

Understanding fragility fracture patients' decision-making process regarding bisphosphonate treatment

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Abstract

Summary We aimed to understand how patients 50 years and older decided to persist with or stop osteoporosis (OP) treatment. Processes related to persisting with or stopping OP treatments are complex and dynamic. The severity and risks and harms related to untreated clinical OP and the favorable benefit-to-risk profile for OP treatments should be reinforced. **Introduction** Older adults with fragility fracture and clinical OP are at high risk of recurrent fracture, and treatment reduces this risk by 50 %. However, only 20 % of fracture patients are treated for OP and half stop treatment within 1 year. We aimed to understand how older patients with new fractures decided to persist with or stop OP treatment over 1 year. **Methods** We conducted a grounded theory study of patients 50 years and older with upper extremity fracture who started bisphosphonates and then reported persisting with or stopping treatment at 1 year. We used theoretical sampling to identify patients who could inform emerging concepts until data

saturation was achieved and analyzed these data using constant comparison.

Results We conducted 21 interviews with 12 patients. Three major themes emerged. First, patients perceived OP was not a serious health condition and considered its impact negligible. Second, persisters and stoppers differed in weighting the risks vs benefits of treatments, where persisters perceived less risk and more benefit. Persisters considered treatment “required” while stoppers often deemed treatment “optional.” Third, patients could change treatment status even 1-year post-fracture because they re-evaluated severity and impact of OP vs risks and benefits of treatments over time.

Conclusions The processes and reasoning related to persisting with or stopping OP treatments post-fracture are complex and dynamic. Our findings suggest two areas of leverage for healthcare providers to reinforce to improve persistence: (1) the severity and risks and harms related to untreated clinical OP and (2) the favorable benefit-to-risk profile for OP treatments.

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Introduction

Osteoporosis (OP) is a chronic condition associated with increased morbidity and mortality and decreased quality of life [1, 2]. Older adults who fracture have a 20 % risk of another fracture within 1 year [1–3] and treatment with a bisphosphonate reduces this risk by 50 % [4–6]. As such, the focus of the 2010 Osteoporosis Canada Guidelines (as well as guidelines endorsed by the National Osteoporosis Foundation and the

International Osteoporosis Foundation) is secondary prevention. This entails identifying patients with fragility fractures of the upper extremity, spine, or hip, ordering bone mass density (BMD) tests and offering treatment to those at the highest risk of another fracture [7–9]. Regardless of this guidance, less than 20 % of people are treated for OP in the year post-fracture [1, 2, 6, 9]. Equally worrisome, of those written a prescription for OP treatment, 30 % will not fill their prescription (primary non-adherence) [10] and of those who do fill their first prescription, at least half will stop treatment within 1 year [11, 12]. Indeed, even in the setting of a randomized trial to improve testing and treatment of OP after a fragility fracture, 18 % of those who started treatment in the intervention arm had stopped treatment within 1 year [13]. Several models address how individual factors, such as knowledge and attitudes, and social processes, including identity and support, influence behaviors [14]. However, the patient-level factors related to starting and stopping OP treatments remain relatively under studied and yet critically important to understand [15–17].

To better understand long-term persistence (and non-persistence) with OP treatments, we capitalized on participants in the Comparing Strategies Targeting Osteoporosis to Prevent Recurrent Fractures (C-STOP) trial. This trial, based on a positive pilot study [18], is currently enrolling patients with upper extremity fragility fractures in an active-comparator randomized controlled trial of nurse case management vs a multifaceted intervention directed at patients (i.e., printed materials, education, telephonic counseling) and their physicians (i.e., reminders, opinion leader endorsed guidelines). The nurse case-manager identifies and interviews patients from clinic settings (Emergency Departments and Fracture Clinics), arranges BMD tests, and offers in-person education, counseling, and guideline-based prescription treatments as needed, and then follows patients up for 1 year.

Patients in the case-manager arm of this study represented the “best-case scenario.” For example, they are relatively healthy although they have all recently suffered a fragility fracture and are all at similar risk of re-fracture based on the most recent major osteoporotic fracture and calculated FRAX with BMD scores of moderate to high risk. In addition, they all received standardized print materials with in-person counseling and were all offered treatment based upon standardized treatment algorithms [18]. In this setting of uniform care, we hypothesized we might be able to gain important and nuanced insights into patient-specific reasons for continuing or quitting OP medications. Therefore, rather than use surveys or secondary analyses of various databases as has been done previously [3, 15, 16, 19–21], we undertook a qualitative grounded theory study to understand the processes and reasoning that adults 50 years and older with recent fragility

fractures go through when deciding to persist with or stop bisphosphonates in the 1-year post-fracture.

