Patient vignettes in osteoporosis: Fracture prevention with bone formation (anabolic) therapy

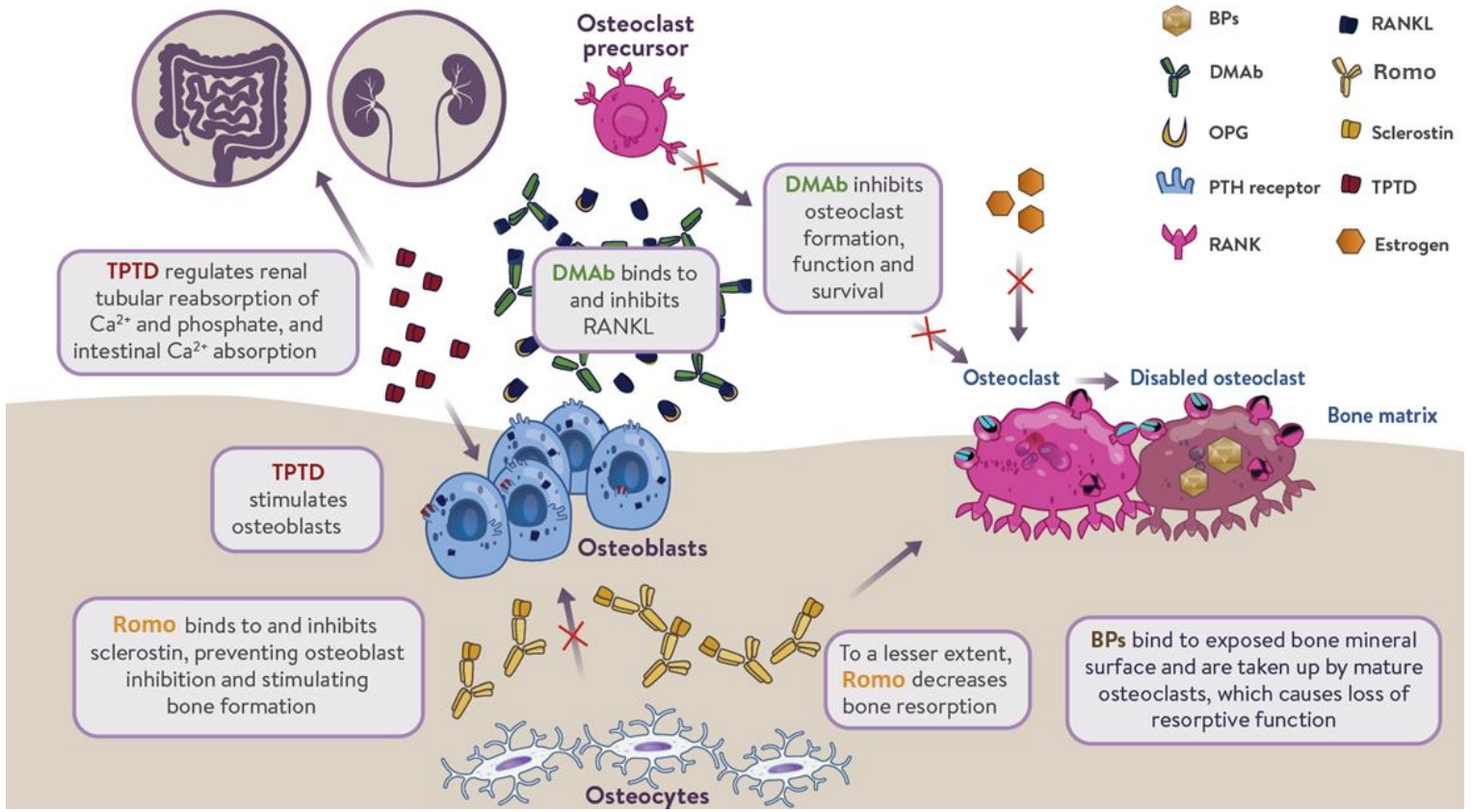
Scientific planning committee member: Dr Aliya Khan

Introduction

Bone formation (BF) therapies

- BF therapies (e.g., romosozumab or teriparatide) have anabolic effects that lead to bone microstructure improvements and significantly greater BMD gains and fracture risk reductions over 12–24 mo of treatment vs antiresorptive therapies[1-6]
- BF therapies tend to achieve greater BMD improvements when administered in a treatment-naive setting rather than after antiresorptive treatment, owing to mechanism of action of both classes of therapy[7-10]
- Recent North American guidelines[11-17] recommend BF therapies for appropriate patients, including those with very high fracture risk

Mechanism of action of BF and antiresorptive therapies[18]



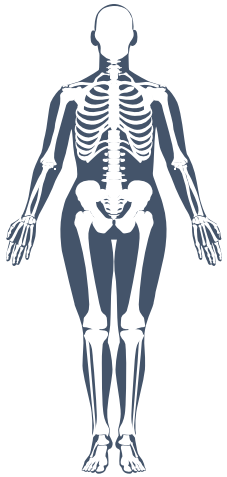
BP, bisphosphonate; BMD, bone mineral density; DMAb, denosumab; OPG, osteoprotegerin; PTH, parathyroid hormone; RANK, receptor activator of nuclear factor kappa-B; RANKL, RANK ligand; romo, romosozumab; TPTD, teriparatide.

1. Brown JP, et al. *J Bone Miner Res*. 2021;36(11):2139-2152; **2.** Eastell R, et al. *J Bone Miner Res*. 2009;24(4):726-736; **3.** Fan G, et al. *Medicine (Baltimore)*. 2020;99(15):e18964; **4.**McClung MR. *Osteoporos Sarcopenia*. 2018;4(1):11-15; **5.** McClung MR, et al. *N Engl J Med*. 2014;370(5):412-420; **6.** Saag KG, et al. *N Engl J Med*. 2017;377(15):1417-1427; **7.** Cosman F, et al. *Osteoporos Int*. 2022;33(6):1243-1256; **8.** Langdahl BL, et al. *Lancet*. 2017;390(10102):1585-1594; **9.** McClung MR, et al. *JBMR Plus*. 2021;5(7):e10512; **10.** Obermayer-Pietsch BM, et al. *J Bone Miner Res*. 2008;23(10):1591-1600; **11.** Camacho PM, et al. *Endocr Pract*. 2020;26(Suppl 1):1-46; **12.** Khan AA, et al. *J Obstet Gynaecol Can*. 2022;44(5):527-536.e5; **13.** LeBoff MS, et al. *Osteoporos Int*. 2022;33(10):2049-2102; **14.** Morin SN, et al. *CMAJ*. 2023;195(39):E1333-E1348; **15**. North American Menopause Society. *Menopause*. 2021;28(9):973-997; **16.** Qaseem A, et al. *Ann Intern Med*. 2023;176(2):224-238; **17.** Shoback D, et al. *J Clin Endocrinol Metab*. 2020;105(3):dgaa048; **18.** CPD Network. Treat Osteoporosis Sooner and Longer. Accessed July 5, 2024. https://www.cpdnetwork.org/cpd-microsites/treat-osteoporosis-sooner-and-longer.

Product monograph indications for BF therapies[1,2]

Romosozumab (sc, qm for 12 mo)

- Postmenopausal women: osteoporosis + osteoporotic fracture hx or ≥2 risk factors for fracture
- Contraindications: uncorrected hypocalcemia or hypersensitivity
- Serious warning: not recommended in patients with a hx of MI or stroke



Teriparatide (sc, qd for ≤24 mo)[a]

- Postmenopausal women: severe osteoporosis[b] with high fracture risk
- Men/postmenopausal women: severe osteoporosis[b] + failure/intolerance to prior therapy
- Contraindications: preexisting hypercalcemia, hypersensitivity, severe renal impairment, metabolic bone disease (other than osteoporosis), unexplained elevations in alkaline phosphatase, skeletal radiotherapy, or malignancy
- Warning: should not be prescribed to patients who are at increased risk for osteosarcoma (e.g., Paget's disease, hx radiation therapy involving the skeleton, etc.)

[a]Primary osteoporosis indications (additional secondary osteoporosis indication: osteoporosis associated with sustained systemic glucocorticoid therapy in men and women at increased fracture risk).
[b]Confirmed by the finding of low bone mass or the presence/history of osteoporotic fracture.[2]
BF, bone formation; hx, history; MI, myocardial infarction; qd, daily; qm, monthly; sc, subcutaneous.
1. EVENITY® (romosozumab-aqqg). Product Monograph. Amgen Inc.; 2020; **2.** Pr FORTEO® (teriparatide (rDNA origin) injection). Product Monograph. Eli Lilly and Co; 2021.

Fractures in women and men after age 50 y, Canada

Women have a higher fracture risk than men[1]

1 in **3** women

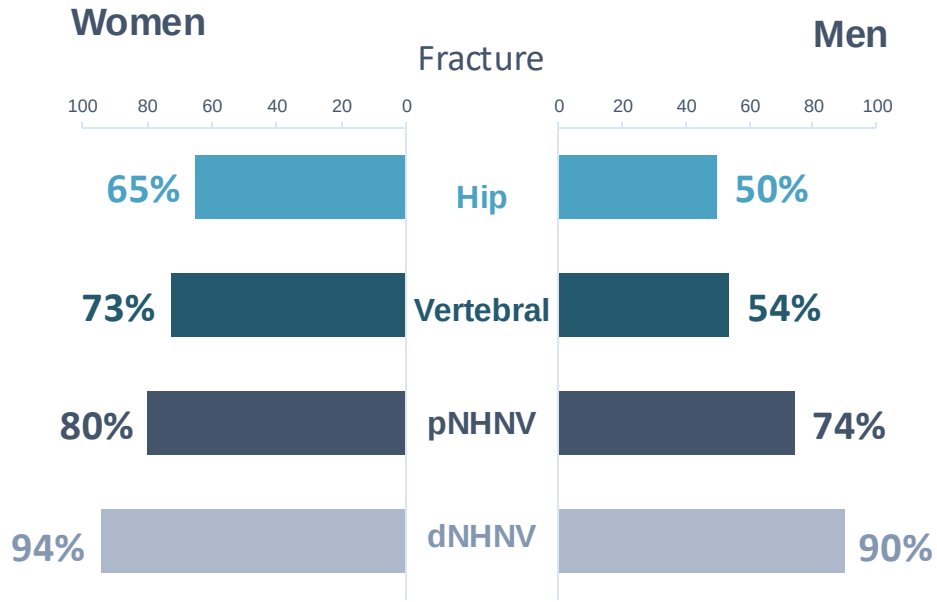
vs

1 in **5** men

will break a bone due to osteoporosis

Men experience more reduced survival after a fracture compared to women[2]

5-y relative survival rate[a]
after a fracture, Ontario, age >65 y



[a]Calculation: (% survived within 5 y among individuals with a fracture)/(% survived within 5 y among age-, sex-, comorbidities-matched individuals without a fracture).
dNHNV, distal non-hip non-vertebral fracture (tibia/fibula/knee, radius/ulna, and wrist); pNHNV, proximal non-hip non-vertebral fracture (pelvis, femur, sternum/rib/clavicle, and humerus/shoulder).
1. Osteoporosis Canada. Risk factors. Accessed July 1 ,2024. https://osteoporosis.ca/risk-factors/; **2.** Vincent G, et al. *JBMR Plus*. 2024;8(5):ziae002.

