Current Treatment Options in Rheumatology (2022) 8:19–35
DOI 10.1007/s40674-021-00190-1

Osteoporosis (K Saag, Section Editor)

The Effectiveness of Fracture Liaison Services in Improving Fragility Fracture Outcomes

Nitasha Khullar, MD
Maria I. Danila, MD, MSc, MSPH[*]

Address
[*]Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, USA
Email: mdanila@uabmc.edu

Published online: 31 March 2022

This article is part of the Topical Collection on *Osteoporosis*

Keywords Fragility fracture · Osteoporosis · Fracture prevention · System-based intervention

Abstract

Purpose of review Fragility fractures are associated with significant morbidity, mortality, and societal costs. A fracture liaison service (FLS) is a multidisciplinary approach that identifies people with fragility fractures with the goal to ensure optimal osteoporosis treatment. In this review, we summarize recent data on the FLS effectiveness in improving osteoporosis diagnosis, bone density testing, and osteoporosis treatment, as well as reducing the rates of secondary fragility fracture, subsequent fall, and mortality in individuals with fragility fractures.
Recent Findings We identified one randomized controlled trial and ten observational studies published within the last 5 years that reported on relevant outcomes. FLS was associated with favorable outcomes, depending on the intensity of the FLS approach used. Secondary fragility fracture rate was the most common reported outcome. Most studies were conducted outside of the USA, included highly variable duration of follow-up and comparators, and focused on heterogeneous patient populations. Most recent studies of FLS have important limitations given the study design and risk of bias.
Summary Our findings support the need for randomized controlled trials of FLS in the USA to rigorously examine to what extent the implementation of FLS in the complex US healthcare system may improve outcomes of patients with fragility fracture.

Introduction

The first sign of osteoporosis in many individuals is a low-trauma fragility fracture, occurring from a fall from standing height or less [1]. The National Osteoporosis Foundation estimates that 53 million Americans are at risk for fragility fractures [2]. In the USA, approximately 2 million fragility fractures occur every year [3] and the rates of fragility fractures are projected to continue to rise [4••]. Adults aged 65 years and older are particularly at risk for fragility fractures, which lead to important losses in function [5], independence [5], income [6], and quality of life [2]. Beyond the significant morbidity and mortality associated with fragility fractures, they also contribute substantially to societal costs. According to Medicare data, the total fragility fracture care-related expenditures in the USA in 2018 was 57 billion dollars and the economic impact associated with fragility fractures is estimated to increase to 95 billion dollars by 2040 [7].

Timely diagnosis of osteoporosis, initiation of effective osteoporosis medications, and robust treatment adherence can decrease the risk of a re-fracture by up to 70% after 30 months of treatment, thus decreasing overall healthcare costs and societal burden [8]. But while accurate tools to assess fracture risk exist (e.g., FRAX ® Fracture Risk Assessment Tool) and many medications that increase bone mineralization are widely available, osteoporosis treatment rates continue to remain low even in high-risk individuals with past fragility fractures [9–11]. In fact, despite the very high risk for subsequent fracture in the first year after a fracture [12], more than 80% of adults who have had a fracture are not offered osteoporosis screening and/or treatment [13, 14]. The lack of timely osteoporosis assessment and treatment leads to an increased risk of subsequent fragility fractures: as much as a threefold increased risk in hip fractures and a twofold increased risk of any new fracture [15].

A fracture liaison service (FLS) is a healthcare system approach to prevent fracture that focuses on coordinating bone healthcare after fracture repair [16]. However, the uptake of FLS by healthcare systems in the USA and worldwide has been lagging and a global care gap in post fragility fracture care remains. Key system barriers to FLS adoption include concerns related to the complexity, cost, and time commitment needed for their implementation and the absence of a "champion" medical or surgical specialty to oversee and follow up on bone health management. In an attempt to mitigate some of these barriers to care and increase medical community and public awareness about the critical need to address bone health problems after a fracture, in 2012, the International Osteoporosis Foundation launched the "Capture the Fracture" campaign, which has promoted mentoring programs for implementing FLS and has broadly disseminated a best practice framework to guide real-world FLS implementation [17]. The FLS model of care supports a multidisciplinary and systematic approach to secondary fracture prevention that includes identification of individuals who sustain fragility fractures, prompt referral for fracture risk assessment (e.g., bone mineral density [BMD] measurement), and appropriate treatment initiation [18]. In the USA, the National Orthopedic Association has rolled out the "Own the Bone Initiative," an FLS quality improvement program to improve osteoporosis diagnosis and treatment [19]. As of 2018, 9 years after the launch of the "Own the Bone Initiative," 240 clinical sites in the USA had registered to start FLS programs and improve coordination of care, counseling, and treatment for patients after fragility fractures [20].