Methods

We used a grounded theory approach as outlined by Corbin and Strauss [22] to understand the processes and reasoning people engage in when deciding to persist with or stop OP medications in general, and more specifically, bisphosphonate treatment after suffering a fragility fracture of the upper extremity. Grounded theory is an inductive approach where models or concepts are “grounded” in the data collected without an a priori hypothesis. We chose to use a grounded theory approach to understand how patients approach a diagnosis of OP and how they negotiate persisting with or stopping treatment. We considered all of these patients (50 years and older with fragility fracture of the distal radius or proximal humerus and low bone mass at one or more skeletal sites) to have a clinical diagnosis of OP [23] and refer to this as OP throughout. When referring to BMD test results alone, we refer to osteopenia (T-score ≤ 1.0 to -2.5) or OP (T-score ≤ 2.5) [18, 23] and always make this distinction explicit.

Data collection and measurements

The primary study outcomes of the larger C-STOP trial were ascertained at 6 months, and the research team remained blinded to these data. That said, during 1-year follow-up of this population, we identified nurse case-management patients who had started bisphosphonate treatment at any time up to their 1-year data collection. We enrolled 150 patients in the nurse case-management arm of the larger study. Thus, all patients seen in the clinic were potentially eligible, and the only patients seen in the clinic were trial patients. We did not sample patients “randomly” for the purposes of generalizability of the results as conceptualized in quantitative research. Instead, we sampled patients based on their ability to act as key informants (i.e., someone with direct experience with the phenomenon who is able to reflect on and articulate their experience) for the purposes of transferability of the results to similar populations and contexts. At this time, we purposefully sampled patients who had started bisphosphonate treatment (by study treatment algorithm, either generic alendronate or risedronate prescribed weekly [18]) and reported whether they were still persistent with treatment at 1 year (“persisters”) or they had stopped treatment (“stoppers”). We verified all self-reported treatment data independently by using local pharmacy dispensing records.

As the study progressed, we used theoretical sampling, one of the core strategies of grounded theory [22, 24]. Theoretical sampling is responsive to the data in that the researchers sample concepts and not persons [22]. Since the nurse case-

manager had met and remained in contact with all trial patients, she helped identify potential patients who could talk directly to our various emerging concepts. For example, we recruited patients diagnosed with either osteopenia or OP as defined strictly by BMD test results to elicit a deeper understanding of perceived severity, when this specific concept emerged from analysis. As well, we re-interviewed several patients as themes and concepts emerged.

A trained researcher conducted qualitative in-person interviews using a semi-structured interview guide (Appendix), which was refined as data analysis progressed. Interviews were conducted in the same location as case-management appointments at a single center and lasted up to 45 min. Interviews were digitally recorded for subsequent analysis and verified for accuracy. The University of Alberta Health Ethics Research Board approved the parent trial and this qualitative sub-study, and all subjects provided written informed consent.

Analysis

We used constant comparison to analyze the data, using open coding and memos [22, 25, 26]. One analyst (LW) identified emerging codes and concepts. The research team held regular meetings to review code definitions, emerging concepts, and memos and to refine the interview guide. We conducted data collection and analysis concurrently until theoretical data saturation [27, 28] was achieved, that is, the major concepts were well defined and explained and no new concepts or themes emerged [22]. We implemented several strategies throughout the research process to ensure rigor including methodological coherence [29], peer debriefing [24], reflective writing [22], and maintaining an audit trail [24]. Data were managed and analyzed using Atlas.ti version 7 (Berlin, Germany, Scientific Software Development GmbH) [30].

