Fracture Liaison Service

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Introduction

Osteoporosis is characterized by a reduction in bone mass and strength, predisposing patients to an increased risk of fragility fractures [1]. The condition is asymptomatic, and therefore its first clinical manifestation is often a low-trauma (fragility) fracture. Fragility fractures cause significant morbidity and mortality and therefore are a considerable public health burden (Fig. 14.1) [2]. The National Osteoporosis Foundation estimated that one in two women and one in five men will experience an osteoporotic-related fracture during their lifetime [3]. Furthermore, a previous low-trauma fracture, at any site, increases the risk of a subsequent fracture by approximately twofold in women and men (Fig. 14.2) [4, 5].

Fracture liaison services (FLS) are considered the coordinator-based model of secondary fracture prevention services with a broad remit. FLS have been designed to identify patients who are at increased risk of secondary fractures, carry out comprehensive assessment, and ensure that the appropriate treatment is initiated through improved care coordination and communication [6–8]. Several organization bodies including the International Osteoporosis Foundation (IOF), the American Society for Bone and Mineral Research (ASBMR) [9], and European League Against Rheumatism(EULAR)/European Federation of National Associations of Orthopaedics and Traumatology (EFORT) have endorsed the provision of FLS services in standard practice for the prophylaxis of secondary bone fractures [10]. Meta-analysis studies confirmed the positive role of FLS and its impact on rates of BMD assessment as well as osteoporosis treatment initiation [11, 12].

However, it is acknowledged that treatment gaps remain [11] and pharmacological prevention remains suboptimal. In 2013, the International Osteoporosis Foundation (IOF) initiated the promotion of FLS programs, continually being implemented worldwide; however, so far, their outcomes show wide variability in the literature. This chapter will discuss the concept of fracture liaison service, its different models and components, and outcomes. It will expand to discuss the cost-effectiveness of fracture liaison services and its impact on bone mineral density testing, initiation, as well as adherence to therapy. It will conclude by presenting the best practice published by the International Osteoporosis Foundation for fracture liaison services.

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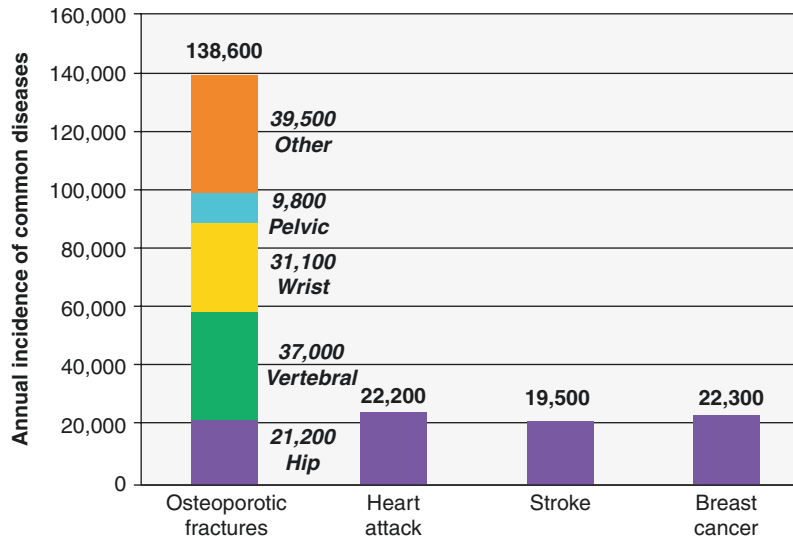

Fig. 14.1 Incidence of osteoporotic fracture, heart attack, stroke, and breast cancer in Canadian women. References for the figure: Leslie et al. [102], Burge et al. [103], Public Health Agency of Canada [104], Canadian Cancer Society/National Cancer Institute of Canada [105]

Fig. 14.2 Fracture Liaison service: approach to prevent secondary fractures

Fracture Liaison Service: The Concept

Given the global problems leading to and caused by osteoporosis, fracture liaison services came about to help diagnose and begin long-term management in these patients who sustain a fragility fracture as their initial presentation of osteoporosis. The World Health Organization (WHO) has identified fragility fracture as one which occurs due to forces equivalent to a fall from a standing height or less and are not attributed to high-energy traumas like motor vehicle accidents or

high velocity mechanism of injuries [13]. In a healthy individual, the result of such a fall may be bruised skin and a bruised ego. In patients with osteoporosis, such a fall may result in fractures [14]. The most common initial fracture in younger adults tends to be distal, e.g., distal forearm. In older adults, the most common fragility fractures occur at the hip, wrist, spine, humerus, or pelvis. Fracture liaison services seek to seamlessly transition these patients from surgical care of the fracture to long-term management of the disease in order to treat the disease process and prevent future fracture.

A fracture liaison service (FLS) systematically identifies, treats, and refers to appropriate services for all eligible patients aged 50 and older within a local population who have suffered fragility fractures, with the aim of reducing their risk of subsequent fractures.

