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ORIGINAL ARTICLE

Rationale, study design, and descriptive data of the Lucky Bone™ Fracture Liaison Service

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Abstract

Summary The study design of a multidisciplinary Fracture Liaison Service (2-year follow-up) aiming to optimize fragility fracture management in an outpatient setting is presented. Patient characteristics, investigation, and treatment initiation data at baseline were recorded. Results corroborate the care gap in osteoporosis management, reinforcing the need for secondary fracture prevention programs.

Purpose This paper describes the study design, implementation, and baseline characteristics of a multidisciplinary Fracture Liaison Service (FLS) in Quebec (Canada).

Methods A FLS was implemented as a prospective cohort study. After identification, fracture risk was assessed and patients were started on treatment or referred, according to guidelines and risk assessment. Thereafter, patients were systematically followed over 2 years. Clinical data (fractures, bone density, blood testing (bone turnover markers), quality of life, physical disability) as well as administrative data (pharmacological, health services, hospitalization) was collected. Baseline descriptive data was analyzed and presented.

Results Of 542 recruited participants, 532 underwent baseline assessment (85.7% female, mean age 63.4 years). Overall, 29.7% of participants either withdrew from the study or were lost to follow-up. Almost 27% were referred to a specialist, while > 70% received anti-osteoporosis medication prescriptions through the FLS at baseline. Mean femoral *T*-score was − 1.6 ± 1.0 and vertebral *T*-score was − 1.7 ± 1.4. Nearly 19% of subjects reported being under anti-osteoporosis medication at the time of incident fracture. Thirty-three percent of participants reported a prior fracture history, of which 29.7% reported being given anti-osteoporosis therapy. Most fracture sites were to the wrist and ankle, while < 19% were hip/femur or vertebral fractures.

Conclusions These results highlight the important care gap in fragility fracture management and reinforce the need for secondary fracture prevention programs. This prospective study will allow the evaluation of key performance indicators for outpatient clinic-based FLS, such as medication usage, by combining prospective clinical and administrative data.

Keywords Osteoporosis · Fragility fracture · Secondary fracture prevention · Fracture liaison service · Fracture management · Cohort study

Introduction

Osteoporosis is a silent chronic disease that ultimately manifests as a fragility fracture. The occurrence of these osteoporosis-related fractures, combined with aging, greatly enhances the risk of subsequent fractures [1, 2]. This risk can also be exacerbated by factors such as a family history of osteoporosis, low bone mineral density (BMD), lifestyle habits (lack of exercise,

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smoking, excessive alcohol consumption), low calcium and vitamin D intake, and the use of specific pharmacological agents such as glucocorticoids [3]. Fortunately, multiple clinical trials have demonstrated that therapeutic agents, known as antiresorptive drugs, can substantially reduce the risk of subsequent fragility fractures over time [4–6]. Nevertheless, fragility fractures are largely underdiagnosed and undertreated [7, 8]. Furthermore, half the "treated" population is known to discontinue treatment 1 year after initiation [9, 10], which is alarming considering that there is a two to threefold increased mortality risk in the first year following a hip fragility fracture. Finally, expenses related to the management and treatment of fragility fractures in the Canadian healthcare system amount to $5 billion annually [11, 12].

Numerous initiatives are being pursued worldwide to decrease the care gap in osteoporosis-related fracture management [13]. Among these, secondary fracture prevention refers to the identification of at-risk patients through an incident fracture event, followed by investigation and treatment to prevent subsequent fragility fractures [14]. These efforts have led to the emergence of dedicated programs, commonly known as Fracture Liaison Services (FLS) [15, 16]. These combine various interventions led by different health professionals with heterogeneous associated training. Most papers reporting on the performance of these programs conclude that patient identification, investigation, and initiation of treatment show improved rates compared to usual care [17]. Several studies have also demonstrated the cost-effectiveness and reduced number of subsequent fragility fractures associated with these programs [18]. However, evidence of their impact on patient behavior, in terms of persistence and adherence to treatment, is less clear, especially in Canada [19, 20].

The Lucky Bone™ FLS prospective cohort study was designed to systematically compile information on clinical outcomes and fracture risk, quality of life (QoL), physical disability, and compliance to treatment. Here, we present the study's rationale and design with the 2-year analysis plan, as well as baseline data, osteoporosis investigation, and treatment initiation according to gender, for FLS participants.

Methods

Study design and setting

A cohort study design was selected to conduct this multidisciplinary follow-up, implemented in two community hospitals in Montreal, QC, Canada, in 2010. Patients with an incident fragility fracture were recruited prospectively from July 2010 to June 2013. The osteoporosis case-management systematic follow-up Lucky Bone™ Program was built in accordance with Osteoporosis Canada guidelines [21],within the framework of a 4i FLS: (1) *identify* patients with a fragility fracture, (2) *investigate* for bone fragility with osteoporosis risk assessment, (3) *initiate* preventive drug therapy and supplements, and (4) *integrate* to a 2-year follow-up and monitoring of adverse events.

This study was approved by the CIUSSS Nord de l'Ile de Montréal ethics research committee. Informed consent was obtained from all individual participants included in the study.

Study population

Study participants included women and men 40 years of age or older, presenting at the outpatient orthopedic clinic of either study hospital with a fracture to predefined body sites, sustained following a trauma that would not normally cause such an injury (minimal). Selected fracture sites included the vertebrae, sternum, sacrum, wrist, forearm, clavicle, scapula, humerus, ribs, ankle, femur, tibia/fibula, hip, and pelvis. Cases with a fracture to the skull, face, hand, foot, or patella were not eligible for participation. Traumas were identified as minimal when a patient fell from standing height, from a sitting position, from a horizontal position, from one to three steps (1 m), or occurred spontaneously. Patients younger than 40 years of age, with an open fracture, a fracture sustained through major trauma, a pathological fracture (underlying cancer or cancer treatment), with severe kidney insufficiency, with cognitive impairment, pregnant or breastfeeding women, or those unable to complete a questionnaire in English or French were not eligible to participate.

Recruitment

Participants were recruited between July 2010 and June 2013 by FLS nurses at the two hospitals (81.2% at the largest location and 18.8% at the secondary location). Patients were followed for 2 years, up to June 2015. Over the 3-year recruitment period, FLS managers identified potential participants at the outpatient orthopedic clinics of the two hospitals by screening the medical files of fracture patients and directly interrogating them to ascertain if they met the inclusion criteria. Clinical staff (surgeons, nurses, residents) was also encouraged to contribute to the identification process by referring potential cases to the FLS managers. Eligible fracture patients were recruited in the study and scheduled for baseline assessment with a FLS nurse. A small number of patients with a foot fracture were also recruited because they presented other risk factors suggesting a high risk for osteoporosis (e.g., fracture history, low BMD).