Results

From April 2014 through March 2015, we conducted 21 interviews with 12 different patients, including a second follow-up interview with the initial 9 patients to address questions that emerged through concurrent data collection and analysis. Of the 12 patients recruited, 7 persisted with bisphosphonates and 5 stopped. Treatment status was determined at the last point of contact (e.g., a patient who was a persister at her first interview but a stopper at her second interview was classified as a stopper). Of note, three patients changed their treatment status during the study. Two thirds of patients were 60 years or older, 75 % were women, 67 % had osteopenia (T-score \leq 1.0) at one or more skeletal sites according to BMD testing, and 92 % had better-than-average OP-related knowledge compared with the average score (57 %) reported previously in a

similar trial population [31] (Table 1). By trial design, no patient had been taking OP medications at the time of fracture.

Three major themes emerged. We provide a list of codes, sub-codes, and supplemental illustrative quotes that comprise each theme in Table 2, and we detail each theme below.

Theme 1: negligible appreciation of risk regarding severity and impact of OP

Regardless of treatment status, patients identified similar reasons for deciding to start bisphosphonates. These reasons included: (1) being advised to do so by a healthcare professional, (2) to prevent the progression of their condition or to maintain current bone health, or (3) to stay healthy.

Nonetheless, and despite the fact that all but one of these patients had better-than-average OP-related knowledge, they did not consider OP to be a serious health condition, particularly compared with other diseases like cancer. Furthermore, based on their understanding of their own BMD test results, patients (all of whom had a fragility fracture) perceived a test result of osteopenia as less serious than OP and defined it as pre- or borderline-OP, at the beginning stages of OP, or within acceptable range. In addition, patients were not concerned about their bone health or OP prior to their fracture. Many patients believed OP was a natural part of aging, especially for women, and some commented that they did not experience symptoms or feel differently because they now had an OP diagnosis.

Of particular note, patients generally perceived minimal susceptibility to the potential negative consequences of OP in the future. They believed that it was in their control to prevent future fractures by being more careful or avoiding falls. From their perspective, the fracture was their fault. However, some patients said the fracture was unavoidable or would have happened to anyone, indicating that it was not a result of compromised bone health. Generally, patients explained that an upper extremity fracture did not affect their lives substantially in the way that a hip fracture would.

Theme 2: ongoing evaluation of risks vs benefits of treatments

The main difference between patients who persisted with or stopped taking bisphosphonates was in their evaluation of its risks and benefits. Patients who persisted perceived greater benefit than risk from taking OP medications. They believed that medication was required or the best option to treat their condition. In addition, they perceived their risk of future fracture without OP treatment as high and said they would continue taking prescription treatment even if they had another fracture. Lastly, they did not report experiencing any side effects.

Table 1 Patient characteristics according to treatment status

Treatment status ^a	Total (n = 12) # (%)	Persisted (n = 7) # (%)	Stopped (n = 5) # (%)
Age >60 years	8 (67)	5 (71)	3 (60)
Female	9 (75)	5 (71)	4 (80)
White	12 (100)	7 (100)	5 (100)
BMD test results			
Osteoporosis (T-score less than -2.5)	4 (33)	2 (29)	2 (40)
Osteopenia (T-score -1.0 to -2.4)	8 (67)	5 (71)	3 (60)
FRAX score			
High 10-year risk	2 (17)	1 (14)	1 (20)
Moderate 10-year risk	10 (83)	6 (86)	4 (80)
Above average OP-related knowledge ^b	11 (92)	6 (86)	5 (100)

^a Treatment status was determined based on status at the last point of contact (e.g., a patient who was a persister at her first interview but a stopper at her second interview was classified as a stopper)

^b The average score (a percentage of correct answers with a higher percentage representing more knowledge) of OP-related knowledge as measured by the 25-item facts on osteoporosis quiz [52] was previously determined in this patient population to be 57 % [31]

In contrast, patients who stopped treatment within 1 year believed that bisphosphonate treatment was optional and no more beneficial than exercising and taking vitamin D and calcium. They perceived their risk of future fracture without treatment as low. In addition, they reported concerns about side effects and this was enough to tip the balance towards non-persistence.

Theme 3: re-evaluation of severity and impact of OP vs risks and benefits of treatment over time

Patients reported changing (or having the potential to change) treatment status even 1-year post-fracture because they reassessed the severity and impact of OP as well as the risks and benefits of bisphosphonate treatment over time. Two patients who restarted OP medications after initially quitting explained that they have OP (rather than just osteopenia according to a BMD test) and that prescription treatment was now *required* rather than optional. Conversely, the patient who persisted with bisphosphonates but then stopped 1-year post-fracture explained that she had osteopenia, and not OP, according to her BMD tests and that there had been no further decline in her bone health as far as she could tell. In addition, she explained prescription treatment was but one option and not necessary to treat OP. Lastly, she reported experiencing what she perceived as side effects of bisphosphonates, including pain in her hip when laying down.