Several FLS models of care have been utilized for secondary fracture prevention [16]. Although each FLS type varies in terms of complexity and by the degree of involvement from different clinical care team members, they all leverage a multidisciplinary approach to coordinate care post fragility fracture. A "type A" FLS is an all-encompassing high-intensity service that typically utilizes a dedicated FLS coordinator (i.e., fracture liaison coordinator) to identify, assess and manage bone health for patients with a low trauma fracture. These FLS coordinators work closely with the orthopedic surgeons to identify qualifying patients, perform BMD measurement using via dual-energy X-ray absorptiometry (DXA), undertake rigorous laboratory workup to rule out secondary causes of osteoporosis, and initiate osteoporosis treatment. A "type B" FLS model of care is similar to "type A" FLS in that FLS coordinator is responsible for identifying and evaluating patients with fragility fractures, but they do not initiate a specific treatment, rather they make treatment recommendations to the primary care provider, who becomes responsible for prescribing osteoporosis therapy and following up with the patient for bone health issues. A "type C" FLS is less comprehensive and offers patients admitted for fragility fractures education about osteoporosis, fragility fractures, and fall prevention strategies, while at the same time passively alerting their primary care provider about the occurrence of a fragility fracture. As a result, the onus is on the primary care provider to coordinate osteoporosis diagnostic evaluation and initiate appropriate treatment. Finally, the "type D" FLS model is the least comprehensive type of FLS, as it only provides patient education about osteoporosis and relies on patients and caregivers to report fragility fractures to a patient's primary care provider for further management recommendations. Thus, "type D" FLS places fracture care coordination responsibility upon the patient and/or their caregivers. In practice, there is a wide variability in the FLS models utilized, depending on feasibility of implementing a specific FLS model of care in the context of local resource allocation and specific healthcare system organization [16]. The purpose of this narrative review is to summarize the findings of recent studies of FLS implementation effectiveness as a key system approach to secondary fracture prevention. We divided the findings of our review by outcomes of interest including rates of new diagnosis of osteoporosis, secondary fragility fracture, mortality, osteoporosis treatment, BMD testing, subsequent fall(s), referral to fall prevention clinic, quality of life, and cost of care. We aimed to understand which types of FLS were most successful, with the goal to inform the design and deployment of future FLS programs.

Methods

We conducted a literature search in PubMed using the search terms "fracture liaison service" OR "secondary fracture prevention" AND "outcomes" to identify studies that evaluated the effectiveness for any type of FLS for specific outcomes of interest. We included the following outcomes: new diagnosis of osteoporosis, secondary fragility fracture, mortality, osteoporosis treatment, BMD testing, subsequent fall(s), referral to fall prevention clinic, quality of life, and program cost. Because our review was focused on recently published manuscripts, we restricted our search to the last 5 years (January 2016–December 2020). We also performed a manual search through references of recent review articles to include any other relevant studies.

Discussion

Our literature search resulted in 11 studies published between January 2016 and December 2020 that examined outcomes of interest for different types of FLS. In Table 1, we summarize the findings of our literature search by type of outcomes of FLS reported in the included studies.

New diagnosis of osteoporosis

Timely identification of osteoporosis in people who have a fragility fracture is critical to initiating appropriate osteoporosis treatment. One way to rapidly identify individuals who sustain fragility fractures is to use electronic medical record alerts. For example, a type A FLS implemented at a US urban academic medical center used such an electronic alert to detect patients who sustained fractures and who were admitted or discharged from the emergency department with planned outpatient follow-up in orthopedics or neurological surgery clinics. This electronic alert triggered an automatic endocrinology consultation. Of the 226 patients referred due to a new fragility fracture or for having "soft bone" during surgical intervention, the authors found that 73.1% had

Table 1. Fracture liaison service approaches to improve fragility fracture outcomes

Reference	Study design	Country	Population	Intervention (FLS type)	Outcome/timing of assessment	Sample size intervention/control	Results
Diagnosis of osteoporosis							
Gupta et al. [21]	Cross-sectional	USA	Adults ≥ 50 years with any fracture **OR** "soft bones" at surgery	Type A	New diagnosis of osteoporosis	$N = 226$	73.1%
Secondary Fracture							
Singh et al. [22•]	Controlled before and after	Canada	Adults ≥ 50 years with MOF (hip, humerus, wrist, spine, pelvis)	Type A	New fracture at 6 months	$N = 130$ (FLS) $N = 65$ (pre-FLS)	3.0% (FLS) vs 1.8% (pre-FLS), $p < 0.664$
Inderjeeth et al. [23]	Prospective cohort	Australia	Adults ≥ 50 years with MTF	Type A	New MTF over 12 months	$N = 241$ (FLS) $N = 55$ (non-FLS) $N = 105$ (pre-FLS)	97 (FLS) vs 200 (non-FLS) vs 203 (pre-FLS) per 1000 PY Age- and sex-adjusted OR = 0.40 (95% CI 0.16, 1.01) vs non-FLS Age- and sex-adjusted OR = 0.38 (95% CI 0.18, 0.79) vs pre-FLS
Axelsson et al. [25•]	Retrospective cohort	Sweden	Adults ≥ 50 years with MOF (hip, humerus,	Type B using medical secretaries	New MOF over 2.2 years median follow up	$N = 13,946$ (FLS) $N = 7,137$ (pre-FLS)	33.7 (FLS) vs 35.8 (pre-FLS) per 1000 PY Adjusted HR = 0.82, 95% CI

Table 1. (Continued)

