Paradigm Shifts in the Care of Patients With Osteoporosis

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Foreword

Osteoporosis management has evolved in the past decade, with considerably more focus now being placed on fractures. As discussed in this report, fractures are highly predictive of future fractures and cause significant patient and systemic burden; therefore, they ***must inform*** osteoporosis management together with other risk factors. The following 7 North American osteoporosis guidelines have been recently published (2020–2023), focusing on patients with a history of a fracture: American Association of Clinical Endocrinologists (AACE),[1] American College of Physicians (ACP),[2] Bone Health and Osteoporosis Foundation (BHOF; formerly National Osteoporosis Foundation),[3] Endocrine Society (ES),[4, 5] North American Menopause Society (NAMS),[6] Osteoporosis Canada (OC),[7] and Society of Obstetricians and Gynaecologists of Canada (SOGC).[8] The main clinical audiences varies between these guidelines, with ACP, BHOF, NAMS, and OC focusing on primary osteoporosis management and/or family care (**Table 1A**). In terms of target patient population, only BHOF and OC considered older men (≥50 years) in addition to postmenopausal women.

As reflected across these guidelines, important paradigm shifts have occurred in osteoporosis care in the past decade, which we discuss here. We also provide a practical summary of the recent recommendations (provided by at least 2 guidelines), as detailed in **Table 1B-F**, focusing on patient identification, diagnosis, and pharmacologic treatments.

As our main audience is primary care, we conclude with clinical pearls from our own practice aimed at family practice. However, much of this report also provides helpful information to other healthcare professionals managing patients with osteoporosis in Canada, such as endocrinologists, rheumatologists, internal medicine specialists, geriatricians, gynaecologists, postmenopausal/women's health specialists, nurse practitioners, and orthopaedic surgeons.

Table 1. Key Clinical Questions for Diagnosis and Treatment of Osteoporosis in Adults ≥50 Years of Age: Summary of Recent (2020–2023) Guidelines

Clinical Questions	Answer provided by ≥2 guidelines						
	AACE[1]	ACP[2]	BHOF[3]	ES[4,5]	NAMS[6]	OC[7]	SOGC[8]
(A) Guideline scope							
What is the main clinical audience of a guideline?							
Physicians managing primary or secondary osteoporosis							
Physicians managing primary osteoporosis							
Family care							
What target patient population did a guideline focus on?							
Postmenopausal women							
Postmenopausal women and men ≥50 years of age		A					
(B) Identification of at-risk patients							
Who should be clinically assessed for osteoporosis risk?							
All postmenopausal women ≥50 years of age		–		–			
All men ≥50 years of age		–		–			
How should osteoporosis and fracture risk be assessed?							
Using the following clinical assessments:							
• Fracture history after age 40–50 years		–		–			
• FRAX fracture risk calculation		–		–			
• Silent spine fracture assessment (e.g., height loss: prospective, >2 cm; historic, >4–6 cm[3, 6, 7])		–		–			
• Falls risk assessment		–		–			
When should BMD testing be performed?							
Age ≥65–70 years		–		–			
Age <65–70 years: using a targeted approach based on risk profile to inform decisions regarding therapy		–		–			
When should osteoporosis and fracture risk be reassessed in patients who do not have high risk?							
If a new fracture occurs	–	–		–	–		–
Otherwise, every 3–10 years (depending on fracture risk [i.e., shorter timing with higher risk])	–	–		–	–		–
(C) Diagnosis							
When is osteoporosis diagnosed?							
When ≥1 is present:							
1. Hip or spine fracture (occurring after age 40–50 years or menopause)	B	–		–		B	
2. BMD T-score ≤–2.5 (lowest score of femoral neck, total hip, or lumbar spine)		–		–			
3. Proximal humerus, pelvic, or distal forearm fracture and BMD T-score –1.0 to –2.5		–		–		C	
4. ≥20% FRAX MOF fracture risk and BMD T-score –1.0 to –2.5		–		–			
5. ≥3% FRAX hip fracture risk and BMD T-score –1.0 to –2.5		–		–			
What is considered a fragility fracture in adults aged ≥50 years?							
Any fracture except hands, feet, and cranium fracture		–		–			–
Low-trauma fracture except hands, feet, and cranium fracture		–		–			–
When should secondary osteoporosis be investigated with laboratory workup?							
When someone is diagnosed with osteoporosis to differentiate between primary and secondary osteoporosis		–		–			
If a secondary cause is found (especially if complex), consider referring for additional investigations to a specialist		–		–			
(D) Risk stratification in treatment-naive patients							
At what fracture risk level is treatment initiation recommended?							
Patients with a **very high** fracture risk, defined by **≥1** of the following, are recommended for bone formation therapy							
1. Recent fragility fracture (within past 12 months)		D		E		F	
2. Multiple spine fractures			D			F	
3. FRAX MOF risk >30%							
4. FRAX hip fracture risk >4.5%							
5. BMD T-score ≤–3.0 (lowest score of femoral neck, total hip, or lumbar spine)						F	
Patients with a **high** fracture risk, defined based on **≥1** of the following, are recommended for therapy							
1. FRAX MOF risk ≥20%	G		G		G		
2. BMD T-score ≤–2.5 (lowest score of femoral neck, total hip, or lumbar spine)						H	
3. Multiple fragility fractures—any site	I	I, D		I, D	G	B	I
4. Spine or hip fracture	B						
5. FRAX hip fracture risk ≥3%	G		G		G		
6. Proximal humerus, pelvic or distal forearm fracture and BMD T-score –1.0 to –2.5							