Even patients who did not change treatment status reported the potential to change status at almost any time post-fracture. For example, patients who persisted with treatment described “lapses” in adherence, primarily when traveling. One patient commented that she forgot to take her medication while traveling because OP is not life threatening. In addition, patients

who persisted reported the potential to stop taking OP medications in the future if, for example, they started experiencing side effects or saw no improvement in their BMD test results. On the other hand, several patients who stopped explained that they would consider re-starting treatment in the future if, for example, they were diagnosed with OP (rather than osteopenia) based on their BMD results, believed that OP could affect their life negatively, or were informed that bisphosphonates were their best treatment option. For example, the patient who stopped prescription treatment 1-year post-fracture said that she would re-start if her family physician diagnosed her with OP and told her that OP medications were required to treat it.

Discussion

In this grounded theory study examining how patients’ understand the clinical problem of OP and how they decided to persist with or stop treatment 1-year post-fracture, three broad themes emerged. First, patients perceived that OP was not a serious health condition and that its impact was negligible regardless of their decision to start treatment. Second, the main difference between persisters and stoppers was in their ongoing evaluation of the risks vs benefits of bisphosphonate treatment, where patients who persisted perceived more benefit and less risk than patients who stopped. Third, we found that patients had the potential to change treatment status even 1-year post-fracture because they re-evaluated the severity and impact of OP vs the risks and benefits of treatments over time. We have attempted to represent and conceptualize this decision-making process in Fig. 1.

Table 2 Codes, sub-codes, and selected supporting quotes by three main themes

Codes and sub-codes	Selected supporting quotes
Theme 1: negligible appreciation of risk regarding severity and impact of OP	
Reason for deciding to start prescription treatment	
Advised by healthcare professional	I think it's to do with the way I was brought up, to do what the doctor tells me (laughing) (female, age 67, persister). [I decided to start prescription treatment] just because [the case-management RN] recommended it or said that it would might be helpful to strengthen the bones (male, age 67, stopper).
Prevent progression or maintain bone health	Just the whole idea that I want to prolong the osteopenia and not actually be classified as osteoporotic. So I guess that's your "carrot dangled in front of you", because you don't want it to get any worse. (female, age 55, changed to stopper).
To stay healthy	I think you know when you get to my age, you've got enough to worry about. Like with health issues you know. There's breast cancer and there's heart problems. So I mean I think if we can try to keep ourselves healthy, I think that's a really good thing (female, age 67, persister).
Clinical OP is not serious	
Compared with other life-threatening diseases	Cancer to me is kind of a death sentence. It doesn't have to be, but it's more like that whereas I think high blood pressure and OP are more the quality of life kind of a thing (male, age 60, persister). It could be cancer for heaven's sake. So this is way better (female, age 55, changed to stopper). Cancer seems to be more life threatening than OP (male, age 67, stopper).
Osteopenia is pre- or borderline-OP, at the beginning stages, or within an acceptable range	I don't think it's pronounced—I mean, I'm just in the beginning stages... So it's not an advanced case (female, age 68, persister). I guess to me the easiest way of saying it was when my husband's doctor said, you don't have diabetes yet, you have pre-diabetes. So it is that we have a problem that we are seeing coming, it's not really there yet, but it's heading in that direction so... Flag there is a problem, but it isn't as bad as OP (female, age 68, changed to persister). I don't believe I have OP. I might have had some bone loss with the bone density, but it's still within an acceptable range (female, age 70, stopper).
Not concerned about bone health or clinical OP before fracture	I had broken this bone about seven or eight years before and they said that there was a weakness of bone but over that time it didn't bother me. I wasn't concerned about it (male, age 67, stopper). I mean I've always been active, I do a lot of walking, I do a lot of exercise. I keep active. I have a pretty good diet. So it was not anything I thought I needed to think about (female, age 68, changed to persister).
Clinical OP is a natural part of aging for women	I guess all women's bones must deteriorate. I mean I'm sure they do after a certain age and maybe a surprisingly young age (female, age 67, persister). I know that it happens as you get older (female, age 70, stopper).
No symptoms or I don't feel different	To be honest I was very surprised when they tested me and I was low on calcium and vitamin D and the bone density was down, borderline-OP. It was just a big surprise. I didn't have any symptoms (male, age 60, persister). Arthritis takes away your independence too, and it takes away your comfort... [With OP,] you don't even know it's there (female, age 70, stopper).
Minimum perceived susceptibility	
Future fractures are preventable	I was just walking in the neighborhood and it was literally ice that was covered with snow. But it was largely my own fault. I just wasn't being as cautious as I should have been. You know (laughing), that's always easy to see the mistake after (female, age 67, persister). But with broken bones, I just write it off to my clumsiness (laughing)... You still have to be careful and sometimes I'm not. Nod off sometimes when I should be paying attention (male, age 67, stopper).
Unavoidable fracture	They said it was an unusual [fracture] because I was just falling from standing, but I was also carrying some heavy stuff and it all came down mostly on the one arm. And it was right on concrete so it was hard and it was slippery so it was harder, so everything (male, age 60, persister).