Intervention setting

Figure 1 shows the conduct of the study. The FLS was managed by nurses (one at each location), a dedicated coordinator,

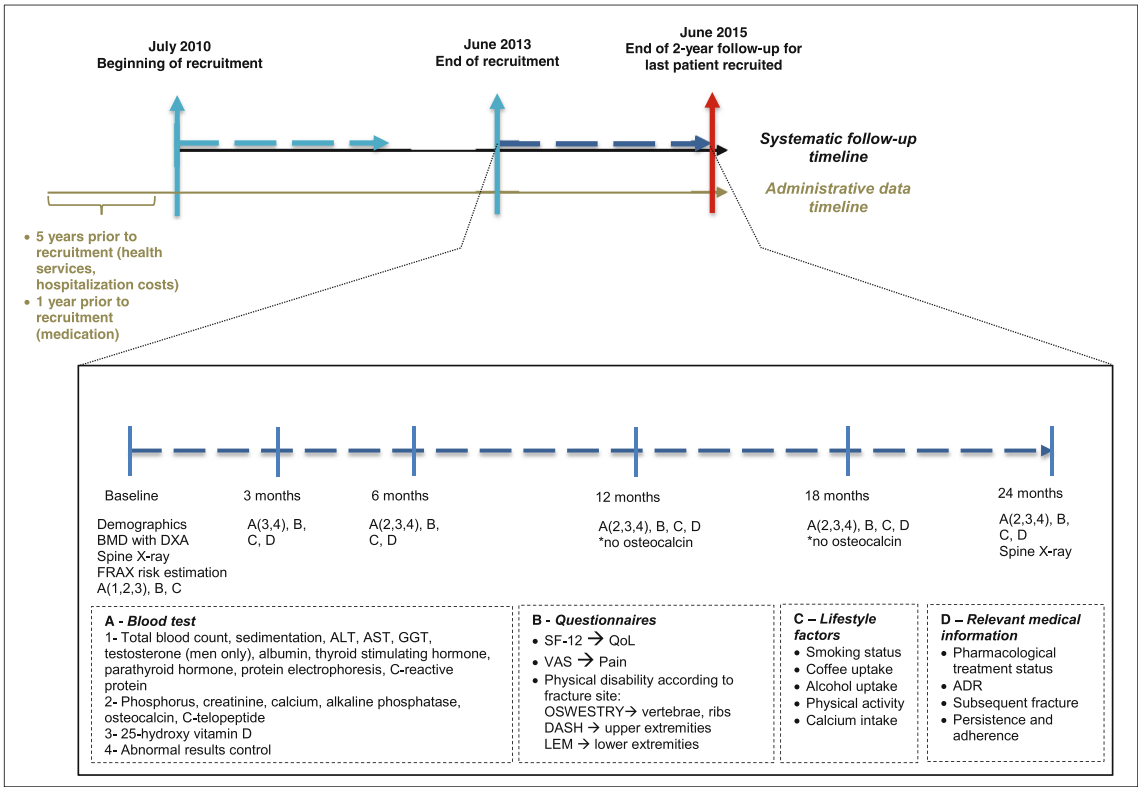

Fig. 1 The Lucky Bone™ Fracture Liaison Service timeline and data collection. ADR, adverse drug reactions; BMD, bone mineral density; DXA, dual-energy X-ray absorptiometry; QoL, quality of life

and a bone champion (orthopedic surgeon). Secondary FLS stakeholders were the physicians accepting referrals for special cases (rheumatologists and internists), the orthopedic surgeons identifying fragility fractures, referring patients to the FLS and prescribing medications, and the staff of the orthopedic outpatient clinics involved in fragility fracture identification and follow-up visits. The care algorithm has been the subject of a previous publication [22].

FLS managers underwent a 6-h training session on osteoporosis disease and diagnostic, fragility fractures, available therapies, secondary fracture prevention, and FLS management, prior to the commencement of the study. Participants' baseline assessment began with the collection of demographic data and a medical evaluation, including the request for a radiological assessment of the fracture site provided by an orthopedic surgeon. Spine radiographs were performed to identify prevalent vertebral fractures, defined as such in the radiologists' report or as a vertebral compression of 25% or more. Blood serum tests and BMD were performed to assess secondary causes and the severity of bone fragility. Blood samples were taken between 8 and 10 am, after patients had been fasting since 8 pm the evening before. Markers measured in the serum at each visit are shown in Table S1 (Online Resource 1). Blood test analyses were performed in accordance with clinical practice guidelines for the diagnosis and management of osteoporosis [23, 24]. BMD was determined by dual-energy X-ray absorptiometry (DXA), which measures the BMD standard deviation from peak bone mass in a young Canadian adult, reported as a *T*-score. The World Health Organization defined a *T*-score of − 2.5 or below as a diagnosis of osteoporosis and a *T*-score between − 1.0 and − 2.5 as a diagnosis of osteopenia (mild bone fragility) [23, 25]. Risk assessment was completed by measuring the 10-year probability of major and hip osteoporotic fractures using the Fracture Risk Assessment Tool (FRAX®) at https://www.sheffield.ac.uk/FRAX/tool.aspx?country=19 for a Canadian population. This tool uses several indicators such as age, gender, fragility fracture history, smoking status, or the use of glucocorticoids, to predict the risk of osteoporotic fractures for individuals aged between 40 and 90 years old and is recommended by the national guidelines for risk assessment [26].

Functional recovery was assessed with validated questionnaires: the SF-12 measures two QoL scores, ranging from 0 to 100 (physical and mental composite scores), where a higher score means a better QoL [27]. The visual analogue scale (VAS) ranges from 0 to 10 and gives an approximation of pain severity as experienced by the patient, where 10 represents the highest level of pain [28]. Three different questionnaires were used for physical disability of the injured limb, depending on incident fracture site: lower extremity measure (LEM, scale 0–100), upper extremity measure (DASH, scale 1–5, converted to a score of 0–100), and the vertebral measure (Oswestry,

scale 0–50, converted to a score of 0–100). The disability is smaller when the LEM score is higher and when the DASH score is lower [29, 30]. Oswestry scores are categorized as follows: 0–20% = minimal disability, 21–40% = moderate disability, 41–60% = severe disability, 61–80% = crippled, and 81–100% = bed-bound [31].