	AACE[1]	ACP[2]	BHOF[3]	ES[4,5]	NAMS[6]	OC[7]	SOGC[8]
What about patients who do not have a high fracture risk?							
Individualized decision-making for treatment initiation is recommended if							
• BMD T-score is –1.0 to –2.5 and patient is not deemed to have high fracture risk	–						
• FRAX MOF risk: OC, >15% and <20%, or SOGC, >10% and <20%							
(E) Treatment initiation							
What therapies are recommended for treatment initiation based on high risk vs very high risk?							
Very high risk							
• Bone formation therapy: romosozumab (SC, QM) or teriparatide (SC, QD)						F	
High risk							
• Any one of: bisphosphonate (oral, QD/QW; IV, Q12M) or denosumab (SC, Q6M)							
• 1L: bisphosphonate (oral, QD/QW; IV, Q12M); 2L: denosumab (Q6M)		J				J	
(F) Treatment duration, monitoring, and sequence							
What is the recommended treatment course duration?							
Bisphosphonates: 3–5 years (IV, 3 years; oral, 5 years), then reassess for follow-on approach							
Denosumab: long-term uninterrupted (may be continued for >10 years)		–					
Romosozumab: long-term uninterrupted therapy for 12 months followed by antiresorptive treatment		–					
Teriparatide: long-term uninterrupted therapy for ≤24 months followed by antiresorptive treatment		–					
What are considered as appropriate follow-on treatment approaches?							
End of treatment: antiresorptive therapy							
• Bisphosphonate: If high on-treatment risk, switch to another therapy or continue with bisphosphonate for ≥6–10 years		K				K	
• Bisphosphonate: If on-treatment risk is not high, consider temporary drug holiday for ~2 years, then reassess for fracture risk and reinitiate treatment if fracture risk returns to high		K				K	
• Denosumab: Follow on with alternative treatment		–					
End of treatment: bone formation therapy							
• Follow on with antiresorptive therapy							
Inadequate treatment response							
• Switch to another therapy and/or consider specialist referral		–	–				
What is considered as high on-treatment risk?							
Consider high on-treatment risk based on **≥1** of the following							
1. On-treatment BMD T-score ≤–2.5		–				L	
2. History of hip or spine fracture		–				L	
3. Recent on-treatment fracture		–				L	
4. FRAX MOF risk ≥20%		–				L	
What is considered as inadequate response to treatment?							
Consider inadequate response to treatment if							
• No secondary cause or adherence issues are present **AND**		–	–				
• **≥1** of the following occurs during treatment							
• ≥2 fractures		–	–				
• 1 fracture and no adherence issues		–	–				
• Continuous BMD decline		–	–				

1L, first line; 2L, second line; AACE, American Association of Clinical Endocrinologists; ACP, American College of Physicians; BHOF, Bone Health and Osteoporosis Foundation (formerly National Osteoporosis Foundation); BMD, bone mineral density; ES, Endocrine Society; FRAX, fracture risk assessment tool; IV, intravenous; MOF, major osteoporotic fracture; NAMS, North American Menopause Society; OC, Osteoporosis Canada; Q6M, every 6 months; Q12M, every 12 months; QD, daily; QM, monthly; QW, weekly; SC, subcutaneous; SOGC, Society of Obstetricians and Gynaecologists of Canada.