Table 2 (continued)

Codes and sub-codes	Selected supporting quotes
Upper extremity fracture had a minimal impact; hip fracture could be worse	<p>I think that the stupid way I fell - I don't know if it would have been any different if I had been 20 or 18 or 12. It might have just been the way I fell versus a concern about osteo' (female, age 68, changed to persister).</p> <p>I mean the wrist was a wrist. If it had been a hip it's going to have a more an impact. If it's an ankle a bit more of an impact too. It didn't prevent me from doing what I wanted to do (female, age 68, changed to persister).</p> <p>My adopted mom, she was watering her flowers and all of a sudden, her hip gave way. Well, that's a red flag (female, age 70, stopper).</p>
Theme 2: ongoing evaluation of risks vs benefits of treatments Benefits outweighed risks for patient who persisted Prescription treatment is required to treat clinical OP	<p>Well I don't know that there's a lot else you can do for OP other than exercise and taking the Alendronate (female, age 67, persister).</p> <p>I didn't have an option [to take prescription treatment], that's the way it occurred, I didn't have an option. I'm not going to any health food medicine or this or that. No way. Oh maybe some of them are very good, but no, I'm not going to do that. I'm going to do what conventional medicine said I should do (male, age 76, persister).</p>
Perceived high to medium risk of future fracture without prescription treatment	<p>Just from what they've told me and cause I'm active in doing things and with loss of 20 % of your bone density it's probably a good chance you're going to break something (male, age 60, persister).</p> <p>Without any treatment, I would probably have a higher risk [of a future fracture] (female, age 51, persister).</p> <p>Oh very high, yeah. Super high, yup (male, age 76, persister).</p>
Continue prescription treatment even if future fracture occurs No to minimal risk (i.e., no side effects)	<p>If it wasn't getting better or at least not getting worse, I guess I could be happy with that (male, age 60, persister).</p> <p>I've been on [prescription treatment] for, I don't know how long, two years. And I don't seem to be suffering any ill effects from anything that I'm taking that I'm aware of any way (female, age 68, persister).</p> <p>I just took it and like I say I didn't experience any side effects (female, age 58, persister).</p>
Risks outweighed benefits for patients who stopped Prescription treatment is optional	<p>I wasn't up against the wall because my condition was just sort of borderline, you know. If I had had OP per se, I'd probably would've kept going [with prescription treatment], tried a bit more (female, age 70, stopper).</p> <p>[Prescription treatment] might have been recommended but there's a subtle difference between recommendation and requirement. And so, you know, I don't feel that I was required to take this drug. It was suggested to me so... I know of course it's not an infectious disease. But if you have tuberculosis, you know treatment is required. It's not recommended. You know? There's a difference there (female, age 57, stopper).</p>
Perceived low risk of future fracture without prescription treatment	<p>I think it's low because I don't do anything risky. I don't do anything that I think would cause the any broken bones or fractures. So I think it would be low (male, age 67, stopper).</p> <p>Probably between medium and low. Because I'm not gonna stop doing things. So but I'm more aware of safety. Yep (female, age 70, stopper).</p>
Perceived risk: reported side effects	<p>Well that one [medication] made me sick and I talked to the person who prescribed [it to] me and they said "Well if you're getting sick with it, just discontinue it" and I decided that it might help me in the long run, but I think I'll just uh do what does not make me feel ill... Especially if you can't really see the results (laughing) (male, age 67, stopper).</p> <p>I was quite game to try something to make my bones stronger, sure. But, I was aware that I had got an ulcer once with [prescription OP] medication and I had tried, I think they had another medication that had Fosamax in it that had something to protect the stomach and it didn't work either and it's just as I kept trying something I just decided this is not worth it (female, age 70, stopper).</p>

