (vs with additional FRAX). In addition, patients who did not take antiosteoporotic drugs showed a tendency to be older (p = 0.09), living in a nursing home (p = 0.07) or had sustained a fracture other than of the radius or the femur (p = 0.07; table 2). Patients with an existing osteoporosis diagnosis at the time of fracture (20.4%, table 1) were found at follow-up to take their antiosteoporotic medicaments more consistently compared with patients without a previous diagnosis of osteoporosis (p = 0.002, table 2).

Stepwise regression analysis verified that the type of diagnosis for osteoporosis, patients' comorbidities and a preexisting osteoporosis diagnosis at the time of fracture were

Table 1: Characteristics of patients who responded to the survey (n = 193) versus cases where only their general practitioner responded (n = 62).

		Response to survey by			
		Patient	General practitioner	Total	
		n = 193	n = 62	n = 255	
		n (%) or mean ± SD			p-value
Age at the time of fracture (years)		72.4 ± 11.5	75.3 ± 12.0	73.1 ± 11.6	0.094
Gender	Male	43 (22.3%)	11 (17.7%)	54 (21.2%)	0.447
	Female	150 (77.7%)	51 (82.3%)	201 (78.8%)	
Living status	Living at home	176 (91.2%)	41 (67.2%)	217 (85.4%)	0.000
	Nursing home	17 (8.8%)	20 (32.8%)	37 (14.6%)	
Age unadjusted Charlson Score		0.57 ± 1.00	1.35 ± 1.83	0.76 ± 1.30	0.000
Trauma energy	Low	163 (84.5%)	57 (91.9%)	220 (86.3%)	0.137
	High	30 (15.5%)	5 (8.1%)	35 (13.7%)	
Osteoporosis known at the time of fracture	No	155 (80.3%)	47 (77%)	202 (79.5%)	0.582
	Yes	38 (19.7%)	14 (23%)	52 (20.5%)	
Type of diagnosis for indication of osteoporotic therapy	Osteopenia + FRAX	64 (33.2%)	19 (30.6%)	83 (32.5%)	0.713
	Osteoporosis (DXA)	129 (66.8%)	43 (69.4%)	172 (67.5%)	
Receiving specific osteoporotic therapy	No	92 (47.7%)	31 (50%)	123 (48.2%)	0.749
	Yes	101 (52.3%)	31 (50%)	132 (51.8%)	

DXA = dual energy x-ray absorptiometry; FRAX = World Health Organization Fracture Risk Assessment Tool

Table 2: Impact of variables on the utilisation of specific antiosteoporotic therapy.

		Use of specific osteoporotic therapy		
		No	Yes	
		n = 123	n = 132	
		n (%) or mean ± SD		p-value
Age at the time of fracture (years)		73.7 ± 12.1	72.5 ± 11.22	0.094
Age category	below 60 years	22 (48.9%)	23 (51.1%)	0.268
	60–69 years	29 (50%)	29 (50%)	
	70–79 years	25 (39.1%)	39 (60.9%)	
	over 80 years	45 (55.6%)	36 (44.4%)	
Gender	Male	25 (46.3%)	29 (53.7%)	0.748
	Female	98 (48.8%)	103 (51.2%)	
Living status	Living at home	100 (46.1%)	117 (53.9%)	0.070
	Nursing home	23 (62.2%)	14 (37.8%)	
Age unadjusted Charlson score		0.97 ± 1.50	0.57 ± 1.04	<0.001
Trauma energy	Low	105 (47.7%)	115 (52.3%)	0.684
	High	18 (51.4%)	17 (48.6%)	
Fracture	Femur	36 (45%)	44 (55%)	0.229
	Pelvis	5 (50%)	5 (50%)	
	Lower limbs except femur	18 (48.6%)	19 (51.4%)	
	Radius	22 (37.9%)	36 (62.1%)	
	Upper extremities except radius	27 (57.4%)	20 (42.6%)	
	Others	2 (100%)	0 (0%)	
	Several	13 (61.9%)	8 (38.1%)	
Fracture category	Femur	36 (45%)	44 (55%)	0.070
	Radius	22 (37.9%)	36 (62.1%)	
	Others	65 (55.6%)	52 (44.4%)	
Osteoporosis known at the time of fracture	No	107 (53%)	95 (47%)	0.002
	Yes	15 (28.8%)	37 (71.2%)	
Type of diagnosis for indication of osteoporotic therapy	Osteopenia + FRAX	55 (66.3%)	28 (33.7%)	<0.001
	Osteoporosis (DXA)	68 (39.5%)	104 (60.5%)	

DXA = dual energy x-ray absorptiometry; FRAX = World Health Organization Fracture Risk Assessment Tool

factors significantly associated with greater patient adherence to their prescribed antiosteoporotic regimen (R^2 0.17; p <0.001; table 3).