Reference	Study design	Country	Population	Intervention (FLS type)	Outcome/timing of assessment	Sample size intervention/control	Results
			wrist, spine, pelvis)				0.73–0.92, $p=$ 0.001
Sietsema et al. [27••]	Retrospective cohort	USA	Medicare enrollees with vertebral, hip, pelvic, femoral,	nonvertebral fracture	Type A	Fracture claim at any site $>$90 days after the index fracture	$N=1{,}304$ (FLS) $N=1{,}304$ (non-FLS)
300 (FLS) vs 381 (non-FLS) per 1000 PY HR=0.8, 95% CI 0.7–0.9							
Nakayama et al. [26]	Retrospective cohort	Australia	Adults≥ 50 years with an MTF	Type A	New MTF over 3 years New MOF (hip, spine, femur, pelvis or humerus) over 3 years	$N=515$ (FLS) $N=416$ (non-FLS)	MTF: 11% (FLS) vs 16% (non FLS), HR 0.67, CI 0.47–0.95, $p=0.025$ MOF: 6% (FLS) vs 10.5% (non-FLS), HR 0.59, CI 0.39–0.90, $p=$ 0.013
Axelsson et al. [24]	Retrospective cohort	Sweden	Adults≥ 50 years with a MOF (hip, spine, shoulder, wrist, pelvis)	Type B using medical secretaries	Re-fracture rate over ~1-year mean follow-up	$N=2{,}713$ (FLS) $N=2{,}616$ (pre-FLS)	8.3% (FLS) vs. 8.4% (pre-FLS), $p=$ 0.85 Adjusted time-dependent Cox analysis: HR 0.95, 95% CI 0.79–1.14, $p=$ 0.60

Table 1. (Continued)

Reference	Study design	Country	Population	Intervention (FLS type)	Outcome/timing of assessment	Sample size intervention/control	Results
Hawley et al. [28•]	Retrospective cohort	UK	Adults ≥ 60 years with hip fractures	Varied by site, not specified	New hip fracture 2 years after first fracture	N=33,152	4.2% new hip fractures
Mortality							
Suarez et al. [30]	Prospective cohort	Colombia	Adults ≥ 65 years with hip fracture	Type A	1-year mortality	N=298 (FLS)	19.9% (years 1–2) vs 10.9% (years 3–4), p =0.038 Adjusted HR= 0.54, 95% CI 0.29–0.99, p= 0.049
Axelsson et al. [25•]	Retrospective cohort	Sweden	Adults ≥ 50 years with MOF	Type B using medical secretaries	Mortality over 2.2-year follow-up	N=13,946 (FLS) N=7,137 (pre-FLS)	94.4 (FLS) vs 91 (pre-FLS) per 1000 PY HR=0.94, 95% CI 0.88–1.01, p= 0.11
Sietsema et al. [27••]	Retrospective cohort	USA	Medicare enrollees with vertebral, hip, pelvic, femoral,	nonvertebral fracture	Type A	Mortality over~2-year follow-up	N=1,304 (FLS) N=1,304 (non-FLS)
117 (FLS) vs 129 (non-FLS) per 1000 PY HR=0.9, 95% CI 0.8–1.1							
Axelsson et al. [24]	Retrospective cohort	Sweden	Adults ≥ 50 years with a MOF (hip, spine,	Type B using medical secretaries	Mortality over~ 1-year follow-up	N=2,713 (FLS) N=2,616 (pre-FLS)	12.2% (FLS) vs. 13.3% (pre-FLS), p= 0.24

Table 1. (Continued)

Reference	Study design	Country	Population	Intervention (FLS type)	Outcome/timing of assessment	Sample size intervention/control	Results
			shoulder, wrist, pelvis)				Adjusted time-dependent Cox analysis: HR 0.88, 95% CI 0.76–1.03, $p=0.11$
Hawley et al. [28•]	Retrospective cohort	UK	Adults ≥ 60 years with hip fractures at 11 sites	Various not specified	30-day and 1-year mortality	$N=33{,}152$	30-day HR = 0.80, 95% CI 0.71–0.91 (FLS) 30-day HR = 0.73, 95% CI 0.65–0.82 (orthogeriatrics) 1-year HR = 0.84, 95% CI 0.77–0.93 (FLS) 1-year HR = 0.81, 95% CI 0.75–0.87 (orthogeriatrics)
Nakayama et al. [26]	Retrospective cohort	Australia	Adults ≥ 50 years with an MTF	Type A	Mortality over 3 years	$N=515$ (FLS) $N=416$ (non-FLS)	Adjusted HR = 1.17, $p=0.23$
Osteoporosis treatment							
Majumdar et al. [32••]	Randomized controlled trial	Canada	Adults ≥ 50 years with upper extremity fracture (wrist, proximal humerus)	Type A, type C	Bisphosphonate initiation at 6 months	$N=180$ (type A FLS) $N=181$ (type C FLS)	48% (type A FLS) vs 28% (type C FLS), $p<0.0001$
Naranjo et al. [31]	Prospective cohort	Spain	Adults > 65 years with a hip fracture	Type A	Bisphosphonate, denosumab, or teriparatide initiation at discharge and at 6 months	$N=80$ (FLS) $N=105$ (non-FLS)	At discharge: 91% (FLS) vs 8% (non-FLS), $p<0.001$ 6 months: 75% (FLS) vs 15%