Alice

A 63-year-old woman with a recent fracture (naive to anti-osteoporosis therapy)

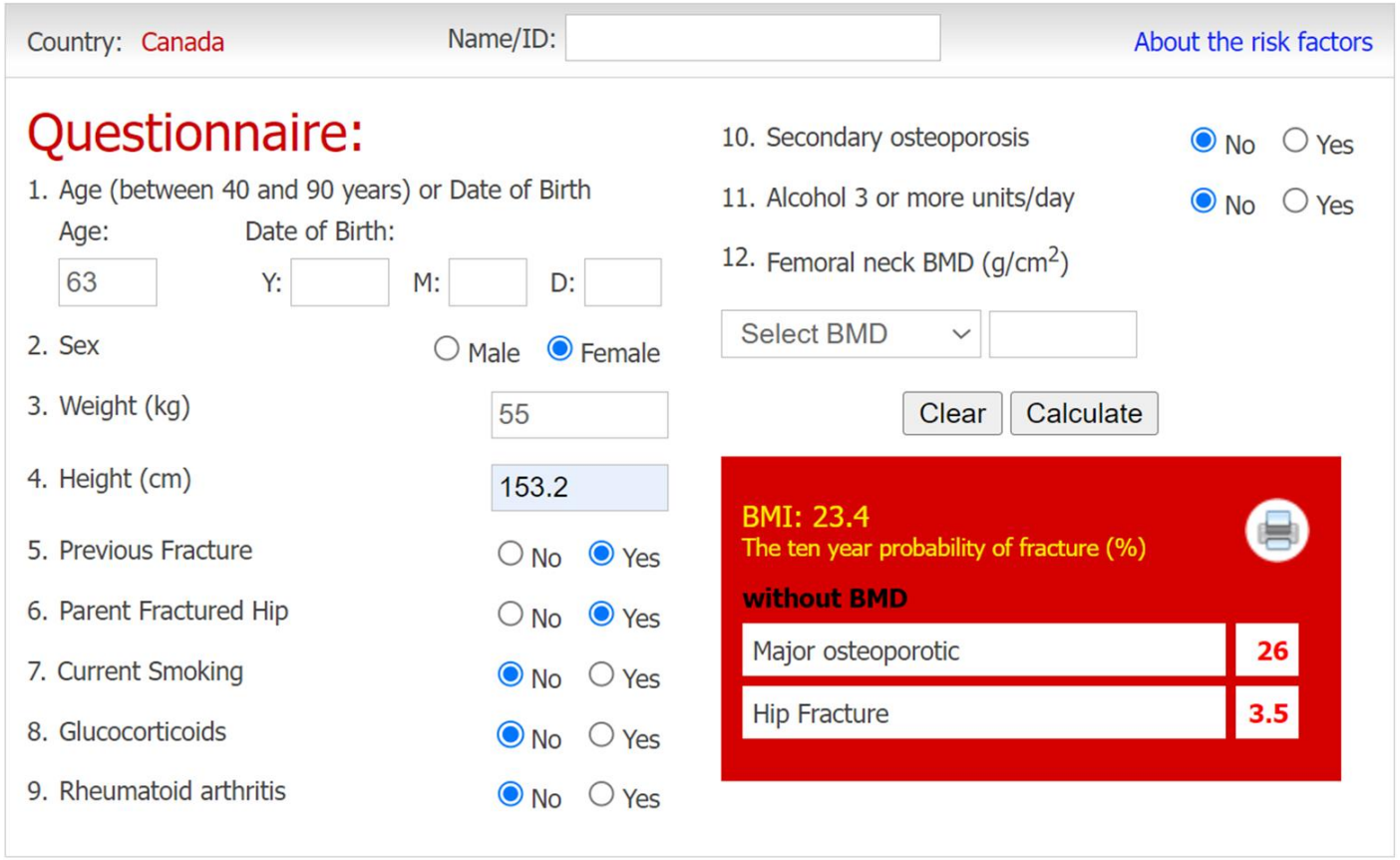
Alice

Age	63 y	**Sex**	Female	**Weight**	55.0 kg	**Height**	153.2 cm
Fracture history	• Clinical spine fracture (confirmed by x-ray), age 63 y			**Medications**	**Current** Steroid asthma inhaler ~2 qw Vitamin D 1000 IU qd and multivitamin qd **Prior** No prior anti-osteoporosis therapy		
BMD T-score	**Lumbar spine** N/A	**Femoral neck** N/A	**Total hip** N/A	**Comorbidities**	IBD (controlled with TCM), age 30 y Mild adult-onset asthma, age 55 y No DM, HTN , or dyslipidemia		
	Assessment date Not yet performed; age, <65 y						
Fracture risk details	• Clinical spine fracture • IBD • Steroids/current/inhaled • Mother had a spine and hip fracture • Highly physically active: walking, ~6 h/week; gym/Zumba classes, 2/week; yoga/Pilates classes, 1/week • No falls within last year • Nonsmoker, rarely drinks alcohol			**Additional notes**	• Spine fracture was observed on a recent (≤1 mo) lateral spine radiograph ordered by a GP after the patient presented with sharp back pain; patient was also worried because her mom had a painful spine fracture • Referral for a specialist assessment was provided to discuss bone formation therapy as an option • Patient saw 'strong bone improvements' when her mom was on bone formation therapy and was wondering if it would also be a suitable option for her • Normal initial blood tests ordered by GP: calcium (corrected for albumin), phosphate, creatinine (eGFR), alkaline phosphatase, thyroid-stimulating hormone, serum protein electrophoresis, 25-hydroxyvitamin D, PTH, magnesium, and TSH		

BMD, bone mineral density; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; GP, general practitioner; HTN, hypertension; IBD, inflammatory bowel disease; qd, daily; qw, weekly; TMC, traditional Chinese medicine.

FRAX: 10-y fracture risk calculator based on Canadian data[1]

Clinical FRAX **without** BMD[a]



Osteoporosis Canada, AACE, BHOF, NAMS, and SOGC guidelines indicate that FRAX can be used without entering BMD when not available;[2-6] FRAX without BMD predicts a hip fracture with ~80% chance[7]

≥20% for MOF[2-6,8] (i.e., hip, spine, humerus, or distal forearm fracture) or **≥3.0%** for hip fracture[2-5,8] indicates **high** future fracture risk

[a]Additional details for the following FRAX entries: 5. adult fracture occurring with low trauma (excluding hands, feet, and cranium); 6. biological mother/father hip fracture; 7. currently smokes tobacco; 8. current/past oral glucocorticoid use, ≥5 mg qd or equivalent; 9. confirmed diagnosis of rheumatoid arthritis; 10. disorders strongly associated with osteoporosis (including type 1 diabetes, osteogenesis imperfecta in adults, untreated long-standing hyperthyroidism, hypogonadism, premature menopause/<45 y, chronic malnutrition, malabsorption, and chronic liver disease); 11. ≥3 units of alcohol daily; 12. enter the T-score if BMD scan is unknown and leave BMD field blank if BMD results are not available.

AACE, American Association of Clinical Endocrinology; BHOF, Bone Health and Osteoporosis Foundation; BMD, bone mineral density; BMI, body mass index; FRAX, fracture risk assessment tool; MOF, major osteoporotic fracture; NAMS, The North American Menopause Society; qd, daily; SOGC, Society of Obstetricians and Gynaecologists of Canada.

1. FRAX® Risk Assessment Tool, Canada. Accessed July 1, 2024. https://frax.shef.ac.uk/FRAX/tool.aspx?country=19; **2.** Camacho PM, et al. *Endocr Pract*. 2020;26(Suppl 1):1-46; **3.** Khan AA, et al. *J Obstet Gynaecol Can*. 2022;44(5):527-536.e5; **4.** LeBoff MS, et al. *Osteoporos Int*. 2022;33:2049-2102; **5.** The North American Menopause Society. *Menopause*. 2021;28:973-997; **6.** Morin SN, et al. *CMAJ*. 2023;195(39):E1333-E1348; **7.** Hoff M, et al. *Osteoporos Int*. 2017;28(10):2935-2944; **8.** Shoback D, et al. *J Clin Endocrinol Metab*. 2020;105(3):dgaa048.

Alice: Clinical management based on recent North American guidelines[1-7]

Osteoporosis and fracture risk

- Needs treatment—at minimum high risk: spine fracture[1-5,7] (also, MOF ≥20%[1-5,7] and hip ≥3.0%[1-3,5,7] FRAX score)
- Recommended for BF therapy—very high risk: recent fracture (≤1 y)[1,2,5,6]
- Osteoporosis diagnosis recorded based on a spine fracture[1-5]

After completing BF treatment, guidelines[1-7] and product monograph[8] recommend switching to antiresorptive therapy to preserve the achieved BMD gains.

What if this patient was a man with a similar risk factor profile? Per product monograph, romosozumab is not indicated in men and teriparatide may be considered after failure/intolerance to prior therapy.[8,9]

Management

- Indicated for romosozumab: osteoporosis + fracture or ≥2 risk factors (fracture and family hx); no hx of MI or stroke and no major CVD risk factors[8]
- Indicated for teriparatide: fracture hx; no known risk factors for osteosarcoma[9]
- DXA scan: ordered to confirm baseline/pretreatment BMD
- Vitamin D: continue supplementing 1000 IU/d; calcium: 1 small yogurt/d + ~2 slices of cheese/d + multivitamin
- Blood tests: reordered (prior tests ~4 mo ago) to exclude contraindications/hypocalcemia and secondary osteoporosis causes[1-5]
- Patient preferences: discussed treatment initiation with BF therapy (qd vs qm dosing) and follow-on antiresorptive treatment after completing BF treatment (bisphosphonates vs denosumab)

BF, bone formation; BMD, bone mineral density; CVD, cardiovascular disease; DXA, dual-energy x-ray absorptiometry; FRAX, fracture risk assessment tool; hx, history; MI, myocardial infarction; MOF, major osteoporotic fracture; qd, daily; qm; monthly.