The most frequently expressed arguments for why patients did not take specific antiosteoporotic remedies (n = 123) were in 43.9% (n = 54) that they were not prescribed any and in 17.9% that they were not interested in taking the medication (table 4).

Discussion

This consecutive survey in fracture patients aged 50 years or older for whom osteoporosis was diagnosed following a standard diagnostic procedure and appropriate therapy was actively recommended to the participating GP revealed three major findings.

First, despite a procedure of active assessment and recommendation efforts, only every second patient with the indication for anti-osteoporotic therapy had received it at one year follow-up.

Recent reports and population-based evaluations from the US [23, 26], Germany [27], Switzerland [18] or the UK [28], for example, show that only in about 10 to 30% are diagnostic tests and/or treatment for osteoporosis adequately executed following fragility fractures or the diagnosis of osteoporosis. Studies on medication use beyond 6 months after initiation of antiosteoporotic therapy mostly report adherence rates ranging from 17 to 56% [29]. In Switzerland, a treatment gap of 58% was found for women at high risk of fracture [30]. A former evaluation in Swiss centres dedicated to the treatment of osteoporosis revealed that only 22% of patients were adequately treated after an acute fragility fracture [18].

Our finding at 1-year follow up of a 52% adherence rate to specific therapy in patients who sustained an osteoporotic fracture appears to be disappointing at first glance. On the other hand, the literature cited above indicates that this rate is in the upper range of reported experiences. This is even more valid given that it was achieved without any dedicated gerontotraumatological procedures, but simply by encouraging routine trauma surgeons to actively identify at-risk patients and recommend appropriate therapy based on an interdisciplinary approach.

A study from the Netherlands comparing a hospital with a dedicated fracture liaison service with one without reported that patients seen at the fracture liaison service had a 56% decreased risk of nonvertebral fracture and a 35% lower mortality than those not seen at the fracture liaison service during the 2-year follow-up period [31]. For intervention programmes, divergent success rates have been reported in the literature (some of them randomised studies) with several interventions showing no success at all [32, 33]. A Cochrane systematic review could not identify one single intervention or bundle of specific combinations that worked best in this field. The authors underlined that the most efficacious multifaceted interventions all involved interactions between study subjects and healthcare professionals: for each of the interventions that led to statistically significant improvements in adherence, the intervention subjects had periodic one-on-one follow-up with trained healthcare professionals [34]. Literature data have shown that it is unrealistic to expect that a one-dimensional intervention such as education or feedback based on response to therapy could significantly improve adherence and reliability across a diverse population [32]. Nevertheless, patients' belief in a particular medication appears to contribute to better adherence and can be improved by firmly associating treatment with expected benefits such as reduced risk of fracture and, consequently, an improved quality of life [35]. Convincing every single patient and their doctor not only to follow the relevant diagnostic procedure but also to implement and persist with therapy, if indicated, continues to be an ongoing and laborious challenge in the field of treatment for osteoporosis.

Second, few studies have investigated possible factors of influence to explain why patients with an indication for antiosteoporotic therapy do not receive it [34, 36, 37]. Looking in more detail at cases where indicated therapy was not implemented in our setting, multivariate analysis disclosed three main factors.

First, it was found that in cases where the indication for therapy was based on FRAX and not on DXA alone, antiosteoporotic therapy was implemented less often. Even though GPs for all of these patients received a written specific therapy recommendation based on the same standard diagnostic procedure, including DXA and additional FRAX scoring in cases of osteopenia, they were more likely to implement the therapy recommendations when osteoporosis was diagnosed by DXA only. Originally, the definition of osteoporosis relied on the WHO-based T-score of bone mineral density (BMD). According to this definition, only subjects with a T-score at or below -2.5 were consid-

Table 4: Reasons given for why patients did not take specific antiosteoporotic remedies (multiple answers possible, n = 123).