An FLS is an essential component of a comprehensive and integrated approach to preventing falls and fractures among people over the age of 50 years. Assessment within an FLS should be part of the pathway for all patients with a fragility fracture. An FLS comprises a dedicated coordinator (often a nurse specialist) who works to preagreed protocols to case-find and then assess patients who have had a fracture. The service may be based in hospital or in the community and requires support from a medically qualified practitioner (typically a hospital doctor or GP with special expertise in bone health and fragility fracture prevention).

Fracture Liaison Service Models

Fracture liaison services (FLSs) are effective models for prevention of osteoporotic fractures. Marsh et al. [15] described 12 different models that have been described in scientific literature to deliver secondary fracture prevention. These ranged from programs aimed at increasing awareness of osteoporosis through to intensive programs that identify, investigate, and initiate treatment (Fig. 14.3). Some programs are completely delivered within the FLS model, and some involve the general practitioner (GP) in

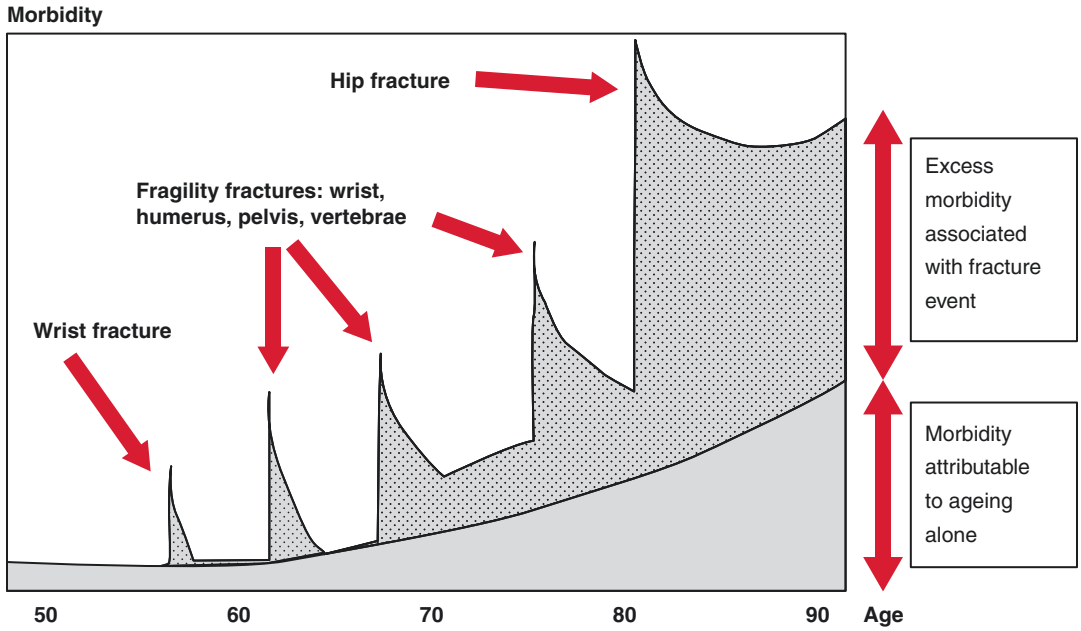

Fig. 14.3 Osteoporosis and fragility fractures throughout the life course. Capture the fracture; each and every fracture was a missed opportunity to diagnose and treat osteoporosis to prevent the subsequent fractures. (Quoted from: British Orthopaedic Association, British Geriatrics Society. The care of patients with fragility fracture 2007. https://www.bgs.org.uk/sites/default/files/content/attachment/2018-05-02/Blue%20Book%20on%20fragility%20fracture%20care.pdf)

primary care. Ganda et al. [16] conducted a similar review and grouped all published programs in scientific literature into four "types" of FLS models, referring to them as types A to D.

- Type A: defined as a service that identifies, investigates, and initiates treatment.
- Type B: services identify and investigate patients but then refer back to the primary care physician for treatment initiation.
- Type C: services identify patients at risk and inform them and their primary care physician. However, they do not undertake any assessment or treatment of the patients.
- Type D: services identify at-risk patients and inform and educate them but take no further part in communicating their findings to other stakeholders in the patient's care.

In the era of artificial intelligence (AI), recent FLS models have been established by smart healthcare systems which can assist clinicians and case managers to identify, investigate, and initiate treatments and improve adherence efficiently. The role of AI will become increasingly important assisted by an efficiently working intelligent healthcare information system. The AI system can automatically analyze reports of X-ray and DXA examinations and identify patients with hip fractures and vertebral compression fractures, osteoporosis, low bone mass, as well as high fracture risk. Moreover, the system's data analysis can not only reduce the rate of missed patients but can also reach a 93.6% rate of 1-year medication adherence [17]. Therefore, the smart healthcare case management system can be a novel model to achieve better outcomes in the fragility fracture prevention program of FLSs. Table 14.1 shows the most common FLS models.