1. Camacho PM, et al. *Endocr Pract*. 2020;26(Suppl 1):1-46; **2.** Khan AA, et al. *J Obstet Gynaecol Can*. 2022;44(5):527-536.e5; **3.** LeBoff MS, et al. *Osteoporos Int*. 2022;33(10):2049-2102; **4.** Morin SN, et al. *CMAJ*. 2023;195(39):E1333-E1348; **5.** North American Menopause Society. Menopause. 2021;28(9):973-997; **6.** Qaseem A, et al. *Ann Intern Med*. 2023;176(2):224-238; **7.** Shoback D, et al. *J Clin Endocrinol Metab*. 2020;105(3):dgaa048; **8.** EVENITY® (romosozumab-aqqg). Product Monograph. Amgen Inc.; 2020; **9.** Pr FORTEO® (teriparatide (rDNA origin) injection). Product Monograph. Eli Lilly and Co; 2021.

Lizzie

80-year-old woman with a history of hip fracture (naive to anti-osteoporosis therapy)

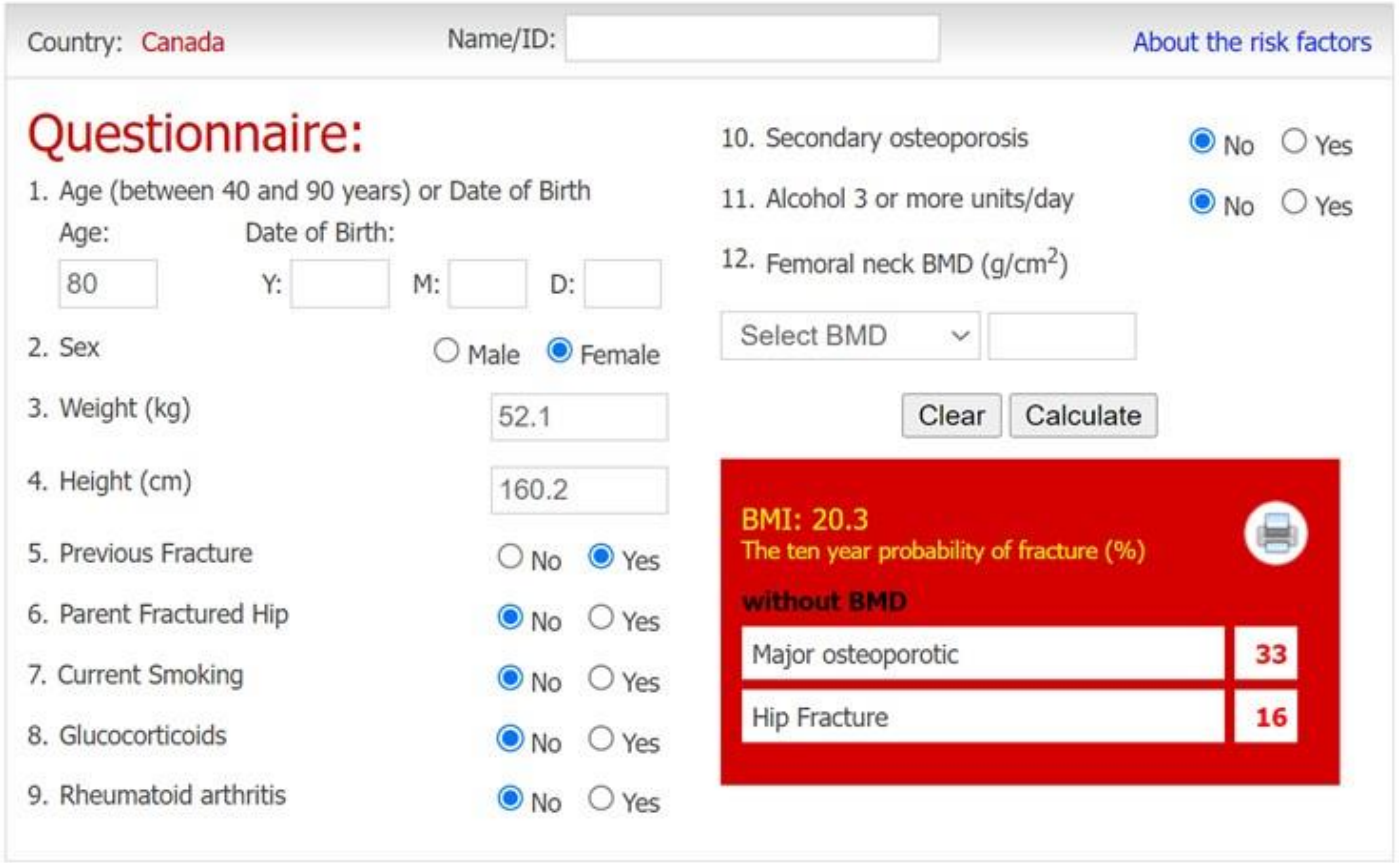
Lizzie

Age	80 y	**Sex**	Female	**Weight**	52.1 kg	**Height**	160.2 cm
Fracture history	• Hip fracture, age 75 y; tripped on a carpet at home			**Medications**	**Current** Escitalopram 10 mg qd Perindopril 8 mg qd Rosuvastatin 10 mg qd No calcium, vitamin D, or multivitamin supplement **Prior** Acetaminophen/codeine/Tylenol 3, age 75–77 y No prior anti-osteoporosis therapy		
BMD T-score	**Lumbar spine** −2.5	**Femoral neck** −2.3	**Total hip** −2.2	**Comorbidities**	Hypertension, age 65 y Frailty, age 75 y Delirium, age 76 y No DM or dyslipidemia		
	BMD assessment date ~5 y ago						
Fracture risk details	• Hip fracture history • Age 80 y • BMD ≤−2.5, ~5 y ago • Frailty and delirium; 3 falls within past year • Family history is unremarkable • Sedentary • Nonsmoker, no longer drinks alcohol			**Additional notes**	• Patient in LTC since age 77 y after hip fracture and delirium • Referred for a specialist assessment due to significant functional decline, increased frailty index, and significant falls history in the past year and a history of hip fracture • Daughter attended visit and worries because the patient does not eat a lot of dairy, meat or vegetables (mostly carbs) • Patient also used to drink heavily (until age ~60 y) • Normal recent blood tests ordered at LTC: calcium (corrected for albumin), phosphate, creatinine (eGFR), alkaline phosphatase, thyroid-stimulating hormone • Low 25-hydroxyvitamin D: 35 nmol/l; high PTH: 10 pmol/l		

BMD, bone mineral density; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; LTC, long-term care home; qd, daily.

FRAX: 10-y fracture risk calculator based on Canadian data[1]

Clinical FRAX **without** BMD[a]



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≥20% for MOF[2-6,8] (i.e., hip, spine, humerus, or distal forearm fracture) or **≥3.0%** for hip fracture[2-5,8] indicates **high** future fracture risk

[a]Additional details for the following FRAX entries: 5. adult fracture occurring with low trauma (excluding hands, feet, and cranium); 6. biological mother/father hip fracture; 7. currently smokes tobacco; 8. current/past oral glucocorticoid use, ≥5 mg qd or equivalent; 9. confirmed diagnosis of rheumatoid arthritis; 10. disorders strongly associated with osteoporosis (including type 1 diabetes, osteogenesis imperfecta in adults, untreated long-standing hyperthyroidism, hypogonadism, premature menopause/<45 y, chronic malnutrition, malabsorption, and chronic liver disease); 11. ≥3 units of alcohol daily; 12. enter the T-score if BMD scan is unknown and leave BMD field blank if BMD results are not available.

AACE, American Association of Clinical Endocrinology; BHOF, Bone Health and Osteoporosis Foundation; BMD, bone mineral density; BMI, body mass index; FRAX, fracture risk assessment tool; MOF, major osteoporotic fracture; NAMS, The North American Menopause Society; qd, daily; SOGC, Society of Obstetricians and Gynaecologists of Canada.

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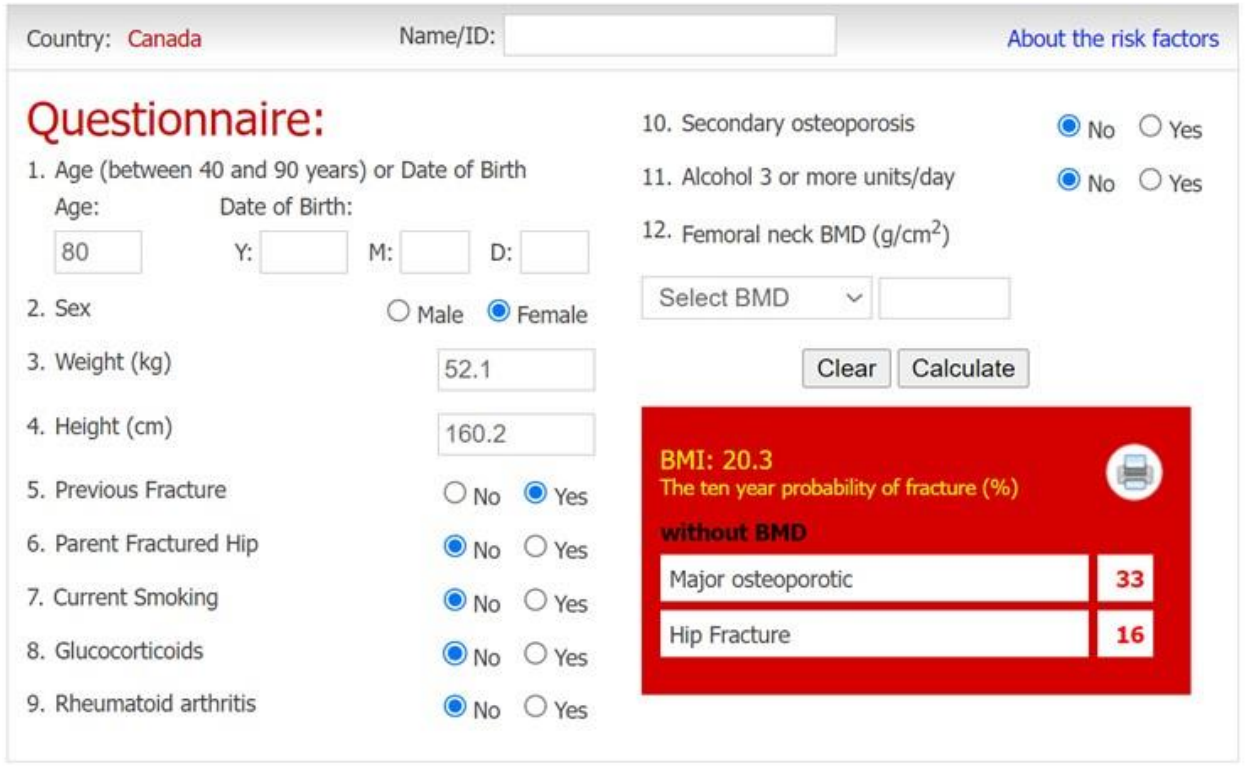