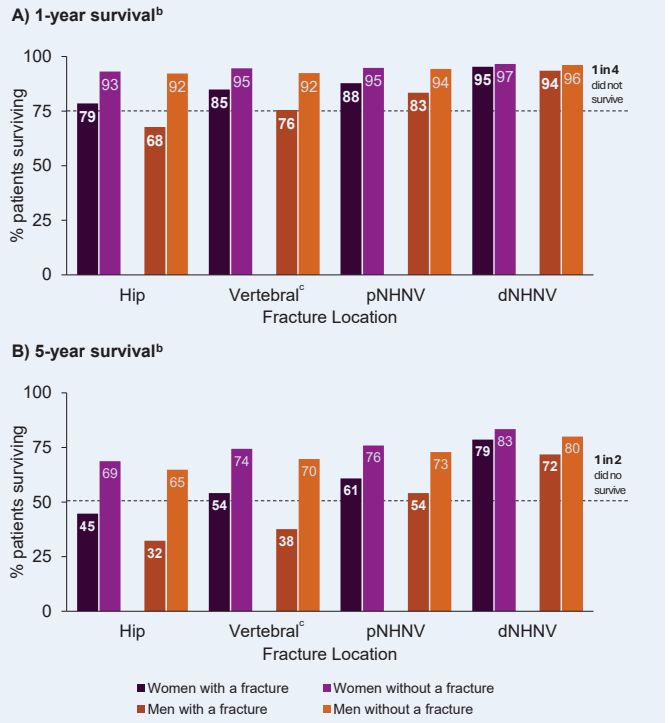
– Question was not addressed by a guideline.
[A]Guideline's target patient population was adults with low bone mass or primary osteoporosis.
[B]Conditional recommendation: if low-trauma fracture.
[C]Guideline recommends only humerus or pelvic fracture and independent of BMD.
[D]Conditional recommendation: if BMD T-score is ≤–2.5.
[E]Guideline recommends initiating therapy without a delay in patients with a recent fracture (within past 2 years).
[F]Guideline does not specify a "very high risk" category but recommends bone formation therapy for those with multiple spine fractures or a recent severe spine fracture and BMD T-score ≤–2.5; it also indicates that fracture risk calculators may underestimate fracture risk in patients with recent fragility fracture or BMD very low spine or total hip BMD.
[G]Conditional recommendation: if BMD T-score is –1.0 to –2.5.
[H]Conditional recommendation: if ≥70 years of age.
[I]Guideline considers multiple fractures as indicating very high risk: AACE, ACP (if BMD T-score is ≤–2.5), ES (if BMD T-score is ≤–2.5), and SOGC.
[J]Denosumab is recommended 1L treatment if barriers to bisphosphonates exist, such as high burden of oral medications, gastrointestinal intolerance, inability to be upright >30 minutes, hypocalcaemia, creatine clearance <30–35 mL/min, or esophageal abnormalities.
[K]Alternative definition provided: OC recommends bisphosphonate holiday if there is adequate response and no ongoing substantial concern for fracture; ACP recommends individualized decision-making for bisphosphonate holiday, based on baseline risk for fracture, type of bisphosphonate and its half-life in bone, and the benefits/harms of discontinuation, including higher risk for fragility fracture.
[L]Alternative definition provided: when there is inadequate response to therapy or ongoing substantial concern for fracture.

Paradigm shifts in the care of patients with osteoporosis

Zero in on fracture

The Public Health Agency of Canada considers osteoporosis a major public health concern, owing to a significant patient and systemic burden caused by osteoporosis-related fractures (**Appendix 1**).[9] Fracture, referred to by some as a "bone attack," is a major complication of osteoporosis like a heart attack is a major complication of cardiovascular disease.[9, 10] Survival declines after a fracture in older Canadian women and men, especially after a hip, spine, upper extremity, or pelvic fracture, and in men (**Figure 1**).[9,11] The survival reductions occur within the initial post-fracture month and persist long term.[11]

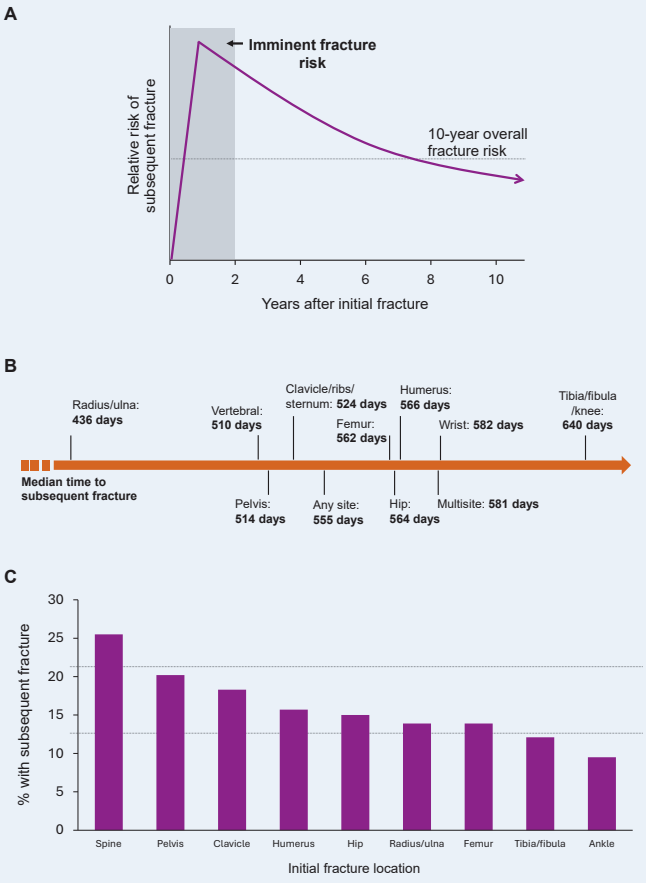
Figure 1. A) 1- and **B)** 5-year survival rate in Ontarians >65 years of age after a fracture compared with matched[a] individuals without a fracture (2011–2015)[11]



pNHNV, proximal non-hip non-vertebral (pelvis, femur, sternum, rib, clavicle, humerus, or shoulder); dNHNV, distal non-hip non-vertebral (tibia, fibula, knee, radius, ulna, or wrist).
[a]Matched 1:1 based on age, sex, and comorbidities.
[b]1 and 5-year relative survival rate (survival probability in patients with fracture divided by survival probability in a control group without fracture), respectively: hip/females, 84%% and 65%; hip/males, 73% and 50%; vertebral/females, 90%% and 73%; vertebral/males, 82% and 54%; pNHNV/females, 93% and 80%; pNHNV/males, 88% and 74%; dNHNV/females, 99% and 94%; dNHNV/males, 97% and 90%.
[c]Clinical/symptomatic.