	No. yes	% yes
Missing prescription	54	43.9%
Not necessary, no interest	22	17.9%
Being too old or too ill	9	7.3%
Medical arguments	8	6.5%
Financial arguments	1	0.8%
Did not tolerate remedies	1	0.8%
No specific reason	38	30.9%

Table 3: Multivariate stepwise logistic regression analysis on the use of specific osteoporotic therapy (n = 255).

Variable	B	Wald	p-value	Odds ratio Exp (B)	95% CI	General		Improvement		
						p-value	Nagelkerke R^2	Chi^2	p-value	Nagelkerke R^2
Osteoporosis (DXA)	1.247	17.93	0.000	3.481	1.954–6.200	0.000	0.084			
Age unadjusted Charlson Score	-0.351	9.11	0.003	0.704	0.561–0.884	0.000	0.135	10.49	0.00	0.051
Osteoporosis known at the time of fracture	0.988	7.91	0.005	2.686	1.349–5.349	0.000	0.174	8.46	0.00	0.039
Constant	-3.187	16.19	0.000	0.041						

CI = confidence interval; DXA = dual energy x-ray absorptiometry

ered to have osteoporosis [38]. Today, almost all guidelines [25, 35] for osteoporosis also include additional risk factors and scores such as the FRAX to indicate therapy and are no longer based solely on DXA measurement. In the Rotterdam epidemiological study, only 44% of women and 21% of men aged 55 and older with a nonvertebral fracture had a T-score lower than -2.5 [38]. A population-based Study of the Osteoporotic Fractures Research Group found that 54% of women aged >65 years without osteoporosis but with a subsequent hip fracture had a T-score of ≤-2.5 at the beginning of follow-up [39]. In this light, restricting therapy only to those patients with a pathological T-Score ≤-2.5 in DXA may be interpreted at least as a very conservative approach towards therapy, if not already as a lack of knowledge on up-to-date treatment of osteoporosis by the GPs concerned. With the chosen patient-centred survey approach we can only speculate on the motivation of participating GPs. In a representative questionnaire survey in 2005/6, every second German GP admitted not knowing the national guidelines and not using them [40]. Recent studies found that few primary care physicians are versed in the use of the FRAX calculator, which would provide guidance regarding a patient's suitability for pharmacological therapy [41]. A recent prospective qualitative study of fragility fracture patients and the barriers to diagnostic testing and treatment of osteoporosis primarily revealed unclear or incorrect information given by the healthcare providers involved [42]. Our finding of a lower prescription rate in cases with a more sophisticated "up-to-date" indication for osteoporosis therapy, despite GPs receiving an identical specialist recommendation, indicates that this more dedicated approach may not be valued equally by participating GPs.

A second group for whom a significantly reduced implementation rate of antiosteoporotic therapy was found in multivariable analysis was more ill according to their Charlson scores. This possible impact was considerably stronger than increasing age, which showed only a trend in univariate analysis. From the geriatrics literature it is known that elderly patients, for example, who have had a hip fracture are especially vulnerable to non-receipt of postfracture secondary prevention [37]. The aforementioned study from the Netherlands comparing a hospital with a dedicated fracture liaison service to one without reported that patients not willing or not able to participate were significantly older and had more often sustained hip fractures than patients who agreed to subsequent therapy [31]. In our cohort study the patients' fracture region did not yield a significant association in multivariate analysis regardless of whether antiosteoporotic treatment was implemented or not. Univariate analysis showed a trend ($p = 0.07$) towards a higher implementation rate in patients after a fracture of the radius or the hip versus all other fracture regions. Multiple comorbidities were described to be associated with decreased persistence with pharmacological antiosteoporotic therapy [43, 44]. In particular, dementia or cognitive impairment [45, 46] were found to be associated with lower prescriptions for osteoporosis pharmacotherapy. From daily experience we know that the motivation to treat for osteoporosis often decreases in situations of clearly reduced quality of life and/or expected limited life expectancy. Given the high risk of further fractures, including subsequent morbidity and mortality, especially in these subgroups of patients, in our eyes such an attitude has to be questioned.