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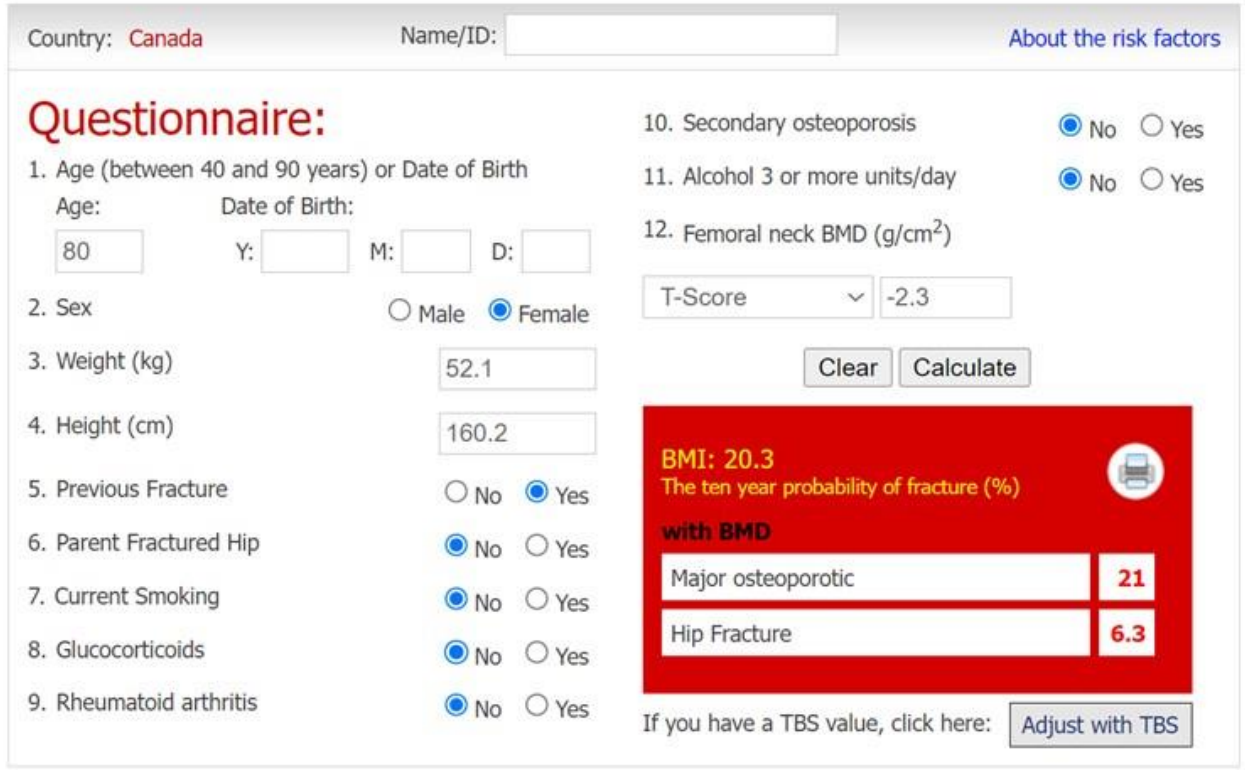

Note: outdated DXA scan (5 y ago and high-risk patient)

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1. FRAX® Risk Assessment Tool, Canada. Accessed July 1, 2024. https://frax.shef.ac.uk/FRAX/tool.aspx?country=19.

Lizzie: Clinical management based on recent North American guidelines[1-7]

Osteoporosis and fracture risk

- Needs treatment—at minimum high risk: hip fracture hx[1-5,7] (also, MOF ≥20%[1-5,7] and hip ≥3.0%[1-3,5,7] FRAX score)
- Recommended for BF therapy—very high risk: MOF >30%[1,2] FRAX score (also, hip fracture >4.5%[1,2])
- Osteoporosis diagnosed 5 y ago by GP based on a hip fracture[1-5]

After completing BF treatment, guidelines[1-7] and product monograph[8] recommend switching to antiresorptive therapy to preserve the achieved BMD gains.

What if this patient was a man with a similar risk factor profile? Per product monograph, romosozumab is not indicated in men and teriparatide may be considered after failure/intolerance to prior therapy.[8,9]

Management

- Indicated for romosozumab: osteoporosis + fracture or ≥2 risk factors (fracture, age ≥75 y, and BMD ≤−2.5); no hx of MI or stroke and hypertension is controlled[8]
- Indicated for teriparatide: fracture hx or BMD T-score ≤−2.5; no known risk factors for osteosarcoma[9]
- DXA scan: ordered to confirm pretreatment BMD based on recent data
- Vitamin D: supplement 2000–3000 IU/d (low blood level); repeat 25-hydroxyvitamin D blood test in ~3 mo to assess if improved[a]
- Calcium: supplement 800–1000 mg/d
- Blood tests: reordered (prior tests ~3 mo ago) to exclude contraindications/hypocalcemia and secondary osteoporosis causes[1-5]
- Patient preferences: discussed treatment initiation with BF therapy (qd vs qm dosing) and follow-on antiresorptive treatment after completing BF treatment (bisphosphonates vs denosumab)

[a]Regulatory trials of romosozomab corrected serum 25-hydroxyvitamin D concentration ≤40 ng/mL by providing a loading dose of vitamin D2 of 50,000–60,000 IU within 1 week prior to starting romosozumab treatment.[8]

BF, bone formation; BMD, bone mineral density; DXA, dual-energy x-ray absorptiometry; FRAX, fracture risk assessment tool; GP, general practitioner; hx, history; MI, myocardial infarction; MOF, major osteoporotic fracture; qd, daily; qm, monthly.

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Garima

73-year-old woman with a history of multiple fractures (naive to anti-osteoporosis therapy)

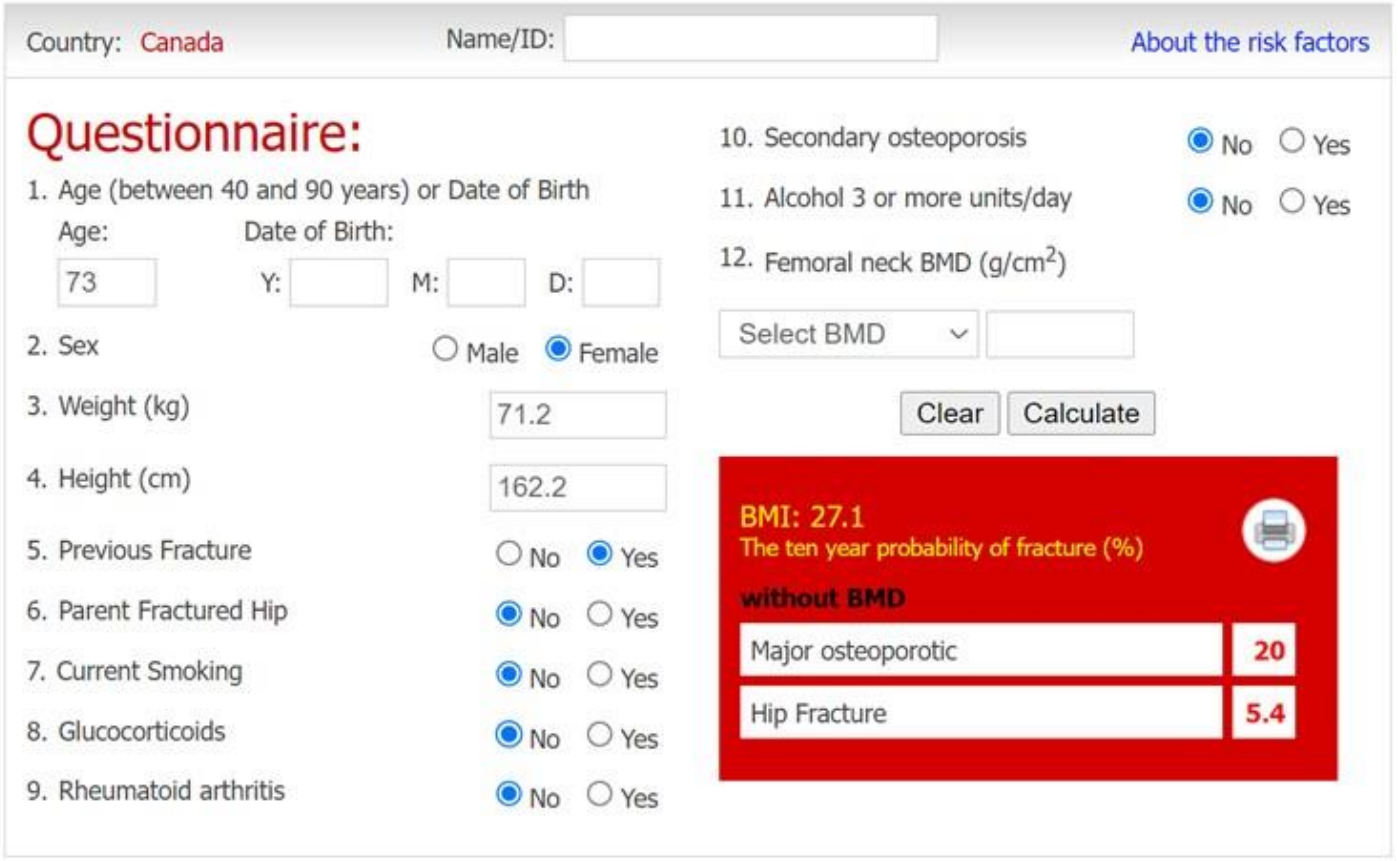
Garima

Age	73 y	**Sex**	Female	**Weight**	71.2 kg	**Height**	162.2 cm
Fracture history	• Humerus fracture, age 72 y; pulled down by her son's dog when holding a leash • Wrist fracture, age 55 y; tripped in the backyard while gardening			**Medications**	**Current** ASA 81 mg Ramipril 5 mg Atorvastatin 40 mg qhs Metformin 500 mg bid Empagliflozin 10 mg qd Multivitamin but no calcium or vitamin D supplement **Prior** No prior anti-osteoporosis therapy		
BMD T-score	**Lumbar spine** −2.6	**Femoral neck** −2.5	**Total hip** −2.4	**Comorbidities**	T2D, age 58 y Dyslipidemia, 65 y AMI, age 70 y No HTN		
	BMD assessment date <6 mo ago						
Fracture risk details	• Multiple fracture history • Type 2 diabetes • Mother had multiple fractures (lower leg, wrist, and spine fracture) • Tai chi or yoga 1–2/week; walking 1–2/week • No falls within past year • Never smoked, drinks only socially (~1/mo)			**Additional notes**	• Patient was referred for a specialist assessment due to low BMD on a recent test, multiple fractures (1 recent, ~1 y ago), family history of osteoporosis, and T2D • Eats mostly Indian vegetarian/vegan foods; she eats paneers once a week and does not consume milk alternatives • Normal initial blood tests ordered by GP: calcium (corrected for albumin), phosphate, creatinine (eGFR), alkaline phosphatase, thyroid-stimulating hormone • Low 25-hydroxyvitamin D: 20 nmol/l; high PTH: 15 pmol/l		

AMI, acute myocardial infarction; ASA, acetylsalicylic acid; bid, twice daily; BMD, bone mineral density; eGFR, estimated glomerular filtration rate; GP, general practitioner; HTN, hypertension; qd, daily; qhs, nightly at bedtime; T2D, type 2 diabetes.