Table 2 (continued)

Codes and sub-codes	Selected supporting quotes
Theme 3—Re-evaluation of severity and impact OP vs risks and benefits of treatment over time	
Prescription treatment restarted 1-year post- fragility fracture	
Diagnosed with OP, not osteopenia and prescription treatment is required	Towards the end of May [2015], I went in for my annual physical and my doctor did the mammogram, bone density, etc. again. And I have gone from osteopenia to OP. So I started the medication (female, age 68, changed to persister).
	I know I have OP (female, age 63, changing to persister).
	The other deciding factor for me with a number of things is always been I have no family history, my doctors have always sort of aired on the side of caution, and where [my family physician] sort of said “it’s up to you [to take prescription treatment]” last year, to “I want to you to be taking it”... She would still never force me, but before it was “you might think about taking this.” This year it was “I really want you to take this” (female, age 68, changed to persister).
Prescription treatment stopped 1-year post-fragility fracture	
Diagnosed with osteopenia, bone health has not deteriorated, prescription treatment is options, experienced side effects	My bone density had not changed in the last two years so I have not receded or I haven’t gone downhill, I guess. So I will just assess again when I have my next one. If I end up being specifically diagnosed with OP, I guess I will have to reassess or see what else is out there and try but at this point in time I’m just gonna hang tough just with the calcium and the Vitamin D (female, age 55, changed to stopper).
	Not at this point in time, no [prescription treatment is not required] (female, age 55, changed to stopper).
	I did continue to take the Alendronate up until about 2 months ago. I was okay but I was noticing I had some discomfort...I had a pain in my left femur... I stopped [taking Alendronate] and I have no discomfort in my leg or my hip at all. I feel fine (female, age 55, changed to stopper).
Potential to stop prescription treatment in the future	
Relapse in taking prescription treatment	Now I have to admit, that we went to Australia and New Zealand and I forgot about 3 [weeks] of them (female, age 67, persister).
	Well, I mean, (laughing) I had a brief hiatus for about 3 months where I was away, I didn’t do it all but then came back to it. So no, in the back of mind I think it’s the right thing to do (laughing)... It’s not an everyday thing and it just happens [I that forget] and since it’s not life threatening it’s like “Oh well, I’ll get it when I come home” (female, age 51, persister).
Other reasons to stop (e.g., experience side effects, no change in bone density)	The only thing would be the side effects or the interactions with other medication that might be more necessary. As you get older, you need sometimes more drugs or the stomach can’t take it anymore or something (male, age 60, persister).
	I haven’t been taking [prescription treatment] that long so you have to give it some time to undo damage or do damage. So right now, I probably still say well, “It’s still working.” If I three or four years from now if I had all the X-rays and things didn’t look any different, then you might question it (female, age 51, persister).
Potential to re-start prescription treatment	
Related to the following conditions: decline in bone density, informed that prescription treatment is best option, or OP could have a negative impact	If I have a change in my bone density and [my family physician] says “Yes, you will or you need to be on it,” okay, I will be, but I’m not now (female, age 55, changed to stopper).
	I’d be willing to do it. I think if it was a dire situation and it was explained to me that it was a dire situation, I’d probably still be on that medication you gave me (male, age 67, stopper).
	To be honest, on the odd occasion I think, “I should go back and start you know integrating [prescription treatment] into my life again.” I should figure out how to take care of this because again, I want to live a healthy life for as long as I live. But in the whoosh of things, it gets swept aside (female, age 57, stopper).