Fracture also significantly increases the risk for a future fracture among older adults over the subsequent 10 years,[12, 13] with the highest relative risk occurring within the initial 1 to 2 post-fracture years (**Figure 2A**).[14-19] In fact, it is estimated that a subsequent fracture occurs on average within 555 days after an initial fracture among Canadians >65 years of age (**Figure 2B**).[14] This near-term risk, termed "imminent fracture risk," is analogous to the near-term risk occurring after a major cardiovascular event and applies to all fractures related to osteoporosis.[14, 15, 20] In postmenopausal women, the 2-year risk is estimated to be 15% to 26% after a spine, pelvic, clavicle, upper arm, or hip fracture and 10% to 14% after a lower arm or leg fractures (**Figure 2C**).[15]

Figure 2. Subsequent fracture within 1 to 2 years after initial fracture: **A)** schematic illustration of "imminent" fracture risk,[14-19] **B)** median time (days) to subsequent fracture among 115,776 Ontarians >65 years of age by anatomic site of initial fracture,[14] **C)** 2-year risk of subsequent fracture among 377,561 postmenopausal women ≥65 years of age in the US by anatomic location of initial fracture[15]

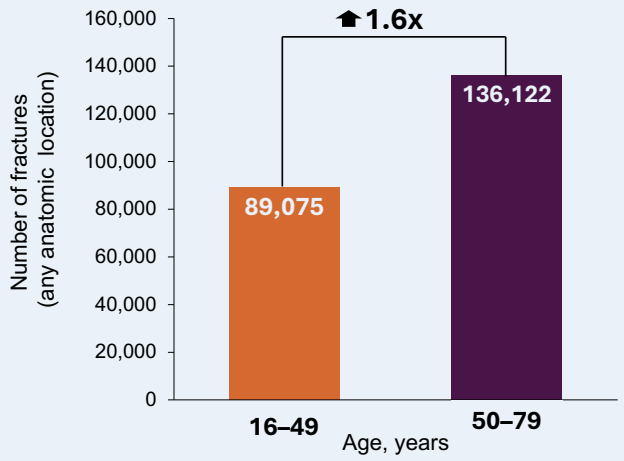


Because fracture is an important risk factor for future fracture, it informs osteoporosis management in postmenopausal women and men ≥50 years of age across its continuum. Guidelines overall agree that the assessments for identifying individuals at risk for osteoporosis need to include an evaluation of fracture history (**Table 1B**). Furthermore, ***a hip or spine fracture requires osteoporosis diagnosis*** regardless of the patient's bone mineral density (BMD; **Table 1C**). This clinical event–driven diagnosis of osteoporosis is analogous to cardiovascular disease, where a diagnosis is made based on an event (e.g., myocardial infarction or cerebral vascular accident) regardless of a patient's cholesterol level. Guidelines also recommend that fracture history should inform risk stratification and treatment decisions. In this regard, history of any fracture is important for a calculation of a 10-year fracture risk based on fracture risk assessment tool (FRAX). All guidelines also agree that, regardless of FRAX results, certain types of fractures (i.e., hip, spine, recent, or >1 fracture) alone indicate high or very high fracture risk (**Table 1D**). Finally, fracture history should also inform clinical decisions during treatment (**Table 1F**), as discussed below.

Fracture signals a need for osteoporosis assessment independent of low trauma

As part of their scope, 4 guidelines specify what is considered a fragility fracture, all confirming that fractures of the hands, feet, and cranium are not to be considered (**Table 1C**). AACE and OC further specify that only fractures associated with low trauma should be considered a clinically significant event as part of osteoporosis management. However, NAMS and BHOF recommend that all fractures occurring among adults ≥50 years of age—independent of trauma—should signal the need for further osteoporosis-related assessments. NAMS and BHOF have provided this recommendation because bone loss increases with age in the general population and, consequently, so do the number of fractures (**Figure 3**), regardless of whether they were caused by a high-trauma injury.[21, 22] Furthermore, even older adults with a history of a fracture resulting from a high-trauma injury were found to a have significantly lower BMD and higher future fracture risk than those without a history of a fracture.[23] Finally, accurately ascertaining if the force experienced during an injury was low impact is challenging;[1] as we often experience in our clinical practice, patients may not sufficiently remember exactly how they injured themselves or overestimate the forces they sustained.