FRAX: 10-y fracture risk calculator based on Canadian data[1]

Clinical FRAX **without** BMD[a]



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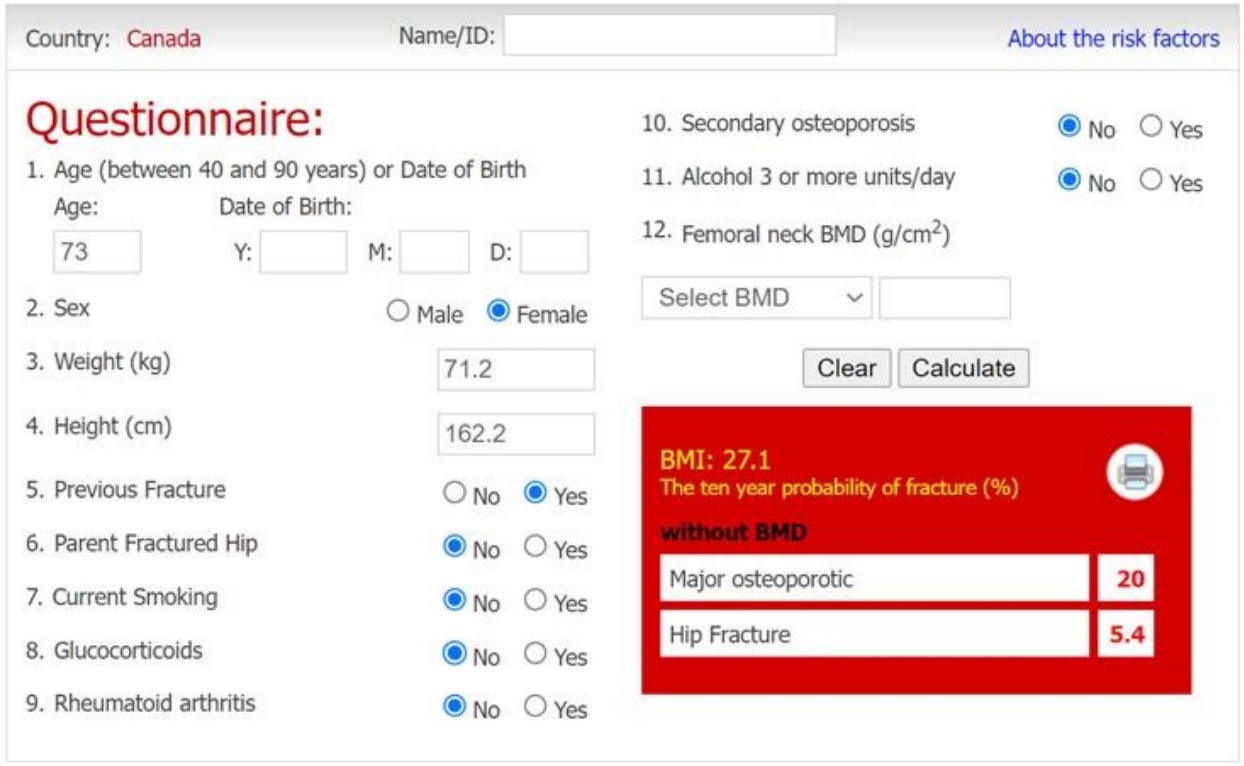
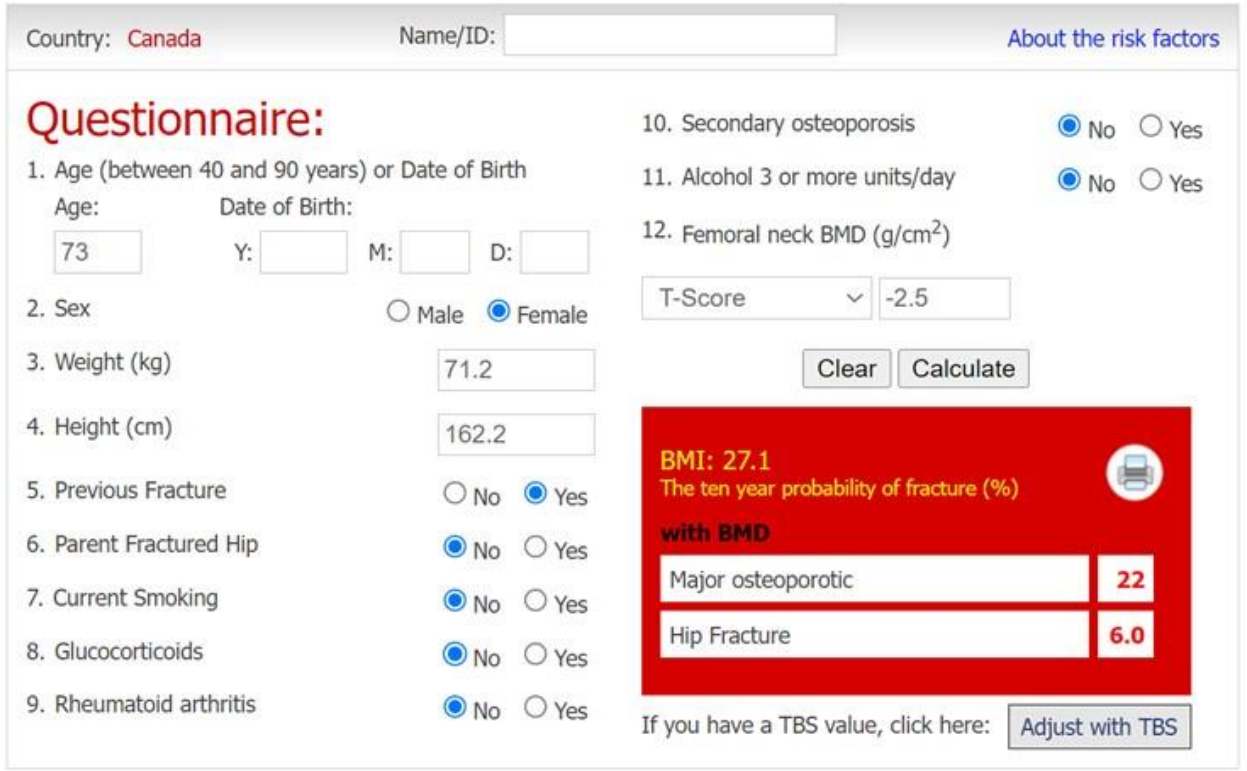


FRAX **with** BMD[a]



[a]Additional details for the following FRAX entries: 5. adult fracture occurring with low trauma (excluding hands, feet, and cranium); 6. biological mother/father hip fracture; 7. currently smokes tobacco; 8. current/past oral glucocorticoid use, ≥5 mg qd or equivalent; 9. confirmed diagnosis of rheumatoid arthritis; 10. disorders strongly associated with osteoporosis (including type 1 diabetes, osteogenesis imperfecta in adults, untreated long-standing hyperthyroidism, hypogonadism, premature menopause/<45 y, chronic malnutrition, malabsorption, and chronic liver disease); 11. ≥3 units of alcohol daily; 12. enter the T-score if BMD scan is unknown and leave BMD field blank if BMD results are not available.

BMD, bone mineral density; BMI, body mass index; FRAX, fracture risk assessment tool; TBS, trabecular bone score.

1. FRAX® Risk Assessment Tool, Canada. Accessed July 1, 2024. https://frax.shef.ac.uk/FRAX/tool.aspx?country=19.

Garima: Clinical management based on recent North American guidelines[1-7]

Osteoporosis and fracture risk

- Needs treatment—at minimum high risk: ≥2 fractures[1,2,4-7] (also, MOF ≥20%[1-5,7] and hip ≥3.0%[1-3,5,7] FRAX score)
- Recommended for BF therapy—very high risk: recent fracture (≤1 y)[1,2,5,6] (also, ≥2 fractures[1,2,6,7] or hip fracture >4.5% FRAX score[1,2])
- Osteoporosis diagnosis recorded based on BMD T-score ≤−2.5[1-5]

⚠ After completing BF treatment, guidelines[1-7] recommend switching to antiresorptive therapy to preserve the achieved BMD gains.

♂ **What if this patient was a man with a similar risk factor profile?** Per product monograph, romosozumab is not indicated in men and teriparatide may be considered after failure/intolerance to prior therapy.[8,9]

Management

- Hx of MI; otherwise indicated for romosozumab: osteoporosis + fracture or ≥2 risk factors (≥2 fractures and BMD ≤−2.5)[8]
- Indicated for teriparatide: fracture hx or BMD T-score ≤−2.5; no known risk factors for osteosarcoma[9]
- DXA scan: not needed/recent BMD data available
- Vitamin D: correct with a loading dose of D2 50,000 IU qw or D3 5,000 IU qd; repeat blood tests in ~3 mo: 25-hydroxyvitamin D to assess if corrected[a] and PTH to assess if normalized with vitamin D correction
- Calcium: supplement 300–600 mg/d + continue with multivitamin
- Blood tests: reordered (prior tests ~5 mo ago) to exclude contraindications/hypocalcemia and secondary osteoporosis causes[1-5]
- Patient preferences: discussed treatment initiation with teriparatide (romosozumab not appropriate owing to MI hx) and follow-on antiresorptive treatment after completing teriparatide treatment (bisphosphonates vs denosumab)

[a]Regulatory trials of romosozomab corrected serum 25-hydroxyvitamin D concentration ≤40 ng/mL by providing a loading dose of vitamin D2 of 50,000–60,000 IU within 1 week prior to starting romosozumab treatment.[8]

BF, bone formation; BMD, bone mineral density; DXA, dual-energy x-ray absorptiometry; FRAX, fracture risk assessment tool; hx, history; MI, myocardial infarction; MOF, major osteoporotic fracture; qd, daily; qw, weekly.