According to the Information, Motivation and Behavioral Skills model [32], people are more likely to initiate and

maintain health-promoting behaviors, including medication adherence [33, 34], which produce positive outcomes when

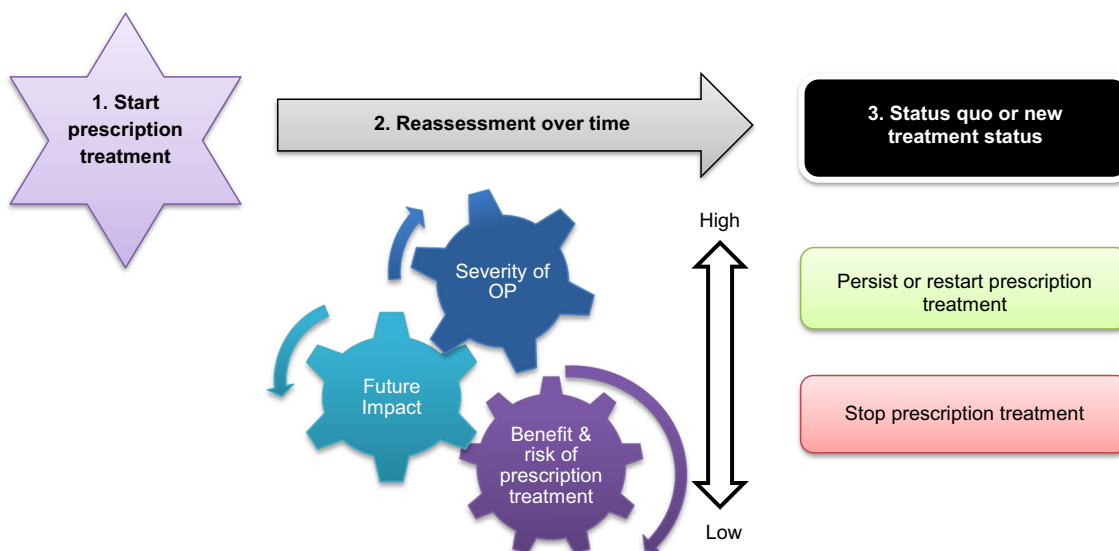


Fig. 1 Conceptualization of the decision-making process to persist with, stop, or re-start prescription treatment for clinical OP over time

they are well-informed, motivated to act, and possess the skills and confidence to take action. Perhaps the most important insight gained from our study is that even in a healthy, knowledgeable, and well-informed high-risk population with recent fragility fracture, the decision to start and then persist with long-term treatment is not a binary “yes-or-no” process situated at one point in time (i.e., the diagnostic moment). Rather, patients appear to re-evaluate and re-frame their willingness to adhere to OP medications over time based on the perceived severity and impact of OP on the one hand vs the risks and benefits of bisphosphonate treatment on the other.

The results also suggest that these risk-benefit re-assessments are driven by multiple factors related to time. First, time from the clinical fracture likely plays some role: as the memory of the clinical fracture event fades, the perceived severity diminishes. Second, the potential negative impact of OP also diminishes over time while the risks of bisphosphonate treatment become more prominent over time, particularly since the absence of another fracture is the only tangible benefit of ongoing treatment. This has implications for facilitating patient-centered decision-making [35, 36] beyond the diagnostic moment where ongoing clinical dialog is going to be needed to support persistence and to continuously re-engage patients who stop treatment. This finding is particularly relevant as demonstrated by a recent front-page article in *The New York Times* reporting that people tend to avoid effective osteoporosis treatment based on the fear of extremely rare side effects and calling for a more balanced perspective in weighing the favorable benefit-to-risk profile of treatment [37].

Similar to our findings, others have found that patients misunderstood their diagnosis in the context of having suffered a fragility fracture [38, 39]. As such, as suggested by an

expert consensus [23], our findings indicate we should use the term “clinical OP” and refrain from using or overly emphasizing BMD test result labels such as “osteopenia” when designing patient-directed interventions or educational materials. Others have also found that patients did not consider OP serious [17, 40–42]. For example, Sale et al. found that patients did not consider compromised bone health as serious, although this perception was not related to use of OP medications [17] possibly explaining why we found this opinion common to both persisters and stoppers. In addition, other studies have commented on the challenges of appropriately treating a clinically silent disease [39, 43, 44]. Challenges related to persistence in taking long-term OP medications are not necessarily unique and seem similar to the problems with adherence and persistence demonstrated for other chronic conditions that are also “asymptomatic” such as hypertension or dyslipidemia [45, 46].