Table 1. (Continued)

Reference	Study design	Country	Population	Intervention (FLS type)	Outcome/timing of assessment	Sample size intervention/control	Results
							(non-FLS), $p < 0.001$
Axelsson et al. [25•]	Retrospective cohort	Sweden	Adults ≥ 50 years with MOF (hip, spine, shoulder, wrist, pelvis)	Type B using medical secretaries	Osteoporosis treatment rate within 12 months	$N = 13,946$ (FLS) $N = 7,137$ (pre-FLS)	199.6 (FLS) vs 72.8 (pre-FLS) per 1000 person-year Adjusted HR = 1.62, 95% CI 1.51–1.75, $p < 0.001$
Sietsema et al. [27••]	Retrospective cohort	USA	Medicare enrollees with vertebral, hip, pelvic, femoral,	nonvertebral fracture	Type A	Osteoporosis medication fill rate	$N = 1,304$ (FLS) $N = 1,304$ (non-FLS)
159 (FLS) vs 90 (non-FLS) per 1000 PY HR = 1.7, 95% CI 1.4–2.0							
Axelsson et al. [24]	Retrospective cohort	Sweden	Adults ≥ 50 years with a MOF (hip, spine, shoulder, wrist, pelvis)	Type B using medical secretaries	Osteoporosis treatment rate over ~ 1-year follow-up	$N = 2,713$ (FLS) $N = 2,616$ (pre-FLS)	31.8% (FLS) vs. 12.6% (pre-FLS), $p < 0.001$ Age- and sex-adjusted time-dependent Cox regression: HR = 2.6, 95% CI 2.5–3.2, $p < 0.001$
Bone mineral density (BMD) testing							
		Canada	Adults ≥ 50 years	Type A, type C	BMD testing at 6 months	$N = 180$ (type A FLS) $N = 181$ (type C FLS)	73% (type A FLS) vs 62%

Table 1. (Continued)

Reference	Study design	Country	Population	Intervention (FLS type)	Outcome/timing of assessment	Sample size intervention/control	Results
Majumdar et al. [32••]	Randomized controlled trial		with upper extremity fracture (wrist, proximal humerus)				(type C FLS), $p = 0.03$
Singh et al. [22•]	Controlled before and after	Canada	Adults ≥ 50 years with a MOF (hip, pelvis, vertebra, wrist or humerus)	Type A	BMD testing at 6 months	$N=130$ (FLS) $N=65$ (pre-FLS)	53.0% (FLS) vs 23.6% (pre-FLS), $p<$ 0.001
Sietsema et al. [27••]	Retrospective cohort	USA	Medicare enrollees with vertebral, hip, pelvic, femoral,	nonvertebral fracture	Type A	BMD testing at 2 years	$N=1,304$ (FLS) $N=1,304$ (non-FLS)
562 (FLS) vs 110 (non-FLS) per 1000 PY HR=4.3, 95% CI 3.7–5.0							
Axelsson et al. [24]	Retrospective cohort	Sweden	Adults ≥ 50 years with a MOF (hip, spine, shoulder, wrist, pelvis)	Type B using medical secretaries	BMD testing over~ 1-year follow-up	$N=2,713$ (FLS) $N=2,616$ (pre-FLS)	39.6% (FLS) vs. 7.6% (pre-FLS), $p<$ 0.001 Adjusted time-dependent Cox analysis: HR= 7.1, 95% CI 6.1–8.2, $p<0.001$
Subsequent falls							

Table 1. (Continued)

Reference	Study design	Country	Population	Intervention (FLS type)	Outcome/timing of assessment	Sample size intervention/control	Results
Singh et al. [22•]	Controlled before and after	Canada	Adults ≥ 50 years with MOF (hip, pelvis, vertebra, wrist or humerus)	Type A	New fall at 6 months	N = 130 (FLS) N = 65 (pre-FLS)	13.9% (FLS) vs 23.6% (pre-FLS), p = 0.123
Inderjeeth et al. [23]	Prospective cohort	Australia	Adults ≥ 50 years with MTF	Type A	New fall over 12 months	N = 241 (FLS) N = 55 (non-FLS) N = 105 (pre-FLS)	26.1 (FLS) vs 278 (non-FLS) vs 40 (pre-FLS) per 100 persons RR = 0.09, 95% CI 0.06–0.15 vs non-FLS RR = 0.53, 95% CI 0.33–0.86 vs pre-FLS
Axelsson et al. [25•]	Retrospective cohort	Sweden	Adults ≥ 50 years with MOF (hip, spine, shoulder, wrist, pelvis)	Type B using medical secretaries	Non-skeletal fall injury over 2.2-year median follow-up	N = 13,946 (FLS) N = 7,137 (pre-FLS)	56.6 (FLS) vs 47.4 (pre-FLS) per 1000 PY Adjusted HR = 1.02, 95% CI 0.93–1.13, p = 0.69
Referral to fall prevention clinic							
Singh et al. [22•]	Controlled before and after	Canada	Adults ≥ 50 years with MOF (hip, pelvis, vertebra, wrist or humerus)	Type A	Referral to fall prevention clinic at 6 months	N = 130 (FLS) N = 65 (pre-FLS)	4.0% (FLS) vs. 0.0% (usual care), p = 0.133
Quality of life							