When preventive therapy was indicated, an antiresorptive agent was prescribed by an orthopedic surgeon, along with calcium and vitamin D supplements. Thereafter, patients were scheduled periodic appointments with the FLS manager for further assessments at 3, 6, 12, 18, 24 months. When applicable, all test results were forwarded to the primary care physicians (PCP) with information on the program.

Participants with fractures meeting all fragility fracture criteria except for age (50 years or more) were referred to a bone specialist when aged between 40 and 49 years. Other reasons for referral were abnormal blood screening, contraindication to treatment, or exposure to anti-osteoporosis therapy at the time of fracture. When no referral was needed, the most commonly prescribed pharmacological treatments were risedronate (oral, 35 mg once weekly) or alendronate (oral, 70 mg once weekly). Non-pharmacological treatment was also prescribed; calcium (oral, 500 mg BID) and vitamin D (oral, 10,000 IU once weekly). Recommendations about healthy lifestyle habits were also given at baseline during a brief education session on tobacco and alcohol restrictions, diet, physical activity, and fall prevention strategies. Other anti-osteoporosis therapies could be prescribed by physicians because of contraindications, adverse events, or other, such as zoledronic acid (IV, 5 mg/100 ml each year), denosumab (SC, 60 mg q 6 months), and teriparatide (SC, 20 mcg once daily for 2 years). The cost of medication was covered either by the Health Ministry insurance program or by private insurance companies, except for zoledronic acid, denosumab, and teriparatide, which are only prescribed in exceptional contraindication cases and require government authorization prior to prescription delivery.

During the FLS follow-up, as per-protocol, FLS managers considered clinical indicators to determine if therapy and supplement intake were optimal: (1) vitamin D, 25-OH D $\geq$ 80 nmol/L; (2) bone turnover markers (BTMs), CTX-1 < 0.3 ng/ml; and osteocalcin between 1 and 18 ng/ml.

Data collection and sources

Demographic and clinical data were collected into an electronic case report form (CRF) based on face-to-face meetings and a structured chart review with a trained FLS interviewer during follow-up visits. Several variables were scaled on a structured chart: physical activity (active or not, intensity, frequency, mean number of hours of exercise), diet, coffee and alcohol intake (frequency), and smoking status (past, present).

To complement the clinical data, the data on health services utilization, hospitalization, and pharmaceutical services from administrative Quebec databases was obtained. This made it possible to retrieve detailed medical history and prior fracture history up to 5 years before cohort entry and prescribed medication 1 year prior to study enrolment. The Régie de l'assurance maladie du Québec (RAMQ) database holds information on the medical services (diagnostic and procedures) received by all Quebec residents and covers all expenses for physician visits, emergency visits, and medical procedures, using physician billing codes. It is also a prescription claims database for social assistance beneficiaries, workers and their families without access to a private drug insurance program, and > 80% of individuals aged 65 years or older (approximately 45% of the province's inhabitants) [32]. The MED-ECHO database is a Health Ministry hospitalization registry gathering information on the site, start and end dates, duration, and reasons (primary and secondary diagnosis) for hospitalization as well as on the date and cause of death. However, it does not record medication received during hospitalization. Diagnoses are coded using the International Classification of Disease (ICD), 9th edition for medical services and 9th edition up to March 31st, 2006, and 10th edition upon April 1st, 2006, for hospitalizations. Procedures were classified according to the Canadian Classification of Diagnostic, Therapeutic, and Surgical Procedures (CCP) up to March 31st, 2006, and the Canadian Classification of Health Interventions (CIHI) upon April 1st, 2006. Diagnostic codes combined with procedure codes were found to be sensitive for the identification of fracture sites in the elderly [33].

We were also able to access data on medication prescribed and dispensed by community pharmacies for privately covered individuals using the reMed database [34]. This centralized Quebec information database is filled on a voluntary basis. Participants not covered by the RAMQ during the conduct of this study were invited to join the reMed registry. Data collection was ended at the last follow-up visit attended when a patient decided to withdraw from the FLS.

Variables and definitions

Details on specific collection periods and variables measured are summarized in Fig. 1 and thoroughly described in Table S1 (Online Resource 1). Data collected only at baseline included socio-demographic and patient characteristics: name, contact information, age, gender, pharmacological, PCP, type of medical insurance, ethnicity, housing, medical history, incident fracture description, previous fractures, weight, height, BMD, FRAX® risk, drug intake, and family fracture history. During visits (including baseline), the following variables were collected: health-related events, antiresorptive therapy status, associated comorbidities, medication persistence and adherence, co-medications, blood analyses (total blood count,

liver function, renal function, sedimentation, ALT, AST, GGT, testosterone (men only), albumin, TSH, protein electrophoresis, parathyroid hormone, C-reactive protein, phosphorus, creatinine, calcium, alkaline phosphatase, 25-hydroxyvitamin D, type I collagen C-telopeptide (CTX-1), and osteocalcin), diet, physical activity, smoking status, caffeine, alcohol use, and QoL/physical disability/pain questionnaires.

Data collected from administrative databases included incident and previous fractures, as well as comorbidities. The *incident* fracture was the one identified by FLS managers to recruit the patient. A *previous* fracture was a fragility fracture sustained prior to the incident fracture. Fractures were identified through administrative databases using ICD codes (Table S2, Online Resource 1) and specific procedures. The following fracture sites were screened for the hip, femur, wrist, forearm, humerus/shoulder, vertebral, pelvis, ribs, knee, tibia/fibula, ankle, foot, pathological fractures, and unspecified fracture sites. In order to identify incident fractures using claims data, diagnostic and procedure codes were targeted, starting 6 months before the date of recruitment and 30 days after the same. This detection period covered multiple codes imputable to the same fracture event. Consequently, previous fractures were identified from the same codes for the 5 years of data obtained prior to cohort entry, excluding the 6-month incident fracture screening period. Medical history included cardiovascular, cerebrovascular, musculoskeletal, endocrine, hepatic, renal, inflammatory bowel, and neuromuscular diseases, as well as digestive disorders, cancer, and vascular events. Table S3 (Online Resource 1) presents ICD codes used to identify comorbidities. The Charlson comorbidity index (CCI) was also calculated [35, 36].