1. Camacho PM, et al. *Endocr Pract*. 2020;26(Suppl 1):1-46; **2.** Khan AA, et al. *J Obstet Gynaecol Can*. 2022;44(5):527-536.e5; **3.** LeBoff MS, et al. *Osteoporos Int*. 2022;33(10):2049-2102; **4.** Morin SN, et al. *CMAJ*. 2023;195(39):E1333-E1348; **5.** North American Menopause Society. *Menopause*. 2021;28(9):973-997; **6.** Qaseem A, et al. *Ann Intern Med*. 2023;176(2):224-238; **7.** Shoback D, et al. *J Clin Endocrinol Metab*. 2020;105(3):dgaa048; **8.** EVENITY® (romosozumab-aqqg). Product Monograph. Amgen Inc.; 2020; **9.** Pr FORTEO® (teriparatide (rDNA origin) injection). Product Monograph. Eli Lilly and Co; 2021.

Julie

75-year-old woman with a hip fracture sustained during anti-osteoporosis treatment

Julie

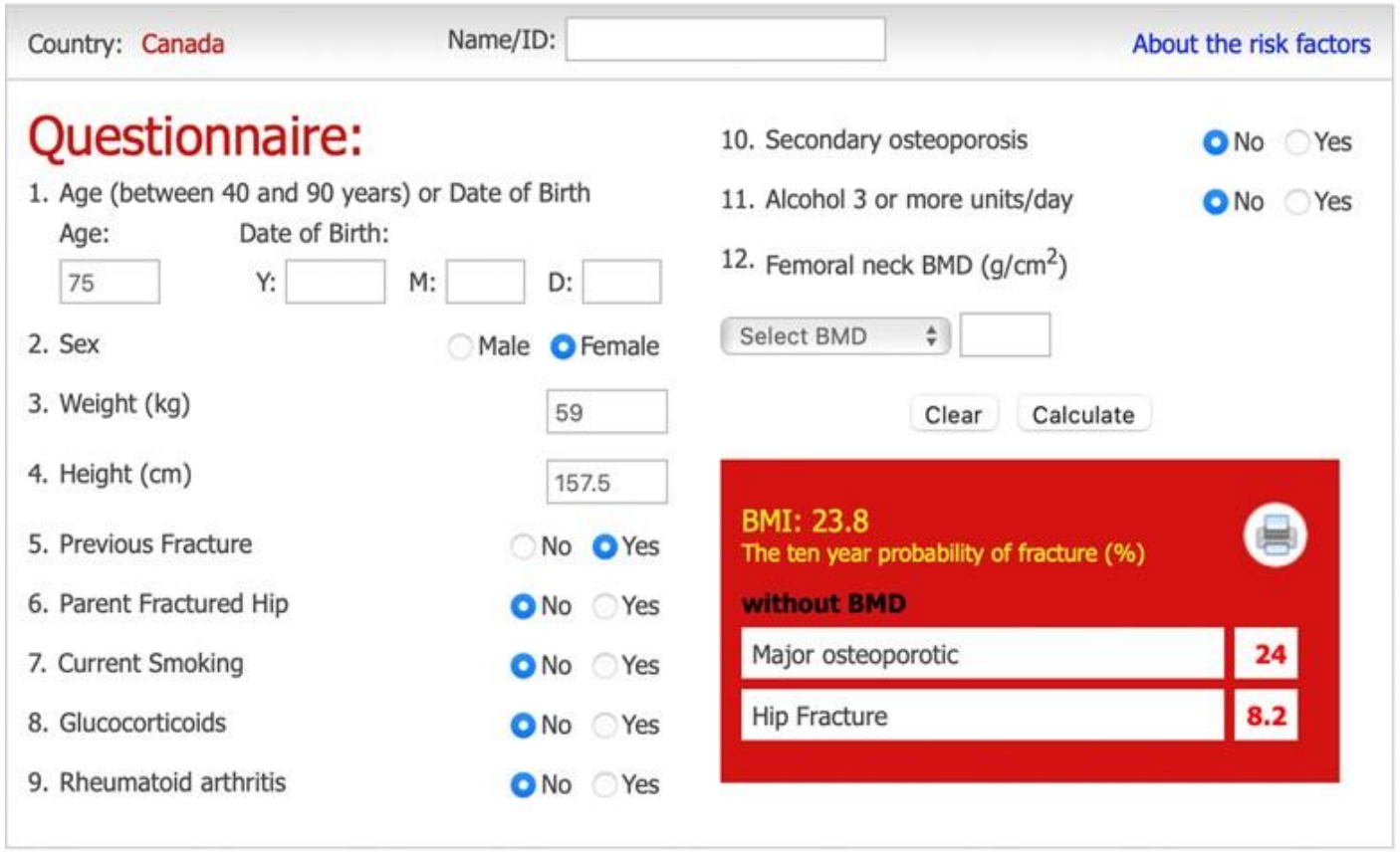
Age	75 y	**Sex**	Female	**Weight**	59.0 kg	**Height**	157.5 cm

Fracture history	• Hip fracture (femoral neck), age 73 y; missed a bottom step at home • Wrist fracture, age 70 y; fell from standing height	**Medications**	**Current** Risedronate DR 35 mg qw (since age 65 y) Citalopram 20 mg qd Pantoprazole 40 mg qd Calcium (600 mg/d) and vitamin D (1000 IU/d) **Prior** Nothing significant
BMD T-score	**Lumbar spine** −3.0 **Femoral neck** −2.8 **Total hip** −2.7 **BMD assessment date** <1 y ago	**Comorbidities**	• GERD • No DM, HTN, or dyslipidemia
Fracture risk details	• Hip fracture/multiple fractures • Age 75 y • BMD ≤−3.0 • GERD/PPIs • Family history is unremarkable • Physically active; walks daily for 1 hour • No falls within past year • Nonsmoker, infrequent alcohol intake	**Additional notes**	• Patient was referred for a specialist assessment due to long-term oral bisphosphonate therapy (~10 y) and a hip fracture sustained while on therapy • Family doctor reports good adherence to bisphosphonates • Normal initial blood tests ordered by GP: calcium (corrected for albumin), phosphate, creatinine (eGFR), alkaline phosphatase, thyroid-stimulating hormone, serum protein electrophoresis, and 25-hydroxyvitamin D

BMD, bone mineral density; DM, diabetes mellitus; DR, delayed release; eGFR, estimated glomerular filtration rate; GERD, gastroesophageal reflux disease; GP, general practitioner; HTN, hypertension; PPI, proton pump inhibitor; qd, daily; qw, weekly.

FRAX: 10-y fracture risk calculator based on Canadian data[1]

Clinical FRAX **without** BMD[a]



Osteoporosis Canada, AACE, BHOF, NAMS, and SOGC guidelines indicate that FRAX can be used without entering BMD when not available;[2-6] FRAX without BMD predicts a hip fracture with ~80% chance[7]

≥20% for MOF[2-6,8] (i.e., hip, spine, humerus, or distal forearm fracture) or **≥3.0%** for hip fracture[2-5,8] indicates **high** future fracture risk

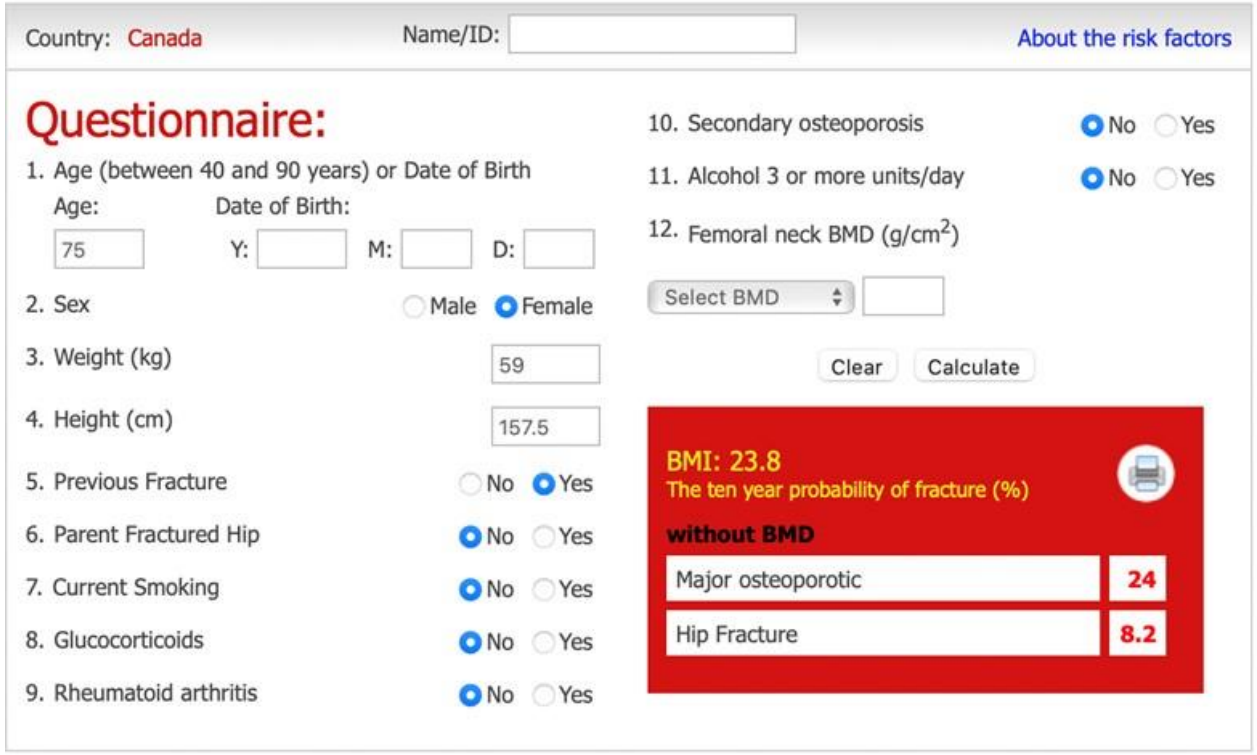
[a]Additional details for the following FRAX entries: 5. adult fracture occurring with low trauma (excluding hands, feet, and cranium); 6. biological mother/father hip fracture; 7. currently smokes tobacco; 8. current/past oral glucocorticoid use, ≥5 mg qdor equivalent; 9. confirmed diagnosis of rheumatoid arthritis; 10. disorders strongly associated with osteoporosis (including type 1 diabetes, osteogenesis imperfecta in adults, untreated long-standing hyperthyroidism, hypogonadism, premature menopause/<45 y, chronic malnutrition, malabsorption, and chronic liver disease); 11. ≥3 units of alcohol daily; 12. enter the T-score if BMD scan is unknown and leave BMD field blank if BMD results are not available.

AACE, American Association of Clinical Endocrinology; BHOF, Bone Health and Osteoporosis Foundation; BMD, bone mineral density; BMI, body mass index; FRAX, fracture risk assessment tool; MOF, major osteoporotic fracture; NAMS, The North American Menopause Society; qd, daily; SOGC, Society of Obstetricians and Gynaecologists of Canada.