Third, on the other hand, the subgroup of patients for whom the diagnosis of osteoporosis was not new at the time of fracture showed a significantly increased adherence to treatment for osteoporosis at the 1-year follow-up. We have insufficient information on how many of these patients already took antiosteoporotic drugs at the time of fracture. In accordance with the literature [20], it appears that the occurrence of a fracture motivated these patients and their doctors to persevere more effectively with adequate therapy than did a recommendation for therapy in patients with a new diagnosis of osteoporosis.

As a third major result, this survey reveals some details about how antiosteoporotic therapy was applied by GPs in the investigated cases. The standard recommendation for therapy given by the rheumatology specialist in our project always included medication alternatives, both with regard to the substance and the form of intake, and were tailored to the patients' individual medical history and possible contraindications. In this way, both GPs and patients were given the liberty to choose the specific treatment. About two thirds of our patients took bisphosphonates and every fourth received denosumab. A recent US national health survey of >12 000 nursing home residents whose osteoporosis prescription data were available showed that the most commonly used therapy was a bisphosphonate, in 73.5% of cases, followed by calcitonin in 16.3%; denosumab was distributed only in 1.4% [47]. In a US setting, rates of persistence and compliance over 12 months were higher among women started on denosumab compared with those receiving other osteoporosis therapies [48].

Only a minority of our patients (42%) reported taking their specific remedies by themselves, most of them on a weekly basis. The distribution of medicaments and the observed dosing regimens appear to be in line with the development of new substances and the increasing trend in the treatment of osteoporosis of delivering therapy through injections by care givers. Retrospective studies indicate that weekly dosing regimens are associated with better persistence than daily regimens [49]. The newer injection treatments given quarterly, 6-monthly or annually should theoretically have the potential to improve adherence. However, to what extent increased use of these drugs will improve adherence and lead to fewer fractures in clinical practice is currently not known. Kothawala et al. presented a meta-analysis of adherence to osteoporosis medication [50]. This review compared results from both self-reported and database studies, and concluded that about one third to half of all patients on osteoporosis medication do not take their medication as directed. Recent investigations report that following the once yearly intravenous infusion of zoledronate about one third of patients still did not receive a second application at the correct time and, in the case of ibandronate given every 3 months, only little more than every second patient continued treatment on this drug after 1 year [14]. A database analysis of over 4000 German women with osteoporosis prescribed oral bisphosphonates in the period from December 2004 to November 2007 showed that compliance and persistence with oral bisphosphonates were inadequate. The 1-year persistence rate was 27.9% and 66.3% of women were compliant. After 2 years of therapy, compliant women had fewer frac-

tures than noncompliant women. In multivariate analysis, treatment compliance was the only factor that significantly decreased fracture risk [15].

One of the strengths of this study is its high follow-up rate of 87% with regard to the outcome parameters under investigation [51], whereby the relevant information was derived from patients in about three quarters of cases and the rest from the participating GPs. We primarily undertook this analysis from the perspective of patients, using their GPs answers as a substitute. Given the need for repeat prescriptions, we are of the opinion that the main question of interest as to who effectively received antiosteoporotic drugs can be sufficiently answered by this approach. In addition, cases in which patients answered for themselves as opposed to those where GPs responded for them differed only with regard to living status and comorbidities (Charlson). It is not surprising that for the majority of more elderly and more ill patients the information had to be obtained from their GPs. Given the assumption that elderly people in nursing homes and/or those who are more ill will obey their GP's prescription at least as much as anyone else, the resulting persistence rates should be reliable and we analysed these data accordingly. In contrast, the more detailed information about why patients did not implement the recommended antiosteoporotic treatment was limited to the subgroup of responding patients. Subsequent interpretation has to take into account this restriction. We cannot say who effectively took medicaments correctly: this study did not look for any detailed data on the pharmacotherapy compliance of patients. We used a simple questionnaire, specifically designed for this quality control study, and so we were not aware at the time of study planning of the recently published first disease-specific adherence measure developed for osteoporosis, the ADEOS-12 [36].