Statistical analysis

Baseline patient-reported cohort characteristics are presented with means and standard deviations when following a normal distribution and with medians and interquartile range (IQR) if otherwise. All variables were compared between women and men using chi-square/Fisher's exact tests for discrete variables and Student *t*/Wilcoxon-Mann-Whitney tests for continuous ones. A p value of ≤ 0.05 was considered statistically significant. Analyses were performed using SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA).

Sample size

The sample size was derived from anti-osteoporosis drug use in terms of medication persistence. The proportion of subjects in the program that would continue treatment for the prescribed period was estimated at 50–55%, compared to 35–40% in the general Quebec population. Using a 5% probability of a type 1 error (alpha), a power of 90% and a difference in proportions of 15%, a sample size of 88 subjects was needed ($n = 54$ with a 20% difference in proportions) [10, 19, 37]. Considering that approximately 65% of the cohort would have drug coverage data, that 70% of patients would initiate treatment in the first 6 months following baseline and that 30% of patients would be lost to follow-up, at least 250 fractured subjects needed to be recruited.

Results

A total of 542 patients were recruited in the FLS, of which 532 (98.1%) had baseline data available. Mean age was 63.4 (± 11.2) years and 85.7% were female (Table 1). Over a 2-year period, 97 patients (18.2%) withdrew from the study, 39 were lost to follow-up (7.3%), 14 were excluded (2.6%), and 8 died (1.5%) (Fig. 2). Between 62 and 77% of participants attended visits over the 2-year follow-up. A prescription for anti-osteoporosis medication was handed to 385 patients (72.4%) by FLS managers at baseline, of which more than 95% was risedronate or alendronate (oral antiresorptive therapies).

Nearly 89% of the cohort benefited from PCP services and 27% of patients were referred to a bone specialist, this proportion being significantly higher in women than in men ($p = 0.018$). More than 85% of patients were Caucasian (more women than men, $p = 0.044$). The majority of subjects lived with a relative, had a low or moderate level of physical activity, and daily calcium intake was below the recommended intake of 1200 mg in 90% of cases [38]. Nearly 18% of patients were current smokers and 41% had a smoking history, with a much higher proportion of men than of women ($p = 0.007$). Overall alcohol consumption was 37.2%, with men also reporting more alcohol consumption and a higher number of drinks per week than women ($p < 0.05$). Almost 90% of participants reported drinking coffee daily (Table 1). More than 7% of subjects reported the need for a walking aid before the incident fracture compared to almost 34% after the incident fracture.

Table 2 presents the results of risk assessment with BMD testing, spine radiography, the FRAX® risk assessment tool, and BTMs. The mean femoral *T*-score was − 1.6 (± 1.0) and did not differ between women and men. According to *T*-score stratification, 62.2% of the cohort had mild bone fragility (osteopenia) and 15.3% had osteoporosis, leaving 22.5% with a normal BMD. Mean vertebral *T*-score was − 1.7 (± 1.4) and was significantly lower in women ($p = 0.005$). According to spine radiographs, a vertebrae depression was detected in 16% of patients, indicating a possible vertebral fracture. The median FRAX® risk for major fractures was 11% (IQR 6.8–17) and was worse in women ($p < 0.001$). More than 48% of the cohort was considered at low risk for major fracture (FRAX® < 10%). The median FRAX® risk for hip fractures was 1.6% (IQR 0.6–4.4), with 34% of patients at high risk for hip fractures. Almost half of the participants had a non-optimal 25-

Table 1 Baseline demographics and lifestyle habits of participants

Variables	Total $N = 532$	Women $N = 456$ (85.7%)	Men $N = 76$ (14.3%)	p value
Age (years), mean ± SD	63.4 ± 11.2	63.4 ± 11.4	62.9 ± 10.5	0.729
40–49 years	59 (11.1)	51 (11.2)	8 (10.5)	0.968
50–59 years	154 (28.9)	131 (28.7)	23 (30.3)	
60–69 years	171 (32.1)	146 (32.0)	25 (32.9)	
70–79 years	94 (17.7)	80 (17.6)	14 (18.4)	
80+ years	54 (10.2)	48 (10.5)	6 (7.9)	
Number with primary care physician	472 (88.7)	408 (89.5)	64 (84.2)	0.179
Number referred to a specialist	143 (26.9)	131 (28.7)	12 (15.8)	0.018
Body mass index (kg/m^2)†	529 (99.4)	453 (99.3)	76 (100.0)	
Mean ± SD	25.9 ± 5.4	25.6 ± 5.2	27.8 ± 6.0	<0.001
< 20	58 (11.0)	53 (11.7)	5 (6.6)	0.016
≥ 20 to < 25	189 (35.7)	171 (37.8)	18 (23.7)	
≥ 25 to < 30	178 (33.6)	147 (32.4)	31 (40.8)	
≥ 30	104 (19.7)	82 (18.1)	22 (28.9)	
Ethnicity†	456 (85.7)	389 (85.3)	67 (88.2)	
Caucasian	390 (85.5)	336 (86.4)	54 (80.6)	0.044
Hispanic	11 (2.4)	10 (2.6)	1 (1.5)	
Black	8 (1.7)	6 (1.5)	2 (3.0)	
Asian	2 (0.5)	0 (0.0)	2 (3.0)	
Arab/West Asian	45 (9.9)	37 (9.5)	8 (11.9)	
Living status†	454 (85.3)	389 (85.3)	65 (85.5)	
Home alone	166 (36.6)	149 (38.3)	17 (26.2)	0.136
With a relative	286 (63.0)	238 (61.2)	48 (73.8)	
Nursing home	2 (0.4)	2 (0.5)	0 (0.0)	
Physical activity†	439 (82.5)	377 (82.7)	62 (81.6)	
Inactive	101 (23.0)	89 (23.6)	12 (19.4)	0.461
Active	338 (77.0)	288 (76.4)	50 (80.6)	
Physical activity level				
Little	57 (16.8)	46 (16.0)	11 (22.0)	0.647
Low	128 (37.9)	111 (38.5)	17 (34.0)	
Moderate	120 (35.5)	104 (36.1)	16 (32.0)	
Intense	33 (9.8)	27 (9.4)	6 (12.0)	
Calcium daily intake (mg)†	433 (81.4)	371 (81.4)	62 (81.6)	
Mean ± SD	763.1 ± 294.9	770.7 ± 296.5	717.9 ± 282.8	0.192
< 1200	393 (90.8)	333 (89.8)	60 (96.8)	0.096
≥ 1200	40 (9.2)	38 (10.2)	2 (3.2)	
Smoking status—present†	528 (99.2)	453 (99.3)	75 (98.7)	
Current smoker	96 (18.2)	79 (17.4)	17 (22.7)	0.277
Smoking status—past†	395 (74.2)	339 (74.3)	56 (73.7)	
Former smoker	161 (40.8)	129 (38.0)	32 (57.1)	0.007
Alcohol intake†	530 (99.6)	455 (99.8)	75 (98.7)	
Drinker	197 (37.2)	159 (34.9)	38 (50.7)	0.009
Number of drinks/week				
≤ 7	145 (73.6)	124 (78.0)	21 (55.3)	0.016
8 to 15	35 (17.8)	24 (15.1)	11 (28.9)	
≥ 16	17 (8.6)	11 (6.9)	6 (15.8)	
Caffeine intake†	429 (80.6)	368 (80.7)	61 (80.3)	
Coffee drinker	381 (88.8)	328 (89.1)	53 (86.9)	0.606
Number of cups/day†	370 (69.5)	317 (69.5)	53 (86.9)	
Median (IQR)	2.0 (1.0–3.0)	2.0 (1.0–3.0)	2.0 (1.0–3.0)	0.747