Table 1. (Continued)

Reference	Study design	Country	Population	Intervention (FLS type)	Outcome/timing of assessment	Sample size intervention/control	Results
Singh et al. [22•]	Controlled before and after	Canada	Adults ≥ 50 years with MOF (hip, pelvis, vertebra, wrist or humerus)	Type A	Change in EQ-5D-5L index between baseline and 6 months	*N*=130 (FLS) *N*=65 (pre-FLS)	Mean difference FLS vs pre-FLS was 0.09, 95% CI 0.22–0.16, $p=0.01$
Inderjeeth et al. [23]	Prospective cohort	Australia	Adults ≥ 50 years with MTF	Type A	3 to 12 months change in EQ-5D Health State VAS 3 to 12 months change in EQ-5D UK index score	*N*=241 (FLS) *N*=55 (non-FLS) *N*=105 (pre-FLS)	+29% (FLS) vs −2% (non-FLS) vs +1% (pre-FLS), $p<0.001$ +15% (FLS) vs −11% (non-FLS) vs −16% (pre-FLS), $p<0.001$
Cost of care							
Majumdar et al. [32••]	Randomized controlled trial	Canada	Adults ≥ 50 with upper extremity fracture (wrist, proximal humerus)	Type A, type C	Direct cost per patient	*N*=180 (type A FLS) *N*=181 (type C FLS)	$66 CDN (type A FLS) vs $18 CDN (type C FLS), $p<0.0001$
Sietsema et al. [27••]	Retrospective cohort	USA	Medicare enrollees with vertebral, hip, pelvic, femoral,	nonvertebral fracture	Type A	Total cost to healthcare system at 12 months	*N*=1,304 (FLS) *N*=1,304 (non-FLS)
$25,306 (FLS) vs $22,896 (non-FLS), $p=0.082$							

CI, confidence interval; *FLS*, fracture liaison service; *HR*, hazard ratio; *MOF*, major osteoporotic fracture (hip, clinical spine, humerus/shoulder, radius, and pelvis); *MTF*, minimal trauma fracture; *PY*, person-year; *RR*, relative ratio undiagnosed osteoporosis [21]. While this was a small study and a single academic medical center and thus with limited generalizability, it is notable that this FLS program used an automated alert to identify those with fractures, which minimizes the burden placed on clinical staff and limits the cost of the program.

Rates of secondary (subsequent) fractures

The rate of new fractures after an initial fragility fracture is perhaps the most critical outcome to demonstrate the value of any FLS program. We identified six studies that reported on this outcome, including one quasi-experimental controlled before and after study [22•] and five observational studies: one prospective [23] and five retrospective cohort studies [24, 25•, 26, 27••, 28•]. Most studies included participants with major osteoporotic fractures and comparator populations. The majority of the observational studies demonstrated that FLS implementation was associated with lower re-fracture rates compared to either historical controls from the same hospital prior to the start of FLS [23, 25•] or contemporary controls from hospital(s) which did not have an FLS program [23, 26, 27••]. The magnitude of risk reduction in future fracture was variable depending on the type of fracture considered (e.g., any fragility fracture vs. major osteoporotic fracture [MOF]), and other variables included in the model (e.g., age, comorbidities, fragility fracture type, use of pharmacologic or non-pharmacologic treatment, inclusion of time varying covariates). For example, a retrospective study from Australia found a ~30% reduction in the rate of any minimal trauma fracture and a ~40% reduction in the rate of major osteoporotic fractures involving hip, pelvis, humerus, and spine among those enrolled at a hospital with a type A FLS compared to those that received care at the non-FLS hospital [26]. In this study, the number needed to treat to prevent one new minimal trauma fracture over a 3-year period was 20 [26]. In US study that used 100% Medicare data set for Michigan residents, participants who had osteoporosis management by a private orthopedic practice had ~20% lower risk of subsequent fracture and a longer median time to subsequent fracture [27••]. A controlled before and after interventional study conducted in Canada among adults 50 years of age and older with major osteoporotic fractures (e.g., hip, humerus, wrist, spine, pelvis) found no statistically significant differences in proportion of participants who sustained a new fracture during the 6-month FLS period compared to the pre-FLS period. However, this study was of short duration and was not adequately powered for this outcome [22•].

The sample size and duration of follow-up after an initial fragility fracture influences the ability to discern fracture risk reduction among persons who receive post-fracture care via an FLS model of care. An initial analysis from a register-based cohort study from Sweden did not find significant differences in the rates of new fractures after ~1-year mean follow-up [24], but the rate of new MOF was lower among patients who were cared for at hospitals with a type B FLS compared to historical controls [25•]. One large retrospective study included data from over 33,000 participants with hip fractures enrolled at 11 clinical sites across the UK who received post-fracture care either through an FLS program or through an established orthogeriatrics service [28•]. In this study, 4.2% of participants were hospitalized for a second hip fracture within the first 2 years after the index hip fracture [28•]. This study did not have a comparator group and because this study considered only new hip fracture events for which participants were hospitalized at the clinical sites, the cumulative incidence of new hip fracture may have been underestimated.