In summary, the adherence rate after use of a consistent standard procedure as outlined above produced rates that were more than twice as good as those previously reported by Swiss centres. Nevertheless, every second fracture patient still does not receive adequate therapy following an osteoporotic fracture, a fact that calls for further improvement. Our investigation primarily revealed lack of prescription of medicaments as the explanation of this deficit. This survey from the patient's perspective cannot provide detailed medical reasons why GPs might have argued against therapy. Nevertheless, given the high percentage of patients without therapy we are of the opinion that an important increase in the number of practising GPs motivated to comply with recommendations for antiosteoporotic therapy could be achieved. The nonimplementation of therapy was most prevalent in the group of patients for whom osteoporosis was diagnosed with the additional use of FRAX (and not DXA only) and for more ill (and older) patients. In the light of these findings it seems GPs have to be better convinced and informed about new guidelines. In our setting we tried to achieve this by this survey *per se* and additional information attached to every letter detailing recommendations for antiosteoporotic therapy. A completely different approach could be that we as a trauma centre would not only diagnose and recommend specific antiosteoporotic therapy but would also independently initiate and subsequently manage therapy over a longer period. Dedicated fracture liaison services demonstrated success with such an approach [31]. In addition, efficacious multifaceted interventions, including modern techniques such as mobile text messages or remote internet-based treatment support, may further improve the adherence to osteoporosis pharmacotherapy after osteoporotic fracture, especially if regular interactions between patients and healthcare professionals may be provided [34]. Given our restricted resources at the time we could not pursue the latter strategy and instead try to further improve the communication with patients and their GPs on the topic.

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References

1 Consensus development conference: prophylaxis and treatment of osteoporosis. Am J Med. 1991;(1):107–10. http://dx.doi.org/10.1016/0002-9343(91)90512-V. PubMed.

2 Lippuner K. Epidémiologie des fractures ostéoporotiques en Suisse. [Epidemiology of osteoporotic fractures in Switzerland]. Rev Med Suisse. 2009;(207):1304–8. PubMed.

3 Adler RA. Secondary fracture prevention. Curr Osteoporos Rep. 2012;(1):22–7. http://dx.doi.org/10.1007/s11914-011-0090-z. PubMed.

4 Bolland MJ, Grey AB, Gamble GD, Reid IR. Effect of osteoporosis treatment on mortality: a meta-analysis. J Clin Endocrinol Metab. 2010;(3):1174–81. http://dx.doi.org/10.1210/jc.2009-0852. PubMed.

5 Grey A, Bolland MJ. The effect of treatments for osteoporosis on mortality. Osteoporos Int. 2013;(1):1–6. http://dx.doi.org/10.1007/s00198-012-2176-6. PubMed.

6 Hochberg M. Preventing fractures in postmenopausal women with osteoporosis. A review of recent controlled trials of antiresorptive agents. Drugs Aging. 2000;(4):317–30. http://dx.doi.org/10.2165/00002512-200017040-00007. PubMed.

7 Bessette L, Ste-Marie LG, Jean S, Davison KS, Beaulieu M, Baranci M, et al. The care gap in diagnosis and treatment of women with a fragility fracture. Osteoporos Int. 2008;(1):79–86. http://dx.doi.org/10.1007/s00198-007-0426-9. PubMed.

8 Dell RM, Greene D, Anderson D, Williams K. Osteoporosis disease management: What every orthopaedic surgeon should know. J Bone Joint Surg Am. 2009;(Suppl 6):79–86. http://dx.doi.org/10.2106/JBJS.I.00521. PubMed.

9 Giangregorio L, Papaioannou A, Cranney A, Zytaruk N, Adachi JD. Fragility fractures and the osteoporosis care gap: an international phenomenon. Semin Arthritis Rheum. 2006;(5):293–305. http://dx.doi.org/10.1016/j.semarthrit.2005.11.001. PubMed.

10 Leslie WD, Giangregorio LM, Yogendran M, Azimaee M, Morin S, Metge C, et al. A population-based analysis of the post-fracture care gap 1996-2008: the situation is not improving. Osteoporos Int. 2012;(5):1623–9. http://dx.doi.org/10.1007/s00198-011-1630-1. PubMed.

11 Papaioannou A, Giangregorio L, Kvern B, Boulos P, Ioannidis G, Adachi JD. The osteoporosis care gap in Canada. BMC Musculoskelet Disord. 2004;(1):11. http://dx.doi.org/10.1186/1471-2474-5-11. PubMed.