Figure 3. Increase in fracture numbers in older vs younger general adult population (Sweden, 2012–2018)[21]



FRAX: preferred risk calculator

BMD is a significant predictor of future fracture risk, in addition to fracture history and age; however, many adults ≥50 years of age experience a fracture when BMD is not in the osteoporotic range.[24] This is because there are other components of bone strength and fracture risk that BMD results cannot capture.[25] As such, all guidelines providing recommendations for identifying at-risk patients (**Table 1B**) recommend conducting a clinical evaluation of multiple risk factors that includes calculation of 10-year fracture risk using the FRAX calculator (**Table 2**; frax.shef.ac.uk/FRAX/tool.aspx). All guidelines, except for ACP's, also recommend that FRAX major osteoporotic fracture (MOF; i.e., hip, vertebral, forearm and humerus fracture)[3, 7] risk score should be used for treatment initiation decisions, with ≥20% indicating high risk (**Table 1D**). FRAX also calculates 10-year risk of a hip fracture, the prevention of which is at the centre of fracture prevention care in older adults.[9, 11, 14, 26] As such, the AACE, BHOF, ES, NAMS, and SOGC recommend that a FRAX hip fracture risk score of ≥3% also indicates high risk (even when MOF risk is <20%). Finally, FRAX risk calculation can be performed without entering BMD data,[1, 3, 6-8] especially among patients 50–65 years of age, for whom BMD testing is recommended based on their initial clinical risk profile (**Table 1B**). Although the original FRAX calculator does not include certain risk factors (e.g., dose and duration of glucocorticoid treatment and location, number and recency of fracture), solutions are available and include considering a higher actual risk among patients who have these risks factors or using the FRAX Plus online calculator (fraxplus.org) with available adjustments described in **Table 2**.

Table 2. Canadian FRAX Fracture Risk Calculator[64]

Free access	https://frax.shef.ac.uk/FRAX/tool.aspx?country=19
Clinical information needed to calculate fracture risk	Required entries • Age • Sex • Weight (kg) • Height (cm) • Previous fracture[a] • Biological parent fractured hip • Current smoking • Glucocorticoids (oral; current/ever ≥3 months; 5-mg prednisone equivalent) • Rheumatoid arthritis (confirmed diagnosis[b]) • Secondary osteoporosis[c] • Alcohol ≥3 units/day Optional entry • Femoral neck BMD[d]
Results	10-year major MOF risk (%) 10-year hip fracture risk (%)
Limitations and solutions	The calculator does not consider the following factors and risk may be underestimated if any of the following is present: • Hip, spine, recent, or multiple fractures (indicate high fracture risk regardless of FRAX score)[7, 64] • Falls risk[7, 8] • BMD ≤–3.0[7] • Spine BMD considerably lower than hip BMD >-2.5[7] • Type 2 diabetes[3, 6] • Current proton pump inhibitor treatment[3, 6] • High exposure to oral glucocorticoids[65] Potential solutions • Consider higher actual risk as part of decision-making • Use FRAX Plus for recency of fracture, falls history, concurrent spine BMD data, type 2 diabetes, high oral glucocorticoid exposure; available for purchase: https://www.fraxplus.org/frax-plus • FRAX Plus is also available as a desktop or mobile application that includes helpful features (e.g., history log and PDF report)

BMD, bone mineral density; FRAX, fracture risk assessment tool; MOF, major osteoporotic fracture.
[a]Includes radiographic observation of silent vertebral fracture.
[b]Rheumatoid arthritis is a risk factor for fracture but osteoarthritis is not; hence, reliance needs to be placed on confirmed diagnosis and not patient's report of "arthritis."
[c]Type 1 diabetes, adult osteogenesis imperfecta, untreated long-standing hyperthyroidism, hypogonadism or premature menopause (aged <45 years), chronic malnutrition or malabsorption, and chronic liver disease.
[d]Leave blank if unknown or enter T-score (if the make of the scanning equipment is known, enter actual BMD in g/cm^2).

Very high risk: an important categorization of patients at the highest fracture risk

Very high risk of fracture is now defined in the AACE, ACP, BHOF, ES, NAMS, and SOGC guidelines (**Table 1D**), and patients who have very high risk are recommended to initiate treatment with bone formation therapy (**Table 1E**). Although the definition of this risk category varies, ≥4 guidelines agree that patients should also be considered as very high risk based on a fracture occurring within the past 12 months. Additionally, ≥2 guidelines agree that the very high–risk classification should be considered based on a history of multiple (≥2) spine fractures, 10-year MOF risk >30% or hip fracture risk >4.5% or BMD T-score ≤–3.0. AACE and SOGC also consider any type of multiple fractures (not just spine) as very high risk. Although the OC guideline did not define a very high–risk category, it recommends considering treatment initiation with bone formation therapy among patients with multiple spine fractures and a BMD T-score ≤–2.5. It also advises that FRAX risk can be underestimated among patients with a recent fragility fracture or very low spine or total hip BMD.[7]

Bone formation therapies are recommended for treatment initiation among patients with very high risk of fracture, owing to their anabolic effects that translate to bone microstructure improvements and greater BMD increases and fracture risk reductions over 12 to 24 months of treatment compared with antiresorptive therapies.[27-33] Furthermore, the ideal opportunity for maximizing their anabolic effects is in treatment-naive patients, because significantly greater BMD gains have been observed when bone formation therapy is administered in a treatment-naive setting vs after antiresorptive treatment with bisphosphonate or denosumab (owing to the mechanism of action of both classes of medications).[34-37]