Data presented as the number of patients (percentage), unless stated otherwise

IQR, interquartile range; *SD*, standard deviation

† Number of patients with data available

hydroxyvitamin D level (< 80 nmol/L), with only 22% of men with an optimal vitamin D level. Median bone resorption (CTX-1) and formation (osteocalcin) marker levels were slightly elevated at 0.327 ng/mL (IQR 0.219–0.472) and 18 ng/mL (IQR 14–24), respectively.

Table 3 presents comorbidities, patient-reported medication, and fracture history at baseline. A history of osteoporosis was more prevalent in women ($p = 0.002$), whilst a history of hypertension, hypercholesterolemia, diabetes, cerebrovascular disease, kidney disorders, heart failure, and myocardial infarction was more important in men ($p < 0.05$). This was supported by the CCI where 61.8% of men had a CCI higher than 0 compared to 49.3% for women ($p = 0.044$). The median number of drugs prescribed, according to patients at baseline,

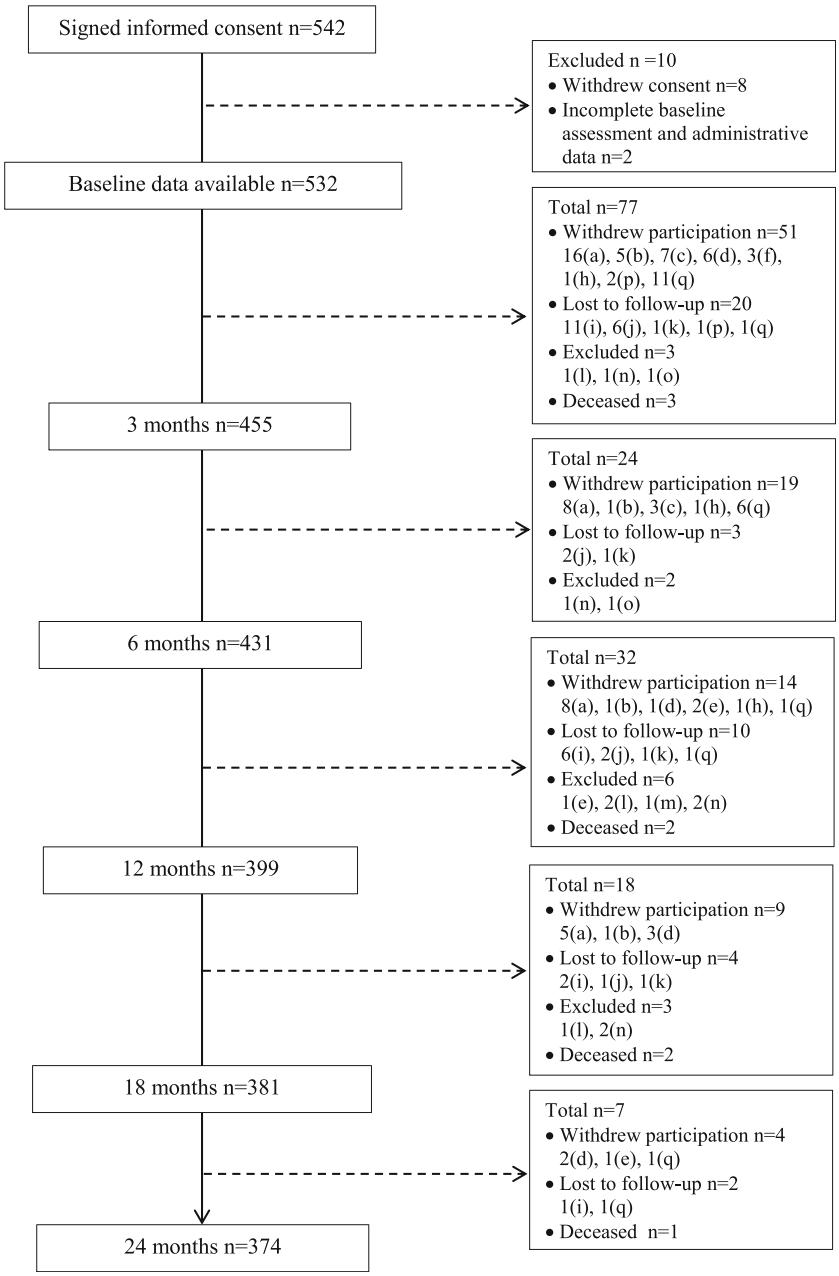

Fig. 2 Study flow diagram. PCP, primary care physician; ADR, adverse drug reaction; FU, follow-up. Reasons: (a) refused FU, no information on treatment; (b) refused FU, treatment continued; (c) wants to be followed by PCP; (d) refused treatment; (e) medical reason; (f) ADR; (g) atypical fracture; (h) PCP refused intervention; (i) no call back; (j) unreachable/ unfound; (k) absent for appointment; (l) cognitive impairment; (m) did not speak French or English; (n) had no bone fragility after risk assessment; (o) other research project; (p) other reason; (q) no reason given

was higher in men than in women ($p = 0.003$). Levothyroxine and corticosteroids were taken by 13% and 11% of patients, respectively. The most frequent incident fracture site, identified from medical files, was to the wrist, followed by the ankle and the humerus (Fig. 3). Major fracture sites such as the hip were more prevalent in men compared with women ($p = 0.005$). Close to 9% of patients presented a vertebral fracture and 10% a hip/femur fracture at baseline. Median number of days between the incident fracture event identified from medical files and the date of recruitment was 59 (IQR 29–138) days ($n = 513$). The percentage of patients suffering a fracture whilst on antiresorptive therapy was 18.6%, with the proportion of women (20.8%) being significantly higher than of men (5.3%) ($p < 0.001$). Almost 33% of patients reported a previous history of fracture. It is to be noted that only 29.7% of patients reporting a history of fragility fracture were following a preventive therapy treatment before the incident event. Patients reported a family history of osteoporosis and fracture in 28% and 33% of cases, respectively.