Patients may also under-estimate their fracture risk or perceive themselves as immune to the effects of OP [43]. Indeed, other studies have shown that patients believed that the fracture was unavoidable and caused by non-preventable circumstances [40, 41] and, therefore, within the realm of normal everyday occurrence. Conversely, patients may also believe the fracture was related to their own unsafe behaviors and, therefore, within their control to modify to prevent the next fracture [41, 43]. However, both of these rationalizations neglect the fact that healthy bones would not have fractured under the same low trauma circumstances.

In addition, patients appear to re-evaluate risks vs benefits of treatments for OP over time, and it is already known that patients are very concerned about possible or perceived (vs actual) side effects of bisphosphonates, and this strongly influences their decisions regarding treatment persistence [47–49]. Our work suggests that a major component of

patients' risk-benefit analysis relates to their belief about whether treatment with bisphosphonates is *required* (rather than "optional") to decrease their risk of another fracture. This finding has implications for the design and content of interventions intended to promote persistence among patients who have started treatment regardless of their concerns related to potential or actual side effects. Clearly, OP medication use varies over time with patients starting, stopping, and re-initiating treatment [15, 20, 47, 50, 51]. This process of re-evaluation might be considered promising by some (because patients who stopped bisphosphonates may re-start) although others believe that it is very concerning [15, 47]. For example, Klop et al. found that persistence after re-starting OP medications remained low and was substantially lower than initial rates of persistence [15].

Despite its strengths (grounded theory approach, theoretical sampling, uniform patient population), our work has limitations. First, even by the standards of qualitative inquiry, some might consider our sample small; however, we sampled until data saturation was reached, employed multiple checks for rigor and validity, and selected participants from both ends of the persistence spectrum. Second, it was somewhat difficult to use the technique of theoretical sampling within the constraints of an ongoing trial. For example, we were unable to sample for patients who changed treatment status more than 1 year after their fracture and we had no access to patients who dropped out of the study altogether. Third, we did not set out to specifically examine sex and gender differences in health behaviors. While this is an important area of inquiry, by our grounded theory design, no sex or gender differences in pill-taking behavior were evident in our study, so we did not pursue increased sampling of constructs related to sex and gender. Last, all subjects were relatively healthy, of good socioeconomic status, had good knowledge related to osteoporosis, had no contraindications to bisphosphonate treatment, and all had an upper extremity fragility fracture, and our findings were based on the experiences of trial patients with universal healthcare coverage from one Canadian province. Thus, some might not consider our results transferrable to other populations, including patients with other types of fractures including hip or spine or settings.

The processes and reasoning related to persisting with or stopping bisphosphonate treatment for OP after a fragility fracture are complex and dynamic over the long term. Our findings suggest two potential areas to leverage for providers and those designing interventions. First, healthcare providers should reinforce the severity and risks and potential harms related to untreated clinical OP and refrain from using BMD test-based labels such as osteopenia, which appears to diminish perceived disease severity among patients. Second, healthcare providers need to review regularly the very favorable benefit-to-risk profile of treatment for this high-risk group of patients. Perhaps what has become most clear through this research is that starting treatment for OP is the

beginning of a long-term negotiation with patients in an effort to prevent the next fracture and its potential consequences.

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Compliance with ethical standards

Conflict of interest None

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Appendix

Table 3 Selected questions from interview guide

Questions posed to all patients

1. Tell me about your understanding of your diagnosis.
2. (If "I don't have OP"): what is the difference between your current condition and OP?
3. Tell me why you decided to start bisphosphonate treatment.
4. Are you concerned about having another fall and breaking another bone? Why?
5. What do you consider your risk of having another fracture without bisphosphonate treatment?
6. How do you think OP or the weakening or thinning of bones, will affect you over the course of your life?
7. Do you think bisphosphonate treatment is required for you to treat OP? Why or why not?
8. How serious is OP as a health condition?

Questions posed to patients who persisted with prescription treatment

1. Tell me about why you decided to keep taking a bisphosphonate as part of your treatment.
2. What, if anything, would make you decide to stop the bisphosphonate?

Questions posed to patients who stopped prescription treatment

1. Tell me about why you decided to stop taking a bisphosphonate as part of your treatment.
2. What, if anything, would make you decide to take a bisphosphonate again?

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