Individualized treatment decisions

With additional treatment options becoming available since the prior OC guideline publication in 2010,[38] treatment-related decision-making has become individualized, as reflected among the recent guidelines. As described above, all guidelines recommend that certain patients should be considered for bone formation therapy (**Table 1D-E**), with 2 therapeutic options being available in Canada (romosozumab and teriparatide).[39, 40] Beyond this, individualized decision-making is recommended by ACP, BHOF, ES, OC, and SOGC for treatment initiation among patients whose fracture risk is approaching a high-risk threshold (**Table 1D**). For context, OC no longer defines a moderate-risk category and instead recommends individualized decision-making among patients with a FRAX MOF risk score of 15.0% to 19.9%.[7] Finally, AACE, BHOF, ES, NAMS, and SOGC guidelines recommend selecting antiresorptive therapy for treatment initiation among high-risk patients based on individualized decision-making (e.g., considering patient preferences for route of administration, dosing schedule, and side effects; contraindications; and cost/access) vs having first- or second-line options (**Table 1E**).

OC and ACP, which focused on a primary care audience (**Table 1A**), have taken a less individualized approach for treatment initiation with antiresorptive therapy by providing recommendations for first- and second-line options (**Table 1E**). The risk–benefit profiles examined as part of their recommendation relied primarily on placebo-controlled clinical trials, which come with certain limitations.[2, 7] More recent placebo-controlled trials typically assessed study populations with a lower baseline fracture risk, potentially underestimating the absolute anti-fracture benefits among those at a high or very high fracture risk. Further, placebo-controlled trials necessitate between-study comparisons of different agents. While head-to-head trials with a large enough study population to examine fracture rates are limited,[41] significantly greater BMD gains were observed with denosumab vs oral bisphosphonates in head-to-head comparisons (and greater on-treatment BMD improvements are associated with greater fracture risk reductions).[27, 42-45]

ACP reported that cost (and availability of generic options) was a key consideration for recommending bisphosphonates as a first-line option but acknowledged that poor adherence to oral bisphosphonates was not considered as part of their assessment.[2, 46, 47] OC reported rapid bone loss after denosumab treatment cessation to be a main consideration;[7, 48] however, this risk is recommended to be managed by not interrupting denosumab treatment without switching to follow-on therapy (**Table 1F**) to help attenuate this bone loss.[49] For risks associated with bisphosphonates, both OC and ACP considered the increased risk of atypical femoral fracture (AFF) associated with long-term bisphosphonate treatment,[2, 7] which can be managed by considering the different follow-on treatment approaches described below.

Treatment course duration and follow-on approaches

There is overall alignment among the recent guidelines regarding the recommended treatment duration and follow-on approaches for different therapies (**Table 1F**). Bone formation agents have a finite treatment duration (romosozumab, 1 year; teriparatide, ≤2 years)[39, 40] that is typically shorter than that of antiresorptive treatments. After finishing bone formation treatment, all guidelines recommend switching to antiresorptive therapy to preserve the achieved BMD gains. Stopping bone formation therapy without a follow-on therapy is accompanied with a loss of anabolic efficacy and BMD declines to pretreatment values within ~1 year.[50] A relatively rapid waning of efficacy after stopping treatment is also characteristic of other medications in this (e.g., denosumab, hormone therapy, and raloxifene) and other (e.g., statins) therapeutic areas[51-53] and is related to these agents' mechanism of action being dependent on adequate blood concentrations. The waning of efficacy with denosumab is associated with an increased risk of multiple spine fractures by ~1 event per 100 person-years on average, particularly in those with a pretreatment history of spine fractures.[54] This risk needs to be attenuated by switching to follow-on antiresorptive or bone anabolic therapy (**Table 1F**). In terms of treatment course duration with denosumab, experts[49] and guidelines agree that there is no defined limit. AACE, BHOF, ES, NAMS, OC, and SOGC recommend long-term uninterrupted treatment without time limits, with OC additionally recommending to reassess patients after 6 to 10 years of treatment and either continuing treatment or switching to another therapy based on individualized decision-making.[7] To help ensure uninterrupted treatment during a denosumab course, various reminder tools and/or patient assistance programs are available for use by patients and/or physicians.

Unlike many other pharmacologic agents requiring sufficient serum concentrations to exert effects, bisphosphonates experience slower waning of efficacy after treatment cessation because they are a unique class of medications that remain embedded within the bone matrix for some time after stopping treatment.[55, 56] In terms of treatment course duration, all guidelines recommend reassessing patients after 3 to 5 years of bisphosphonate treatment (oral, 5 years; intravenous, 3 years; **Table 1F**), owing to a significantly increased risk of rare complications with long-term exposure (i.e., AFF and osteonecrosis of the jaw).[56-58] All guidelines also agree that after 3 to 5 years of bisphosphonate treatment appropriate patients may consider taking a temporary holiday (owing to bisphosphonate unique mechanism of action). AACE, BHOF, ES, NAMS, and SOGC consider the appropriate patients to be those who no longer have a high on-treatment fracture risk; these are patients with an on-treatment BMD T-score >-2.5 who did not experience a recent on-treatment fracture and do not have a history (before or during treatment) of a hip or spine fracture (**Table 1F**). ES and SOGC also indicate that in order to start a bisphosphonate holiday, on-treatment FRAX MOF risk should be <20%. However, some caution against this approach because FRAX (and other fracture risk calculators) was validated based on treatment-naive data.[3] Finally, ACP does not define high on-treatment risk, and OC recommends against a bisphosphonate holiday when there is "ongoing substantial" concern for osteoporosis-related fracture.[2, 7]