As for QoL, disability and pain questionnaires gave the following results at baseline: the Oswestry median score ($n = 38$) was 49 (IQR 26–60), corresponding to a "severe disability," the median LEM score ($n = 185$) was 69.0 (46.3–90.4), the median DASH score ($n = 267$) was 63.6 (38.6–77.3), and the mean mental and physical SF-12 scores ($n = 485$) were 47.8 (± 11.4) and 38.1 (± 10.1), respectively. More

Table 2 Baseline investigation tests and risk assessment tool results

Variables	Total $N = 532$	Women $N = 456$ (85.7%)	Men $N = 76$ (14.3%)	p value
DXA results				
Femoral T-score[†]	458 (86.1)	388 (85.1)	70 (92.1)	
Mean ± SD	− 1.60 ± 0.97	− 1.60 ± 0.94	− 1.58 ± 1.12	0.847
> −1	103 (22.5)	87 (22.4)	16 (22.8)	0.682
≤ − 1 to > − 2.5	285 (62.2)	244 (62.9)	41 (58.6)	
≤ −2.5	70 (15.3)	57 (14.7)	13 (18.6)	
Vertebral *T*-score[†]	459 (86.3)	389 (85.3)	70 (92.1)	
Mean ± SD	− 1.71 ± 1.36	− 1.78 ± 1.32	− 1.29 ± 1.51	0.005
> −1	127 (27.7)	99 (25.5)	28 (40.0)	0.031
≤ − 1 to > − 2.5	192 (41.8)	165 (42.4)	27 (38.6)	
≤ − 2.5	140 (30.5)	125 (32.1)	15 (21.4)	
Spinal X-ray results[†]	357 (67.1)	307 (67.3)	50 (65.8)	0.401
Normal	300 (84.0)	260 (84.7)	40 (80.0)	
Depression	57 (16.0)	47 (15.3)	10 (20.0)	
FRAX risk[α†]	529 (99.4)	453 (99.3)	76 (100.0)	
Major, median (IQR)	11.0 (6.8–17.0)	12.0 (7.5–17.0)	7.2 (4.6–13.0)	< 0.001
< 10%	256 (48.4)	203 (44.8)	53 (69.7)	< 0.001
10–20%	173 (32.7)	156 (34.4)	17 (22.4)	
> 20%	100 (18.9)	94 (20.8)	6 (7.9)	
Hip, median (IQR)	1.6 (0.6–4.4)	1.7 (0.6–4.4)	1.4 (0.4–4.7)	0.325
< 3%	349 (66.0)	299 (66.0)	50 (65.8)	0.971
≥ 3%	180 (34.0)	154 (34.0)	26 (34.2)	
Vitamin D (nmol/L)[β†]	377 (70.9)	318 (69.7)	59 (77.6)	
Mean ± SD	84.0 ± 32.2	87.2 ± 32.0	67.1 ± 28.2	< 0.001
< 80 nmol/L	179 (47.5)	133 (41.8)	46 (78.0)	< 0.001
≥ 80 nmol/L	198 (52.5)	185 (58.2)	13 (22.0)	
CTX-1 (ng/mL)[†]	381 (71.6)	323 (70.8)	58 (76.3)	
Median (IQR)	0.327 (0.219–0.472)	0.325 (0.208–0.480)	0.332 (0.230–0.413)	0.833
≥ 0.300 ng/mL	218 (57.2)	185 (57.3)	33 (56.9)	0.957
< 0.300 ng/mL	163 (42.8)	138 (42.7)	25 (43.1)	
Osteocalcin (ng/mL)[†]	362 (68.0)	306 (67.1)	56 (73.7)	
Median (IQR)	18.0 (14.0–24.0)	18.0 (14.0–25.0)	18.0 (15.0–21.5)	0.505
< 18 ng/mL	167 (46.1)	140 (45.8)	27 (48.2)	0.733
≥ 18 ng/mL	195 (53.9)	166 (54.2)	29 (51.8)	

Data presented as the number of patients (percentage), unless stated otherwise

BMD, bone mineral density; *DXA*, dual-energy X-ray absorptiometry; *IQR*, interquartile range; *SD*, standard deviation

[†] Number of patients with data available

[α] FRAX measured at https://www.sheffield.ac.uk/FRAX/toolaspx?country=19

[β] 25-hydroxyvitamin D

than 50% of the cohort indicated having a pain level higher than 4/10 on the VAS at baseline ($n = 492$).

Table S4 (Online resource 1) compares baseline characteristics between subjects still participating in the study after 2 years ($n = 374$) and subjects that were lost to follow-up ($n = 158$). There were only slight differences between participants and patients lost to follow-up; the latter group had fewer subjects with a history of smoking and current alcohol intake, as well as a higher continuous vertebral *T*-score ($p < 0.05$).

Figure S1 (Online resource 1) illustrates the distribution of comorbidities, incident fracture sites, and history of fracture according to clinical data from the FLS and claims data from administrative databases. Proportions were similar up to a ± 5 percentage point variation for most parameters, except for hypertension, wrist/forearms/elbow, and other types of incident fractures. It is to be noted that the algorithm to identify *incident* fractures using administrative data allowed the identification of a fracture site in 84% of participants ($n = 447$).