Most studies evaluating the impact of FLS on secondary fracture prevention have important limitations. These include observational study design, reliance on hospital sources of data which may have missed fracture events if a patient had second fracture but did not present at the same hospital for care, variable collection of and adjustment for risk factors (e.g., age, sex, comorbid conditions, baseline osteoporotic treatment, vitamin D status), differences in the type of fractures studied, comparator groups, and duration of follow-up.

Mortality

Osteoporotic fractures, particularly hip fractures, have substantial impact on patient risk of death, with approximately 30% of individuals who sustain a hip fracture dying by the following year [29]. The impact of FLS on mortality is difficult to study because of the need for large sample sizes and the necessity of collecting long-term follow-up data. We found one prospective cohort [30] and five retrospective cohort [24, 25•, 26, 27••, 28•] studies that evaluated mortality rates among patients with various types of fragility fractures. Suarez et al. found that 1-year mortality rate among adults 65 years of age and older with a hip fracture decreased from ~20 to 11% 4 years after implementation of a type A FLS program at an academic medical center in Colombia [30]. However, this study had a small sample size and did not have a comparator group, and while stratification by age and year of hospital admission was performed, analyses were not adjusted for other risk factors of mortality [30]. Two studies conducted in Sweden found that among adults ≥ 50 years with a MOF, FLS implementation was not significantly associated with decreasing mortality [24, 25•] after ~1 or ~2 years, as did a study using US Medicare claims data and which followed patients for ~2 years [27••] and a study from Australia with a 3-year follow-up period [26]. In contrast, a large, multi-center retrospective study examined risk of death among over 33,000 patients who sustained their first hip fracture and who were treated at eleven hospitals in the UK, which had implemented various types of secondary fracture prevention programs [28•]. The age- and sex-adjusted 30-day mortality was 20% lower after the introduction of the FLS program, while at 1 year, the age- and sex-adjusted mortality was 16% lower highlighting that participation in an FLS model of care was associated with lower risk of death [28•]. While this study included a large sample size and was conducted at several sites, only patients with hip fractures were included, thus limiting its generalizability to patients with non-hip fragility fractures.

Osteoporosis treatment

Osteoporosis medication initiation and adherence are key indicators of efficacy of FLS programs. We found five recent studies [24, 25•, 27••, 31, 32••] that evaluated the impact of FLS implementation on the rates of osteoporosis treatment. A recent randomized controlled trial compared rates of bisphosphonate use among 361 patients with upper extremity fracture who were randomized to either a type C FLS or a type A FLS model of care [32••]. At 6 months, participants randomized to the type A FLS group had a 70% higher likelihood to be started on bisphosphonate treatment compared to those in the type C FLS group [32••]. As initiation of appropriate osteoporosis treatment is the single best modality to improve further fragility fractures, this trial stresses the role of a high-intensity FLS in improving fragility fracture outcomes. A prospective cohort study conducted in Spain found that at the time of hospital discharge, 91% of hip fracture patients at an FLS hospital were prescribed an osteoporosis medication compared to only 8% patients discharged from a hospital without a post-fracture care infrastructure in place [31]. Furthermore, at 6 months after discharge, the positive impact of the FLS on osteoporosis treatment persisted, with 75% of the patients discharged from the FLS hospital and only 15% of those receiving usual care using osteoporosis therapy [31]. These findings should be interpreted cautiously given the observational study design, its small sample size, and the sparse data collection of participant characteristics, factors that influence the study conclusions. A recent retrospective study using the 100% Medicare data set for Michigan residents found that patients who had type A FLS care post fracture had a 70% higher likelihood of filling osteoporosis medications compared to a propensity score matched group of patients who received usual care [27••]. These findings are in line with osteoporosis treatment rates during FLS periods observed in two studies conducted in Sweden among patients with major osteoporotic fractures [24, 25•]. After adjustment for important covariates, age- and sex-adjusted time-dependent Cox regression analysis found a 1.6- to 2.6-fold increased likelihood of being treated during the FLS period compared to the before FLS implementation [24, 25•]. Taken together, these results emphasize the positive effect of FLS programs on osteoporosis treatment, a necessary step for secondary fracture prevention.

BMD measurement

BMD testing is key for documenting the baseline BMD values at the time of an initial fragility fracture. We found four studies including a randomized controlled trial [32••], a controlled before and after quasi-experimental study [22•], and two retrospective studies [24, 27••] that reported on BMD testing for post-fragility fracture care. The randomized controlled trial found that compared to participants randomized to type C FLS, those assigned to a type A FLS were 17% more likely to have a BMD assessment using DXA [24]. The strengths of this study include the randomized controlled design, but the study population was limited to patients who sustained upper extremity fragility fractures and thus not generalizable to other types of fractures. Similar positive results were demonstrated in a small controlled before and after study [22•] and two large retrospective studies [24, 27••], one using a propensity score-matched comparator group [27••] and the other using historical controls participants [24]. Patients with any fragility fractures had over 4 times higher likelihood to have a BMD testing during when receiving care via an FLS compared to usual care [27••], while participants who sustained a major osteoporotic fracture had over sevenfold higher likelihood to have BMD evaluation during the FLS period versus the before the FLS was implemented [24]. Despite their limitations, as discussed above, these results highlight the role of FLS programs in increasing screening for osteoporosis using BMD testing.