Regarding the duration of bisphosphonate holiday, it is recommended for patients to be reassessed for when anti-osteoporosis treatment needs to be reinitiated at ~2 years after starting the bisphosphonate holiday by using fracture history, BMD assessment, and FRAX risk calculation (note: after 2 years off treatment, FRAX is appropriate, because these patients may be considered as naive to treatment).[1, 3-8] Anti-osteoporosis therapy needs to be restarted when high fracture risk is observed during the bisphosphonate holiday.[1, 3-8]

For the patients who remain at high risk after 3 to 5 years of bisphosphonate treatment, it is recommended to switch to another therapy or continue bisphosphonate therapy (**Table 1F**). Continuing bisphosphonate treatment beyond 3 to 5 years is recommended because the risk of MOF exceeds the concern for AFF;[1-7, 56] however, SOGC recommends switching to a non-bisphosphonate treatment (if possible),[8] which is an especially important consideration for Asian women who have a higher AFF risk.[58]

Clinical pearls

Here, we provide additional tips and insights from our own practice as well as helpful links (**Appendix 2**) that we hope you may find helpful.

A man with one watch knows what time it is

"A man with one watch knows what time it is. A man with two watches is never sure." Considering this saying, we would like to share the following reminders and tips for integrating different data elements into clinical decision-making:

- Only 1 factor listed in **Table 1C** needs to be considered for osteoporosis diagnosis; clinical diagnosis of osteoporosis based on hip or spine fracture does not require BMD- or FRAX-based confirmation
- When determining fracture risk, a history of high-risk fracture alone (i.e., hip, spine, recent, or multiple fractures; **Table 1D**) has greater importance than FRAX risk score, and FRAX assessment using BMD data exceeds BMD data alone or FRAX assessment without BMD
- The FRAX calculator should be utilized for fracture risk stratification to inform treatment initiation[7]
- When evaluating BMD as part of fracture risk assessment, a T-score value ≤–2.5 is an important risk factor
  - Consider the lowest observed score at the femoral neck, total hip, or lumbar spine for osteoporosis diagnosis (**Table 1C**) or when considering BMD as an independent risk factor for high or very high fracture risk stratification (**Table 1D**)
  - Recognize that although the FRAX calculation should use femoral neck BMD, patients can have lower spine BMD than femoral neck or total hip BMD[59] and may be considered as having a higher actual fracture risk; alternatively, adjustments can be made to their score using FRAX Plus (fraxplus.org/frax-plus) if this option is available (as described in **Table 2**)

Prioritizing osteoporosis assessments in a busy practice

How can you quickly identify patients requiring more immediate attention when there is limited time to carry out thorough risk assessments? Three key predictors of future fracture among adults ≥50 years of age are:

1. a prior fracture
2. age ≥65 years
3. BMD T-score ≤–2.5 (lowest score of femoral neck, total hip, or lumbar spine)

If a patient has a history of fracture and either BMD T-score ≤–2.5 or age ≥65 years, a very high fracture risk should be suspected and these patients should be of most concern. If a patient's age is ≥65 years and BMD is ≤–2.5, a minimum of high risk should be considered.

We find FRAX to be a highly useful communication tool when discussing osteoporosis and fracture risk with patients, and FRAX can be completed relatively quickly and easily during a patient visit (**Table 2**). However, when catching up with administrative tasks in a busy family practice, knowing which BMD reports to prioritize for calculating FRAX risk score may be helpful (note: radiologists often have limited patient information available to be able to calculate a FRAX risk score as part of BMD reporting). Remember that high fracture risk needs to be automatically considered and FRAX risk calculation is not needed for patients with a history of high-risk fracture (i.e., hip, spine, recent, or multiple fractures) or BMD <–2.5 (**Table 1D**). For other patients, the 3 main predictors, i.e., a prior fracture, age ≥65 years, and BMD T-score ≤–2.5, are also helpful here. If needed, consider prioritizing FRAX calculation when 2 or more of these factors are present (when only 1 of these risk factors is present, it is less likely that a patient would have high risk). However, after getting used to the FRAX calculator, you may learn that it is easy and quick to use, providing helpful information on a wide variety of patients.