Table 3 Baseline medical, medication and fracture history of participants

Variables[α]	Total $N = 532$	Women $N = 456$ (85.7%)	Men $N = 76$ (14.3%)	p value
Medical history				
Hypertension	245 (46.0)	199 (43.6)	46 (60.5)	0.006
Osteoporosis	174 (32.7)	161 (35.3)	13 (17.1)	0.002
Dyslipidemia	136 (25.6)	102 (22.4)	34 (44.7)	< 0.001
Pulmonary diseases	129 (24.2)	113 (24.8)	16 (21.0)	0.483
Cancer	106 (19.9)	97 (21.3)	9 (11.8)	0.057
Depression	102 (19.2)	91 (20.0)	11 (14.5)	0.261
Diabetes	77 (14.5)	56 (12.3)	21 (27.6)	< 0.001
E/G diseases	72 (13.5)	66 (14.5)	6 (7.9)	0.121
Hypothyroidism	70 (13.2)	62 (13.6)	8 (10.5)	0.463
AI diseases	52 (9.8)	47 (10.3)	5 (6.6)	0.405
ALBF	40 (7.5)	32 (7.0)	8 (10.5)	0.283
Angina	38 (7.1)	29 (6.4)	9 (11.8)	0.086
PV diseases	35 (6.7)	28 (6.1)	7 (9.2)	0.317
CV disease	34 (6.4)	24 (5.3)	10 (13.2)	0.009
Heart failure	34 (6.4)	24 (5.3)	10 (13.2)	0.009
Renal diseases	33 (6.2)	20 (4.4)	13 (17.1)	< 0.001
Hyperthyroidism	29 (5.4)	26 (5.7)	3 (4.0)	0.785
Myocardial infarction	21 (3.9)	14 (3.1)	7 (9.2)	0.011
Rheumatoid arthritis	19 (3.6)	17 (3.7)	2 (2.6)	1.000
NM diseases	15 (2.8)	13 (2.8)	2 (2.6)	1.000
Alz/Dem	15 (2.8)	14 (3.1)	1 (1.3)	0.707
Liver disease	9 (1.7)	7 (1.5)	2 (2.6)	0.623
Hypercalcemia	5 (0.9)	4 (0.9)	1 (1.3)	0.539
CI, median (IQR)	1.0 (0.0–2.5)	0.0 (0.0–2.0)	1.5 (0.0–3.0)	0.050
0	260 (48.9)	231 (50.7)	29 (38.2)	0.044
> 0	272 (51.1)	225 (49.3)	47 (61.8)	
Number of medications[†β]	467 (87.6)	400 (87.7)	67 (88.2)	
Median (IQR)	5.0 (3.0–9.0)	5.0 (3.0–8.0)	7.0 (3.0–12.0)	0.003
Medications at risk for secondary osteoporosis[β]				
Levothyroxine	70 (13.2)	65 (14.2)	5 (6.6)	0.069
Corticosteroids	58 (10.9)	52 (11.4)	6 (7.9)	0.363
Diuretics	41 (7.7)	32 (7.0)	9 (11.8)	0.144
Laxatives	17 (3.2)	15 (3.3)	2 (2.6)	1.000
Heparin	10 (1.9)	8 (1.7)	2 (2.6)	0.641
Tamoxifen	9 (1.7)	9 (2.0)	NA	NA
Antiepileptic	4 (0.7)	4 (0.9)	0 (0.0)	1.000
Lithium	4 (0.7)	4 (0.9)	0 (0.0)	1.000
Facture site[β£]				
Wrist/forearm/elbow	228 (42.9)	207 (45.4)	21 (27.6)	0.005
Ankle	91 (17.1)	74 (16.2)	17 (80.2)	
Shoulder/humerus	76 (14.3)	69 (15.1)	7 (9.2)	
Hip/femur	55 (10.3)	40 (8.8)	15 (19.7)	
Vertebrae	45 (8.5)	37 (8.1)	8 (10.5)	
Other	64 (12.0)	52 (11.4)	12 (15.8)	
Under treatment before incident fracture[β]	99 (18.6)	95 (20.8)	4 (5.3)	< 0.001
Previous fracture(s)[β]	175 (32.9)	155 (34.0)	20 (26.3)	0.187

Data presented as the number of patients (percentage), unless stated otherwise

AI, abdominal inflammatory diseases; *ALBF*, abnormal lower body function; *Alz/Dem*, Alzheimer's disease or other dementias; *CCI*, Charlson comorbidity index; *CV*, cerebrovascular; *E/G*, esophageal- or gastroprotection-related diseases; *IQR*, interquartile range; *NA*, not applicable; *NM*, neuromuscular; *PV*, peripheral vascular; *SD*, standard deviation; *SSRI*, selective serotonin reuptake inhibitors

[†] Number of patients with data available

[α] Variables are all based on provincial administrative databases, unless stated otherwise

[β] Patient-reported

[£] Includes 33 multiple fractures

Discussion

The Lucky Bone™ prospective cohort study is a nurse-led FLS aiming to optimize subsequent fracture prevention through the treatment of underlying osteoporosis, using a case-management systematic follow-up with a multidisciplinary service. FLS managers were able to investigate more than 85% of patients for osteoporosis and initiate or continue anti-

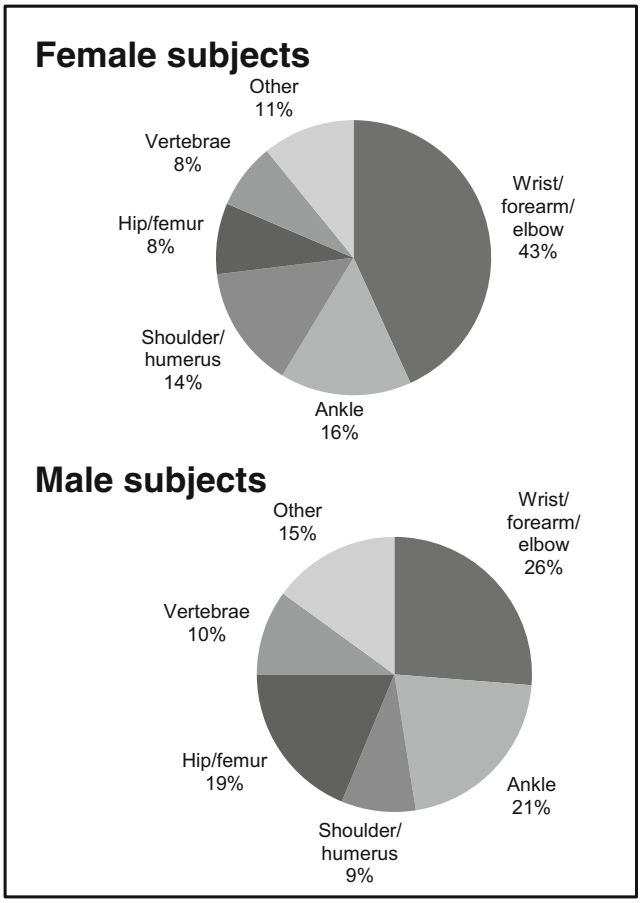

Fig. 3 Distribution of incident fracture sites according to gender. Fracture sites were either patient-reported or identified with the medical file. Most recurrent fractures were to the wrist and ankle. Thirty-three patients had multiple fractures (6.2%)