12 Solomon DH, Finkelstein JS, Katz JN, Mogun H, Avorn J. Underuse of osteoporosis medications in elderly patients with fractures. Am J Med. 2003;(5):398–400. http://dx.doi.org/10.1016/S0002-9343(03)00357-7. PubMed.

13 Kanis JA, Adams J, Borgström F, Cooper C, Jönsson B, Preedy D, et al. The cost-effectiveness of alendronate in the management of osteoporosis. Bone. 2008;(1):4–15. http://dx.doi.org/10.1016/j.bone.2007.10.019. PubMed.

14 Ziller V, Kostev K, Kyvernitakis I, Boeckhoff J, Hadji P. Persistence and compliance of medications used in the treatment of osteoporosis--analysis using a large scale, representative, longitudinal German database. Int J Clin Pharmacol Ther. 2012;(5):315–22. http://dx.doi.org/10.5414/CP201632. PubMed.

15 Hadji P, Claus V, Ziller V, Intorcia M, Kostev K, Steinle T. GRAND: the German retrospective cohort analysis on compliance and persistence and the associated risk of fractures in osteoporotic women treated with

oral bisphosphonates. Osteoporos Int. 2012;(1):223–31. http://dx.doi.org/10.1007/s00198-011-1535-z. PubMed.
16 Majumdar SR. Quality-improvement interventions for osteoporosis: when are the results worth the effort? CMAJ. 2012;(3):279–80. http://dx.doi.org/10.1503/cmaj.111999. PubMed.
17 Majumdar SR, Johnson JA, McAlister FA, Bellerose D, Russell AS, Hanley DA, et al. Multifaceted intervention to improve diagnosis and treatment of osteoporosis in patients with recent wrist fracture: a randomized controlled trial. CMAJ. 2008;(5):569–75. http://dx.doi.org/10.1503/cmaj.070981. PubMed.
18 Suhm N, Lamy O, Lippuner K; OsteoCare study group. Management of fragility fractures in Switzerland: results of a nationwide survey. Swiss Med Wkly. 2008;(45-46):674–83. PubMed.
19 Majumdar SR, Johnson JA, Lier DA, Russell AS, Hanley DA, Blitz S, et al. Persistence, reproducibility, and cost-effectiveness of an intervention to improve the quality of osteoporosis care after a fracture of the wrist: results of a controlled trial. Osteoporos Int. 2007;(3):261–70. http://dx.doi.org/10.1007/s00198-006-0248-1. PubMed.
20 Rosenwasser MP, Cuellar D. Medical management of osteoporosis and the surgeons' role. Injury. 2016;(Suppl 1):S62–4. http://dx.doi.org/10.1016/S0020-1383(16)30014-6. PubMed.
21 Haasters F, Prall WC, Himmler M, Polzer H, Schieker M, Mutschler W. [Prevalence and management of osteoporosis in trauma surgery. Implementation of national guidelines during inpatient fracture treatment]. Unfallchirurg. 2015;(2):138–45. http://dx.doi.org/10.1007/s00113-013-2500-4. PubMed.
22 Chevalley T, Hoffmeyer P, Bonjour JP, Rizzoli R. An osteoporosis clinical pathway for the medical management of patients with low-trauma fracture. Osteoporos Int. 2002;(6):450–5. http://dx.doi.org/10.1007/s001980200053. PubMed.
23 Balasubramanian A, Tosi LL, Lane JM, Dirschl DR, Ho PR, O'Malley CD. Declining rates of osteoporosis management following fragility fractures in the U.S., 2000 through 2009. J Bone Joint Surg Am. 2014;(7):e52, 1–8. http://dx.doi.org/10.2106/JBJS.L.01781. PubMed.
24 Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;(5):373–83. http://dx.doi.org/10.1016/0021-9681(87)90171-8. PubMed.
25 Cosman F, de Beur SJ, LeBoff MS, Lewiecki EM, Tanner B, Randall S, et al.; National Osteoporosis Foundation. Clinician's guide to prevention and treatment of osteoporosis. Osteoporos Int. 2014;(10):2359–81. http://dx.doi.org/10.1007/s00198-014-2794-2. PubMed.