Subsequent falls and referral to a fall prevention clinic

Since a fall is the principal causative mechanism for fragility fractures, and fall prevention is important for secondary fracture prevention, we found three studies that addressed subsequent fall occurrence as an outcome [22•, 23, 25•]. In a prospective study from Australia, among adults 50 years and older with minimal trauma fractures, a type A FLS was associated with lower risk for subsequent falls [23]. However, this study had a small sample size and baseline data on the clinical characteristics, risk factors, and medical history were not collected, which affect the interpretation of the study findings. In contrast, a controlled before and after interventional study conducted in Canada [22•] and a large retrospective cohort study from Sweden [25•] did not find associations between implementation of FLS programs and future falls, findings likely influenced by the short duration of follow-up in these studies. In addition, participants who received post fragility fracture care via an FLS type A were not more likely to be referred to a fall prevention clinic [22•].

Quality of life

Given the substantial morbidity of fragility fractures, two recent studies evaluated whether participation in an FLS program is associated with improved quality of life assessed using various EuroQoL-5D measures [22•, 23]. A small prospective study from Australia found that although the participants in the FLS program had the poorest quality of life at 3 months after a minimal trauma fracture compared to a concurrent or historical controls, they experienced the largest increase in quality of life between 3 and 12 months post fracture [23]. Similarly, an interventional study from Canada found that the quality of life improved between baseline and 6 months post fracture among patients receiving type A FLS care compared to a historical control group from the same institution [22•]. The small sample size and lack of randomization in these studies limit the inferences that can be drawn from these findings.

Cost of care

A major obstacle to implementing FLS in clinical practice has been the need for upfront investment in developing a functional FLS. Our review of the recent literature identified two studies that calculated cost of providing FLS care. In a randomized controlled trial of type A vs. type C FLS, the investigators calculated that the direct cost per participant treated by the FLS, which included only cost of staffing and did account for medication or other healthcare system costs [32••]. As expected, the cost per participant was higher for the type A FLS program compared to the less intensive type C FLS program. However, this study was conducted at a single academic medical center in Canada and, since the cost of the FLS program was estimated based on activity time reported by the research coordinator and local salary rates, the cost may be different in other regions in Canada or in other countries. In contrast, a large study that used Medicare claims data found that total cost to the healthcare system at 12 months was not significantly different between patients receiving osteoporosis management services post-fragility fracture and those receiving usual care [27••]. While this large study provides added data of cost of post-fracture care, a formal cost-effectiveness of the FLS program was not conducted.

Conclusion

Studies summarized in this review found that the patient-centric approach provided by FLS was associated with favorable outcomes, depending on the intensity of the FLS model of care used, but most were conducted outside of the USA, included highly variable duration of follow-up and comparators, and focused on heterogeneous patient populations. Most of the studies published in the last 5 years were observational and have important limitations given the study design and risk of bias. Our findings support the need for randomized controlled trials of FLS conducted in the USA to rigorously examine to what extent the implementation of FLS in the complex US healthcare system may improve outcomes of patients that sustain fragility fracture.

References and Recommended Reading

Papers of particular interest, published recently, have been highlighted as:
• Of importance
•• Of major importance

1. Lewiecki EM, et al. Healthcare policy changes in osteoporosis can improve outcomes and reduce costs in the United States. JBMR Plus. 2019;3(9):e10192.
2. Wright NC, et al. The recent prevalence of osteoporosis and low bone mass in the United States based on bone mineral density at the femoral neck or lumbar spine. Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research. 2014;29(11):2520–6.
3. Singer A, et al. Burden of illness for osteoporotic fractures compared with other serious diseases among postmenopausal women in the United States. Mayo Clin Proc. 2015;90(1):53–62.
4.•• Lewiecki EM, et al. Osteoporotic fracture trends in a population of US managed care enrollees from 2007 to 2017. Osteoporos Int. 2020;31(7):1299–304. (**A recent retrospective analysis from a research database that found that hip fracture rates are not declining, as they were from 2007 to 2013. For some fracture types, rates are rising and further contributing to the healthcare burden.**)
5. Leibson CL, et al. Mortality, disability, and nursing home use for persons with and without hip fracture: a population-based study. J Am Geriatr Soc. 2002;50(10):1644–50.
6. Tajeu GS, et al. Death, debility, and destitution following hip fracture. J Gerontol A Biol Sci Med Sci. 2014;69(3):346–53.
7. Hansen, D., et al. *Medicare cost of osteoporotic fractures*. 2019; Available from: https://www.bonehealthpolicyinstitute.org/s/Medicare-Cost-of-Osteoporotic-Fractures-20190827-hpry.pdf.
8. Mugnier B, et al. Clinical effectiveness of osteoporosis treatment in older patients: a fracture liaison service-based prospective study. J Women Aging. 2019;31(6):553–65.
9. Compston JE, McClung MR, Leslie WD. Osteoporosis. The Lancet. 2019;393(10169):364–76.
10. Skjødt MK, et al. Secular trends in the initiation of therapy in secondary fracture prevention in Europe: a multi-national cohort study including data from Denmark, Catalonia, and the United Kingdom. Osteoporos Int. 2020;31(8):1535–44.
11. Klop C, et al. Anti-osteoporosis drug prescribing after hip fracture in the UK: 2000–2010. Osteoporos Int. 2015;26(7):1919–28.
12. Balasubramanian A, et al. Risk of subsequent fracture after prior fracture among older women. Osteoporos Int. 2019;30(1):79–92.
13. Elliot-Gibson V, et al. Practice patterns in the diagnosis and treatment of osteoporosis after a fragility fracture: a systematic review. Osteoporos Int. 2004;15(10):767–78.
14. Giangregorio L, et al. Fragility fractures and the osteoporosis care gap: an international phenomenon. Semin Arthritis Rheum. 2006;35(5):293–305.
15. Noordin S, Allana S, Masri BA. Establishing a hospital based fracture liaison service to prevent secondary insufficiency fractures. Int J Surg. 2018;54(Pt B):328–32.
16. Ganda K, et al. Models of care for the secondary prevention of osteoporotic fractures: a systematic review