Unmet needs in primary care

It is important to be aware of which patients may benefit from receiving specialist care owing to their complexities and unmet needs in primary care. Patients requiring bone formation treatment may benefit from specialist care because bone formation therapy requires greater expertise to explain to patients and consequently is typically initiated in a specialist setting in North America. Recent North American guidelines also recommend that patients with more complex secondary osteoporosis causes or those with inadequate treatment response (as defined in **Table 1F**), especially when treatment choices are limited, may need additional investigations by a specialist.[3, 6, 7]

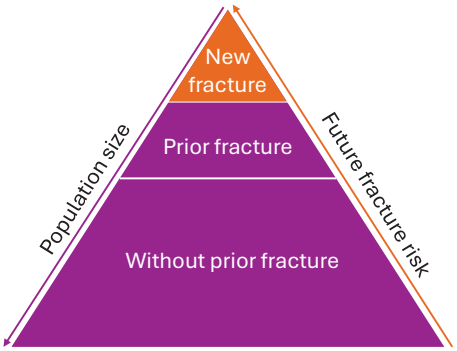
However, perhaps the most pressing unmet need, which applies to all healthcare professionals managing osteoporosis or fractures, is to consider osteoporosis among older adults as seriously as other common chronic diseases (such as heart disease). This inattention to the consequences of fracture will result to significant reductions in the life span (**Figure 1**) and/or quality of life. The large osteoporosis gap that currently exists in Canada (**Appendix 1**) and worldwide is a direct result of the current lack of prioritization of osteoporosis, especially in the light of our rapidly aging population. Experts, advocacy groups, and governments agree that addressing the care gap requires urgent and comprehensive strategies and attention from healthcare systems and multiple healthcare specialties, especially those who see the highest-risk patients.[9, 60-62] In this regard, the American Society of Bone and Mineral Research task force[63] identified key areas to help address the care gap, which include having primary care teams and other clinicians communicate 3 simple messages to patients ≥50 years of age and their family or caregivers throughout fracture care and healing process:

1. *"Their broken bone likely means they have osteoporosis and are at high risk for breaking more bones, especially over the next 1 to 2 years*
2. *Breaking bones means they may suffer declines in mobility or independence—for example, have to use a walker, cane, or wheelchair, or move from their home to a residential facility, or stop participating in favorite activities—and they will be at higher risk of dying prematurely*
3. *Most importantly, there are actions they can take to reduce their risk, including regular follow-up with their usual health care provider as for any other chronic medical condition"*

Appendix 1. Osteoporosis and fracture prevention in Canadian population.

The Public Health Agency of Canada (PHAC) considers osteoporosis a major public health concern owing to significant patient and systemic burden associated with fractures and the growing population of older Canadians who are currently experiencing a major osteoporosis care gap.[9] The PHAC refers to fractures related to osteoporosis as a "bone attack" (as do some experts),[10] because like heart attack, fractures are a major complication of a chronic disease associated with significant morbidity (e.g., frailty),[66-69] loss of independence (e.g., 20% to 25% long-term care admission rate 1 year after a hip fracture),[70] and reduced survival.[9, 11, 22] A recent study found that 1-year mortality after osteoporosis-related fractures observed among Canadians >65 years of age was comparable to that observed after a myocardial infarction.[22] However, unlike patients with myocardial infarction, of whom 80% are estimated by the PHAC to receive medications to prevent future events within 1 year, <25% of patients receive medications within a year to prevent future fractures even after experiencing one of the most serious osteoporosis-related fractures—a hip fracture.[9, 11, 26, 71]

As part of its population-level strategy of fracture prevention in Canada, the PHAC closely surveils fractures among Canadians ≥40 years of age and advocates for the International Osteoporosis Foundation's approach to identifying at-risk individuals within the older adult population. This approach focuses on easy-to-identify individuals, or those presenting with a fracture.[9, 72] As depicted here, these individuals make up a relatively small proportion of the population appropriate for fracture risk assessment yet have a high probability of experiencing another fracture.



While primary prevention is still important, a prioritized approach focusing on secondary prevention was highlighted by the PHAC, partly owing to the extensity of the osteoporosis care gap.[9] Family care plays an important role in identifying patients with a recent fracture in Canada because such patients can present to their primary care practice soon after experiencing the fracture. Although fracture clinics provide orthopaedic care to see patients presenting with a fracture, most of Canada's hospitals do not currently have a clinical pathway to initiate osteoporosis assessment during fracture clinic care.[60] However, considering that Canada's population is aging and experiencing primary care physician shortage, patient identification and assessment warrants a team approach with all levels of medical support need, including an establishment of evidence-based clinical pathway, known as fracture liaison services, at more hospitals.[61, 72, 73]

Appendix 2: Helpful links

Exercise

- https://osteoporosis.ca/exercise/
- https://osteoporosis.ca/wp-content/uploads/OC-Too-Fit-to-Fall-or-Fracture.pdf
- https://www.sailfitness.org/
- https://www.osteoporosis.foundation/health-professionals/prevention/exercise/exercise-depending-on-age

Falls

- https://www.canada.ca/en/public-health/services/publications/healthy-living/you-prevent-falls.html

Nutrition

- https://osteoporosis.ca/nutrition/
- https://osteoporosis.ca/calcium-calculator/
- https://www.osteoporosis.foundation/health-professionals/prevention/nutrition
- https://www.osteoporosis.foundation/patients/recipes
- https://osteoporosis.ca/recipes/

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