osteoporosis treatment in 70% of the cohort at baseline. The baseline descriptive results depict a high-risk cohort (incident fragility fracture). Nonetheless, BMD testing, the FRAX® assessment tool, age (majority < 65 years), and incident fracture site (less than 20% were vertebral or hip fractures) showed the majority of participants to be suffering from osteopenia or having a moderate fracture risk. As expected, men presented more risk factors than women (smoking, alcohol, comorbidities, medication), agreeing with secondary osteoporosis manifestation. Interestingly, less than 30% of patients with a history of fragility fracture reported being treated for the prevention of subsequent fractures before cohort entry, even though a majority of patients had a PCP. This confirms the presence of a care gap in fragility fracture management in the population, underscoring the necessity for this study.

Using administrative billing data for medical services, we were able to identify an incident fracture site for 84% of patients over a predefined timeframe, with fracture sites (wrist/forearm/elbow, ankle, shoulder/humerus, hip/femur, and vertebrae) corresponding to those reported by patients in 83–97% of cases. This result is similar to those of a study validating the use of diagnostic codes to identify fragility fractures through several algorithms, where sensitivity and predictive positive values were high for almost all fracture sites (~ 80 to > 90%) [39]. This will allow us to identify fragility fractures in the future, using diagnostic codes in combination with an algorithm for added precision.

We aimed to remedy the fragility fracture care gap with our personalized model for secondary fracture prevention by reporting on its clinical and economic impacts. The more specific objectives of this study were to (1) report the number of subsequent fragility fractures and describe the evolution of clinical outcomes (QoL, physical disability of the fractured limb and BTMs); (2) assess medication usage, including treatment initiation, persistence, and adherence to antiresorptive therapy; and (3) describe the costs and consequences associated to the program. The analyses of the gathered data are ongoing, i.e., the evolution of patient-reported QoL, functional outcomes, and BTMs over 2 years will be modeled using robust statistical methods for repeated measurements [40] and the incidence of subsequent fragility fractures will be reported. Then, anti-osteoporosis therapy utilization in the FLS (treatment initiation, discontinuation, re-initiation, and adherence) will be assessed in a subgroup of subjects with available pharmacy claims. Predictors of persistence and adherence will also be identified. Finally, a cost-consequence study will be performed by modeling trajectories of health care, health outcomes, and related costs [41, 42].

To the best of our knowledge, very few studies have reported results on FLSs using both administrative and clinical data and the ones that did show a great variability in terms of the level of intervention [19, 20, 43]. Conversely, the Lucky Bone™ FLS benefits from a high level of intervention, where treatment initiation, longitudinal monitoring, and systematic follow-up with visits improve healthcare access for patients. This type of program, provided by dedicated personnel, could be part of standard practice and help fight the osteoporosis care gap. This cohort study stands out by its singular and innovative use of prospective clinical data enhanced by administrative data to measure the evolution of clinical parameters, such as BTMs and medication usage, as well as model trajectories of care and costs in a pre-post fashion.

Several potential limitations need to be considered: first and foremost, the absence of a control group and the prospective observational design which can limit the ability to monitor potential confounders. Furthermore, some of the missing data, from patients refusing to participate and lost to follow-up, might not be randomly distributed which could cause a selection bias. However, the comparison between participants and patients lost to follow-up showed minor differences in baseline characteristics, suggesting a low possibility for selection bias. Hip and vertebral fracture patients are underrepresented in this cohort since case identification was restricted to outpatient clinics and hip fracture patients are generally

hospitalized on wards while vertebral fractures are often under-detected per their asymptomatic manifestation. We acknowledge that this can affect the external validity of the present study and recommend that a FLS should include detecting fractures via the emergency unit and hospital wards in order to address the in-hospital fragility fracture care gap.

Conclusion

Fragility fractures significantly affect the lives of victims and their relatives and can be prevented with efficient and safe therapies. Secondary prevention through a FLS managed by nurses, to identify and investigate patients, initiate treatment and ensure close follow-up, could help resolve the care gap. Key performance indicators are currently being analyzed and will help determine if the Lucky Bone™ FLS can help optimize disease prevention and treatment in individuals with fragility fractures.

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Compliance with ethical standards

All procedures performed in this study involving human participants were in accordance with the ethical standards of the CIUSSS Nord de l'Ile de Montréal ethic research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Conflicts of interest Senay, Perreault, Banica, Beaumont, Jodoin, and Nguyen declare that they have no conflict of interest. Delisle reports support for personal fees from Amgen Canada and Eli Lilly outside of the conducted work. Morin reports grants from Amgen Canada and Merck, support as an advisory board member from Amgen Canada and Eli Lilly outside of the conducted work. Raynauld reports fees as an advisory board member for Amgen Canada outside of the conducted work. Troyanov reports fees as an advisory board member for Amgen, Eli Lilly, and Novartis outside of the conducted work. Laflamme reports research grants from Zimmer, Stryker, and DePuy Synthes, and support as a consultant from Stryker outside of the conducted work. Leduc reports research grants from Stryker, DePuy Synthes, Smith & Nephew, and Zimmer, and support as a consultant from Stryker outside of the conducted work. Mac-Thiong reports acts as co-founder of Spinologics Inc. and head of Medtronic Research Chair outside of the conducted work. Ranger reports grants from Johnson & Johnson, support as a consultant from Smith & Nephew, Corin, Bioventus, Sanofi Canada, and support for development of educational presentations by Horizon Pharma outside of the conducted work. Rouleau reports research and educational grants from Zimmer, Stryker, Smith & Nephew, Tornier, Arthrex, Conmed, and DePuy Synthes outside of the conducted work. Fernandes reports grants from Eli Lilly during the conduct of this study and grants from Baxter outside of the conducted work.

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