26 Parikh S, Mogun H, Avorn J, Solomon DH. Osteoporosis medication use in nursing home patients with fractures in 1 US state. Arch Intern Med. 2008;(10):1111–5. http://dx.doi.org/10.1001/archinte.168.10.1111. PubMed.
27 Vogel T, Kampmann P, Bürklein D, Böhm H, Ockert B, Kirchhoff C, et al. [Reality of treatment of osteoporotic fractures in German trauma departments. A contribution for outcome research]. Unfallchirurg. 2008;(11):869–77. http://dx.doi.org/10.1007/s00113-008-1504-y. PubMed.
28 McLellan AR, Wolowacz SE, Zimovetz EA, Beard SM, Lock S, McCrink L, et al. Fracture liaison services for the evaluation and management of patients with osteoporotic fracture: a cost-effectiveness evaluation based on data collected over 8 years of service provision. Osteoporos Int. 2011;(7):2083–98. http://dx.doi.org/10.1007/s00198-011-1534-0. PubMed.
29 Sale JE, Beaton D, Posen J, Elliot-Gibson V, Bogoch E. Key outcomes are usually not reported in published fracture secondary prevention programs: results of a systematic review. Arch Orthop Trauma Surg. 2014;(2):283–9. http://dx.doi.org/10.1007/s00402-011-1442-y. PubMed.
30 Svedbom A, Ivergård M, Hernlund E, Rizzoli R, Kanis JA. Epidemiology and economic burden of osteoporosis in Switzerland. Arch Osteoporos. 2014;(1):187. http://dx.doi.org/10.1007/s11657-014-0187-y. PubMed.
31 Huntjens KM, van Geel TA, van den Bergh JP, van Helden S, Willems P, Winkens B, et al. Fracture liaison service: impact on subsequent non-vertebral fracture incidence and mortality. J Bone Joint Surg Am. 2014;(4):e29. http://dx.doi.org/10.2106/JBJS.L.00223. PubMed.
32 Gleeson T, Iversen MD, Avorn J, Brookhart AM, Katz JN, Losina E, et al. Interventions to improve adherence and persistence with osteoporosis medications: a systematic literature review. Osteoporos Int. 2009;(12):2127–34. http://dx.doi.org/10.1007/s00198-009-0976-0. PubMed.
33 Solomon DH, Iversen MD, Avorn J, Gleeson T, Brookhart MA, Patrick AR, et al. Osteoporosis telephonic intervention to improve medication regimen adherence: a large, pragmatic, randomized controlled trial. Arch Intern Med. 2012;(6):477–83. http://dx.doi.org/10.1001/archinternmed.2011.1977. PubMed.
34 Nieuwlaat R, Wilczynski N, Navarro T, Hobson N, Jeffery R, Keepanasseril A, et al. Interventions for enhancing medication adherence. Cochrane Database Syst Rev. 2014;(11):CD000011. PubMed.
35 Kanis JA, McCloskey EV, Johansson H, Cooper C, Rizzoli R, Reginster JY; Scientific Advisory Board of the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) and the Committee of Scientific Advisors of the International Osteoporosis Foundation (IOF). European guidance for the diagnosis and management of osteoporosis in postmenopausal women. Osteoporos Int. 2013;(1):23–57. http://dx.doi.org/10.1007/s00198-012-2074-y. PubMed.
36 Breuil V, Cortet B, Cotté FE, Arnould B, Dias-Barbosa C, Gaudin A-F, et al. Validation of the adherence evaluation of osteoporosis treatment (ADEOS) questionnaire for osteoporotic post-menopausal women. Osteoporos Int. 2012;(2):445–55. http://dx.doi.org/10.1007/s00198-011-1555-8. PubMed.
37 Sale JE, Beaton D, Bogoch E. Secondary prevention after an osteoporosis-related fracture: an overview. Clin Geriatr Med. 2014;(2):317–32. http://dx.doi.org/10.1016/j.cger.2014.01.009. PubMed.
38 Schuit SC, van der Klift M, Weel AE, de Laet CE, Burger H, Seeman E, et al. Fracture incidence and association with bone mineral density in elderly men and women: the Rotterdam Study. Bone. 2004;(1):195–202. http://dx.doi.org/10.1016/j.bone.2003.10.001. PubMed.