and meta-analysis. Osteoporos Int. 2013;24(2):393–406.

17. Akesson K, et al. Capture the fracture: a Best Practice Framework and global campaign to break the fragility fracture cycle. Osteoporos Int. 2013;24(8):2135–52.
18. Walters S, et al. Fracture liaison services: improving outcomes for patients with osteoporosis. Clin Interv Aging. 2017;12:117–27.
19. Bunta AD, et al. Own the bone a system-based intervention improves osteoporosis care after fragility fractures. J Bone Joint Surg Am. 2016;98(24):e109.
20. Barton DW, et al. The clinical impact of fracture liaison services: a systematic review. Geriatric Orthopaedic Surgery & Rehabilitation. 2021;12:2151459320979978.
21. Gupta MJ, et al. Rush fracture liaison service for capturing "missed opportunities" to treat osteoporosis in patients with fragility fractures. Osteoporos Int. 2018;29(8):1861–74.
22.• Singh S, et al. Breaking the cycle of recurrent fracture: implementing the first fracture liaison service (FLS) in British Columbia, Canada. Arch Osteoporos. 2019;14(1):116. (**In this small controlled before and after study conducted in Canada, implementation of a high-intensity FLS was associated with improved bone mineral density testing at 6 months.**)
23. Inderjeeth CA, et al. Implementation of the Western Australian Osteoporosis Model of Care: a fracture liaison service utilising emergency department information systems to identify patients with fragility fracture to improve current practice and reduce re-fracture rates: a 12-month analysis. Osteoporos Int. 2018;29(8):1759–70.
24. Axelsson KF, et al. Effectiveness of a minimal resource fracture liaison service. Osteoporos Int. 2016;27(11):3165–75.
25.• Axelsson KF, et al. Association between recurrent fracture risk and implementation of fracture liaison services in four Swedish hospitals: a cohort study. J Bone Miner Res. 2020;35(7):1216–23. (**A large retrospective study conducted in Sweden that found that implementation of a high-intensity FLS using medical secretaries was associated with lower recurrent fracture risk and higher osteoporosis treatment rates.**)
26. Nakayama A, et al. Evidence of effectiveness of a fracture liaison service to reduce the re-fracture rate. Osteoporos Int. 2016;27(3):873–9.
27.•• Sietsema DL, et al. The effectiveness of a private orthopaedic practice-based osteoporosis management service to reduce the risk of subsequent fractures. J Bone Joint Surg Am. 2018;100(21):1819–28. (**In this retrospective study that included Medicare enrollees with vertebral, hip, pelvic, femoral, and nonvertebral fracture who were managed in a practice that used a high-intensity FLS, the authors found decreased risk of fractures claims as well as increased rates of osteoporosis medication use at 1 year and of bone mineral density measurement at 2 years.**)
28.• Hawley S, et al. Clinical effectiveness of orthogeriatric and fracture liaison service models of care for hip fracture patients: population-based longitudinal study. Age Ageing. 2016;45(2):236–42. (**A large multi-center retrospective study of patients with hip fractures found that implementation of an FLS program was associated with a lower risk of death. This study had a large sample size and was conducted at several sites.**)
29. Brauer CA, et al. Incidence and mortality of hip fractures in the United States. JAMA. 2009;302(14):1573–9.
30. Suarez S, et al. Impact on hip fracture mortality after the establishment of an orthogeriatric care program in a Colombian hospital. J Aging Health. 2017;29(3):474–88.
31. Naranjo A, et al. Preventing future fractures: effectiveness of an orthogeriatric fracture liaison service compared to an outpatient fracture liaison service and the standard management in patients with hip fracture. Arch Osteoporos. 2017;12(1):112.
32.•• Majumdar SR, et al. Comparing strategies targeting osteoporosis to prevent fractures after an upper extremity fracture (C-STOP trial): a randomized controlled trial. J Bone Miner Res. 2018;33(12):2114–21. (**The only randomized control trial conducted within the last 5 years. This trial underscores the importance of a high-intensity FLS program, as those participants randomized to a high-intensity FLS had a 70% higher likelihood to be started on a bisphosphonate than those randomized to a low-intensity FLS.**)

Publisher's note