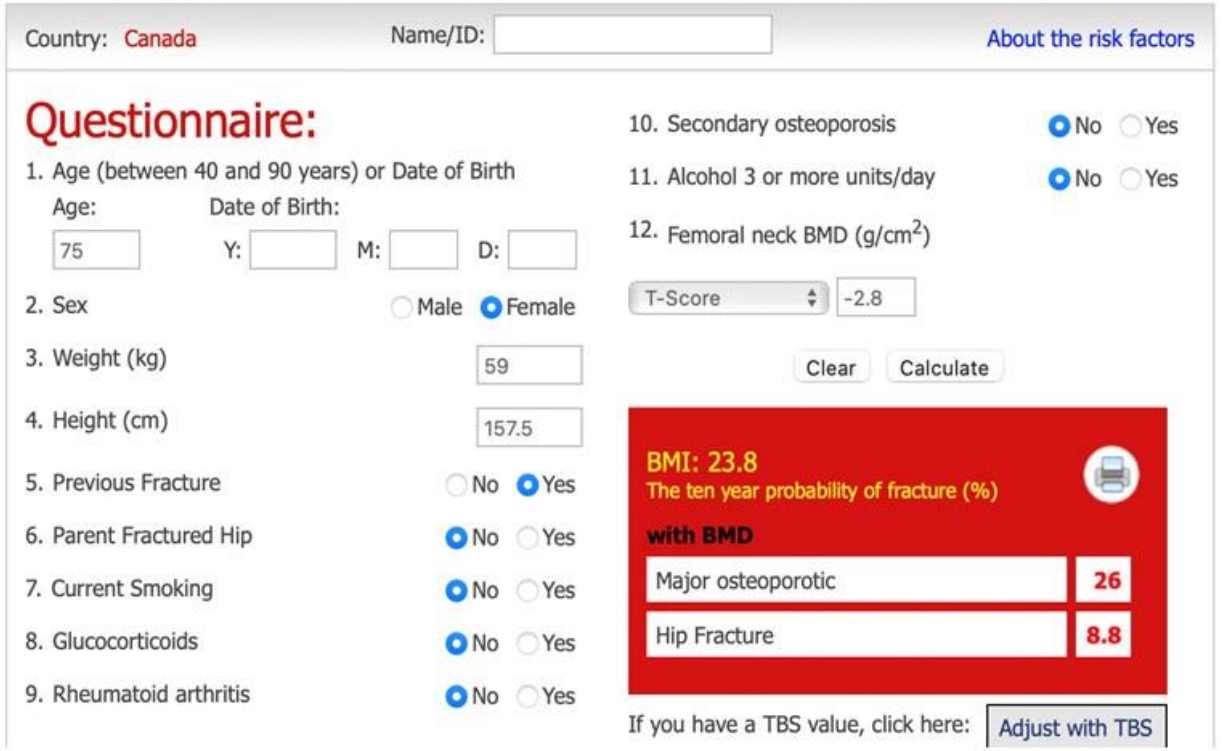
1. FRAX® Risk Assessment Tool, Canada. Accessed July 1, 2024. https://frax.shef.ac.uk/FRAX/tool.aspx?country=19; **2.** Camacho PM, et al. *Endocr Pract*. 2020;26(Suppl 1):1-46; **3.** Khan AA, et al. *J Obstet Gynaecol Can*. 2022;44(5):527-536.e5; **4.** LeBoff MS, et al. *Osteoporos Int*. 2022;33:2049-2102; **5.** The North American Menopause Society. *Menopause*. 2021;28:973-997; **6.** Morin SN, et al. *CMAJ*. 2023;195(39):E1333-E1348; **7.** Hoff M, et al. *Osteoporos Int*. 2017;28(10):2935-2944; **8.** Shoback D, et al. *J Clin Endocrinol Metab*. 2020;105(3):dgaa048.

FRAX: 10-y fracture risk calculator based on Canadian data[1]

Clinical FRAX **without** BMD[a]



FRAX **with** BMD[a]



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1. FRAX® Risk Assessment Tool, Canada. Accessed July 1, 2024. https://frax.shef.ac.uk/FRAX/tool.aspx?country=19.

Julie: Clinical management based on recent North American guidelines[1-7]

Osteoporosis and fracture risk

- Treatment failure: on-treatment fracture,[a] treatment adherent, and no apparent secondary causes[1,2,4,5,7]
- Recommended for BF therapy—very high risk: ≥2 fractures[1,2,6,7] (also, ≤−3.0 BMD T-score[1,5] or hip fracture >4.5% FRAX risk[1,2])
- Osteoporosis diagnosed ~10 y ago by GP based on BMD T-score ≤−2.5[1-5]

After completing BF treatment, guidelines[1-7] and product monograph[8] recommend switching to antiresorptive therapy to preserve the achieved BMD gains.

♂ **What if this patient was a man with a similar risk factor profile?** Per product monograph, romosozumab is not indicated in men and teriparatide may be considered after failure/intolerance to prior therapy.[8,9]

Management

- Indicated for romosozumab: osteoporosis + fracture or ≥2 risk factors (≥2 fractures, age ≥ 75 y, and BMD ≤−2.5); no hx of MI or stroke and no major CVD risk factors[8]
- Indicated for teriparatide: fracture hx or BMD T-score ≤−2.5; no known risk factors for osteosarcoma[9]
- DXA scan: not needed/recent BMD data available
- Vitamin D: continue supplementing 1000 IU/d; calcium: continue supplementing 600 mg/d
- Blood tests: reordered (prior tests ~4 mo ago) to exclude contraindications/hypocalcemia and secondary osteoporosis causes[1-5]
- Patient preferences: discussed treatment initiation with BF therapy (qd vs qm dosing) and follow-on antiresorptive treatment after completing BF treatment (bisphosphonates vs denosumab)

[a]Consider treatment failure if no secondary osteoporosis present and ≥2 on-treatment fractures (regardless of adherence) or ≥1 fracture, if adherent to therapy.[1,2,4,5,7]

BF, bone formation; BMD, bone mineral density; CVD, cardiovascular disease; DXA, dual-energy x-ray absorptiometry; FRAX, fracture risk assessment tool; GP, general practitioner; hx, history; MI, myocardial infarction; qd, daily; qm; monthly.

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Rosaria

68-year-old woman with 2 silent spine fractures sustained during anti-osteoporosis treatment

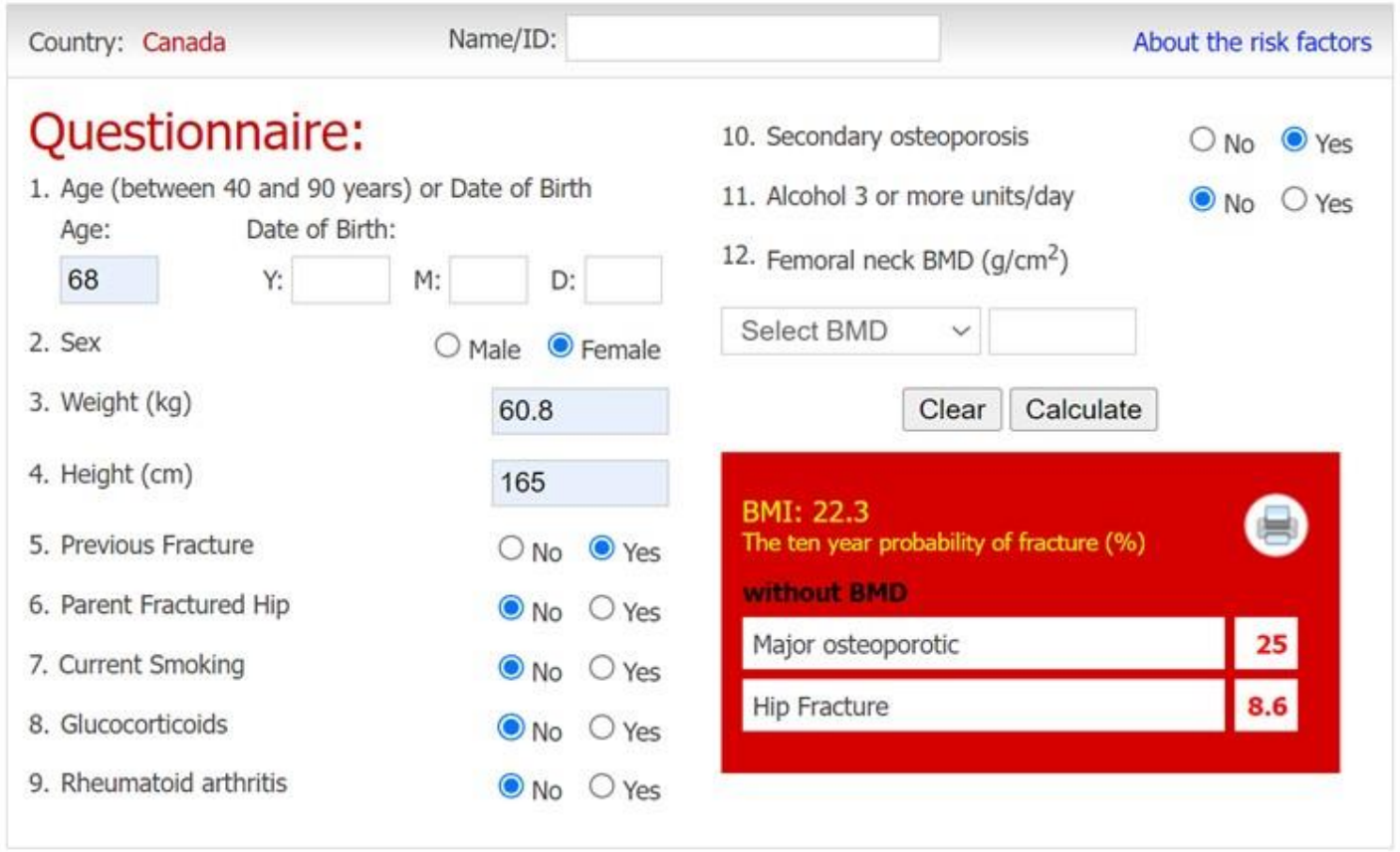
Rosaria

Age	68 y	**Sex**	Female	**Weight**	60.8 kg	**Height**	165.0 cm
Fracture history	• 2 silent vertebral fractures observed on a cxr for pneumonia, age 68 y; no history of trauma and cxr 3 y ago was clear/no fracture			**Medications**	**Current** Alendronate 70 mg qw (since age 66 y) Calcium 600 mg qd and vitamin D 1000 IU qd **Prior** Nothing significant		
				Comorbidities	Osteoarthritis (hands) Spontaneous/early menopause (age 44 y)		
BMD T-score	**Lumbar spine** −2.7	**Femoral neck** −2.3	**Total hip** −2.1	**Additional notes**	• Patient was referred for a specialist assessment due to 2 silent spine fractures observed on a cxr while on oral bisphosphonate therapy • Patient does not recall any significant back injury but remembers minor back pain ~6 mo ago, which she attributed to computer work/muscle tension • Patients is vegetarian but eats a lot of dairy • She reports being highly adherence to bisphosphonate therapy and calcium/vitamin D supplements; with her family history, she wants to make sure she does everything she can • Normal initial blood tests ordered by GP: calcium (corrected for albumin), phosphate, creatinine (eGFR), alkaline phosphatase, thyroid-stimulating hormone, serum protein electrophoresis, and 25-hydroxyvitamin D • Patient mentioned losing height over the past year (~2 cm) and that she does not like how her upper back is rounding and does not want to end up looking like her dad		
	BMD assessment date ~2 y ago						
Fracture risk details	• Multiple spine fractures; potentially recent (1–2 y ago) • BMD ≤−2.5, lumbar spine • Secondary osteoporosis cause: early menopause (<45 y) • Father experienced significant height loss by age 80 y and had a severe forward hunch • Physically active: walks daily for ~0.5 hour; cycles on weekends ~3 hours • Prospective height loss (expected) • No falls within past year • Nonsmoker, infrequent alcohol intake						

BMD, bone mineral density; cxr, chest x-ray; eGFR, estimated glomerular filtration rate; GP, general practitioner; qd, daily; qw, weekly.