39 Wainwright SA, Marshall LM, Ensrud KE, Cauley JA, Black DM, Hillier TA, et al.; Study of Osteoporotic Fractures Research Group. Hip fracture in women without osteoporosis. J Clin Endocrinol Metab. 2005;(5):2787–93. http://dx.doi.org/10.1210/jc.2004-1568. PubMed.
40 Chenot R, Scheidt-Nave C, Gabler S, Kochen MM, Himmel W. German primary care doctors' awareness of osteoporosis and knowledge of national guidelines. Exp Clin Endocrinol Diabetes. 2007;(9):584–9. http://dx.doi.org/10.1055/s-2007-981454. PubMed.
41 Edwards BJ, Koval K, Bunta AD, Genuario K, Hahr A, Andruszyn L, et al. Addressing secondary prevention of osteoporosis in fracture care: follow-up to "own the bone". J Bone Joint Surg Am. 2011;(15):e87. http://dx.doi.org/10.2106/JBJS.I.00540. PubMed.
42 Sale JE, Bogoch E, Hawker G, Gignac M, Beaton D, Jaglal S, et al. Patient perceptions of provider barriers to post-fracture secondary prevention. Osteoporos Int. 2014;(11):2581–9. http://dx.doi.org/10.1007/s00198-014-2804-4. PubMed.
43 Giusti A, Barone A, Razzano M, Oliveri M, Pizzonia M, Palummeri E, et al. Persistence with calcium and vitamin D in elderly patients after hip fracture. J Bone Miner Metab. 2009;(1):95–100. http://dx.doi.org/10.1007/s00774-008-0007-9. PubMed.
44 Solomon DH, Avorn J, Katz JN, Finkelstein JS, Arnold M, Polinski JM, et al. Compliance with osteoporosis medications. Arch Intern Med. 2005;(20):2414–9. http://dx.doi.org/10.1001/archinte.165.20.2414. PubMed.
45 Gruber-Baldini AL, Zimmerman S, Morrison RS, Grattan LM, Hebel JR, Dolan MM, et al. Cognitive impairment in hip fracture patients: timing of detection and longitudinal follow-up. J Am Geriatr Soc. 2003;(9):1227–36. http://dx.doi.org/10.1046/j.1532-5415.2003.51406.x. PubMed.
46 Mauck KF, Cuddihy MT, Trousdale RT, Pond GR, Pankratz VS, Melton LJ, 3rd. The decision to accept treatment for osteoporosis following hip fracture: exploring the woman's perspective using a stage-of-change model. Osteoporos Int. 2002;(7):560–4. http://dx.doi.org/10.1007/s001980200073. PubMed.
47 Zarowitz BJ, Cheng LI, Allen C, O'Shea T, Stolshek B. Osteoporosis prevalence and characteristics of treated and untreated nursing home residents with osteoporosis. J Am Med Dir Assoc. 2015;(4):341–8. http://dx.doi.org/10.1016/j.jamda.2015.01.073. PubMed.
48 Cheng LI, Durden E, Limone B, Radbill L, Juneau PL, Spangler L, et al. Persistance and compliance with osteroporosis therapies among women in a commercially insured population in the United States. J Manag Care Spec Pharm. 2015;(9):824–33, 833a. http://dx.doi.org/10.18553/jmcp.2015.21.9.824. PubMed.
49 Silverman S, Gold DT. Compliance and persistence with osteoporosis medications: a critical review of the literature. Rev Endocr Metab Disord. 2010;(4):275–80. http://dx.doi.org/10.1007/s11154-010-9138-0. PubMed.
50 Kothawala P, Badamgarav E, Ryu S, Miller RM, Halbert RJ. Systematic review and meta-analysis of real-world adherence to drug therapy for osteoporosis. Mayo Clin Proc. 2007;(12):1493–501. http://dx.doi.org/10.1016/S0025-6196(11)61093-8. PubMed.
51 O'Neill TW, Marsden D, Matthis C, Raspe H, Silman AJ. Survey response rates: national and regional differences in a European multicentre

study of vertebral osteoporosis. J Epidemiol Community Health. 1995;(1):87–93. http://dx.doi.org/10.1136/jech.49.1.87. PubMed.