FRAX: 10-y fracture risk calculator based on Canadian data[1]

Clinical FRAX **without** BMD[a]



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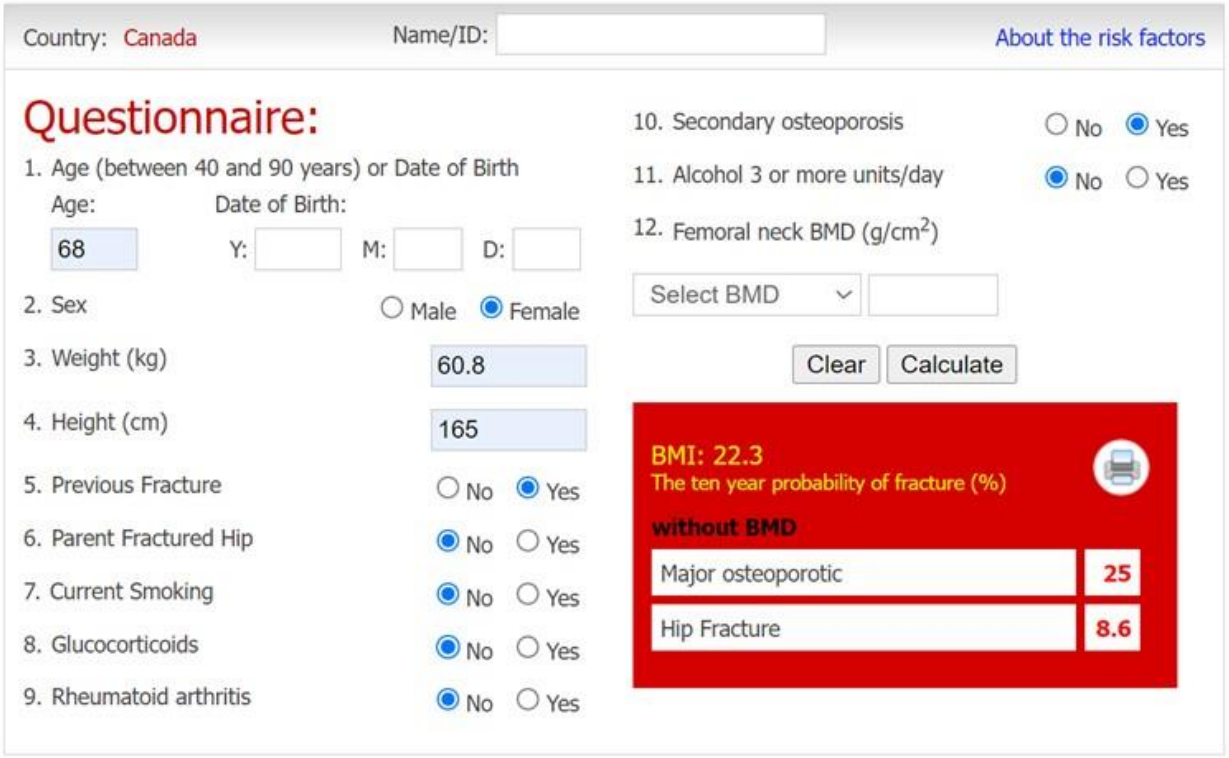
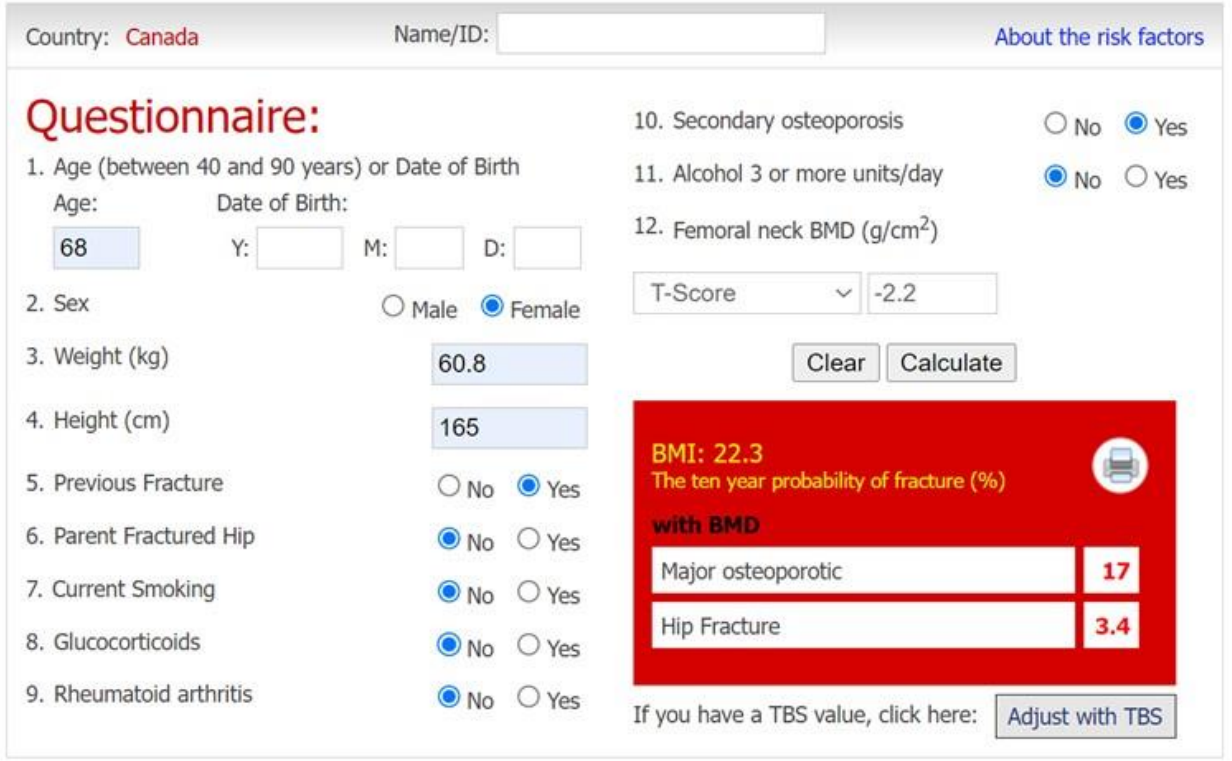


FRAX **with** BMD[a]



Note: outdated DXA scan (2 y ago, high risk, 2 spine fractures since)

[a]Additional details for the following FRAX entries: 5. adult fracture occurring with low trauma (excluding hands, feet, and cranium); 6. biological mother/father hip fracture; 7. currently smokes tobacco; 8. current/past oral glucocorticoid use, ≥5 mg qd or equivalent; 9. confirmed diagnosis of rheumatoid arthritis; 10. disorders strongly associated with osteoporosis (including type 1 diabetes, osteogenesis imperfecta in adults, untreated long-standing hyperthyroidism, hypogonadism, premature menopause/<45 y, chronic malnutrition, malabsorption, and chronic liver disease); 11. ≥3 units of alcohol daily; 12. enter the T-score if BMD scan is unknown and leave BMD field blank if BMD results are not available.

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Rosaria: Clinical management based on recent North American guidelines[1-7]

Osteoporosis and fracture risk

- Treatment failure: on-treatment fracture,[a] treatment adherent, and no apparent secondary causes[1,2,4,5,7]
- Recommended for BF therapy—very high risk: recent fracture (≤1 y) [1,2,5,6] (also, ≥2 spine fractures[1-3,6,7] or hip fracture FRAX score >4.5%[1,2])
- Osteoporosis diagnosed 2 y ago by family doctor based on BMD T-score ≤−2.5[1-5]

⚠ After completing BF treatment, guidelines[1-7] and product monograph[8] recommend switching to antiresorptive therapy to preserve the achieved BMD gains.

♂ **What if this patient was a man with a similar risk factor profile?** Per product monograph, romosozumab is not indicated in men and teriparatide may be considered after failure/intolerance to prior therapy.[8,9]

Management

- Indicated for romosozumab: osteoporosis + fracture or ≥2 risk factors (≥2 fractures and early menopause/<45 y); no hx of MI or stroke and no major CVD risk factors[8]
- Indicated for teriparatide: fracture hx or BMD T-score ≤−2.5; no known risk factors for osteosarcoma[9]
- DXA scan: ordered to confirm pretreatment BMD based on recent data
- Vitamin D: continue supplementing 1000 IU/d; calcium: continue supplementing 600 mg/d and consuming da
- Blood tests: reordered (prior tests ~2 mo ago) to exclude contraindications/hypocalcemia and secondary osteoporosis causes[1-5]
- Patient preferences: discussed treatment initiation with BF therapy (qd vs qm dosing) and follow-on antiresorptive treatment after completing BF treatment (bisphosphonates vs denosumab)

[a]Consider treatment failure if no secondary osteoporosis present and ≥2 on-treatment fractures (regardless of adherence) or ≥1 fracture, if adherent to therapy.[1,2,4,5,7]

BF, bone formation; BMD, bone mineral density; CVD, cardiovascular disease; DXA, dual-energy x-ray absorptiometry; FRAX, fracture risk assessment tool; hx, history; LS, lumbar spine; MI, myocardial infarction; MOF, major osteoporotic fracture; qd, daily; qm; monthly.

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Thank you!