Components of Fracture Liaison Service

FLSs include mainly evaluation of all people aged 50 years or older who have sustained a new fracture or radiological fragility fracture at any skeletal site, though exceptions are justified for fractures of skull, facial, digit, and scaphoid bones that are typically caused by a traumatic injury. A pragmatic approach to the definition of a fragility fracture which is vital to initiate the process with exclusions might only be made in the case of a road traffic collision (or other clearly significant trauma) or where a fall has clearly been from above standing height. Table 14.2 shows a summary of the main components of the fracture liaison service, which include:

Identify

The FLS identifies people aged 50 years or older who sustain a new fragility fracture. This includes:

- Newly identified vertebral fracture.
- Newly identified low trauma fracture.
- A new fracture occurring while a patient is taking an osteoporosis drug therapy.

Identifying people aged 50 years or older with a new clinical fracture is in the core of the FLS process and is a main responsibility of the service. Ideally, this is carried out by an "FLS coordinator" who is a dedicated nurse specialist, although this role may also be undertaken by allied health professionals (AHPs) or nonclinical personnel. Identification of new clinical fracture presentations is achieved according to the approach the patient has been handled by the hospital:

Table 14.1 Examples of fracture liaison service models

3 "I"	4 "I"	5 "I"Q	5 "I"
Identify	Identify	Identify	Identify
Investigate	Investigate	Investigate	Investigate
Initiate	Inform	Inform	Initiate
	Initiate	Initiate	Improving adherence
		Integrate	Intelligence (Artificial intelligence)
		+ Quality	

Table 14.2 Main components of the fracture liaison service

Component		Description
1	Identify	People aged 50 years and over with a fragility fracture are systematically identified
2	Investigate	Investigations to assess risk of fragility fractures and falls and possible underlying secondary causes for osteoporosis are offered to people identified by the FLS
3	Inform	Information and support are offered to people (and where relevant their carers) using the FLS
4	Intervene (initiate)	Interventions to reduce the risk of fragility fractures are offered to people as required
5	Integrate	The FLS will integrate with the wider healthcare system to facilitate an inclusive patient pathway, ensuring effective case-finding, onward referrals, and long-term management of osteoporosis
6	Improving adherence	Improving patients' adherence to therapy and adopt a system to monitor the patient's response to management and adherence to therapy as well as to remind physicians and case managers about non-adherent patients
7	Intelligence	Implementing artificial intelligence takes the FLS into the smart healthcare era. The AI system can analyze reports of X-ray and DXA examinations and identify patients with hip fractures and vertebral compression fractures, osteoporosis, and low bone mass. It can also help professionals to provide adequate control on pharmaceutical treatment to the patients
Q	Quality	The FLS demonstrates clinical accountability, ongoing quality improvement, effective governance, and funded access to continuing professional development

Inpatient Fractures

People who need to stay in hospital after their fracture are not only at highest future fracture risk [18, 19] but also are among the most straightforward to identify. Identification of this group can be carried out either through orthogeriatric inpatients service, setting up a notification system with orthopaedics team, trauma nurse, or using IT/informatics systems. Coordination with the local orthopedics and trauma teams is essential in order to agree roles and responsibilities for identifying people aged 50 or older who have had a fragility fracture and to grant the FLS staff access to the patients under the care of Orthopaedic or Accident and Emergency Departments. Similarly, falls which occur during hospital admission that result in a fracture should be also assessed by the FLS. These can be identified via DATIX (or similar incident reporting systems), seen in fracture clinic or transferred to orthopedics.

Outpatient Fractures

People who are managed in outpatient fractures clinics could be considered as easier identifiable cohort. These can be recognized by reviewing accident and emergency department lists, screening fracture clinic notes, leaving questionnaires with the receptionists to be handed over to the patients to complete while attending the clinics, reviewing primary care records, and linking with virtual fracture clinics.

Silent Vertebral Fractures

Vertebral fractures are among the most common osteoporosis-associated fractures and very important in predicting future osteoporotic fractures. Unfortunately, they are often missed, and studies reveal that they account for less than 5% of clinical fracture presentations to FLS [20]. Best approaches to identify this cohort is through liaising with radiology to agree a notification system highlighting any vertebral fractures identified in X-rays which can be incidental findings on plain X-rays, CT, and MRI scans images, also to carry out vertebral fracture assessment (VFA) [20, 21]. Liaising with physiotherapy-led musculoskeletal back pain services or other interface might also be helpful to identify any case lost from the record.

Organization bodies recommend that radiologists should (1) review the spine in all images of the chest, abdomen, and pelvis; (2) report

vertebral fractures clearly using the term "vertebral fracture"; and (3) recommend further assessment and management to reduce fracture risk. This would help using electronic software that are able to search or the word "fracture" or "vertebral fracture" and generate an automatic electronic letter to the FLS.

Referrals

Referrals to the FLS from other services, such as GPs, pain clinics, interface services, and falls services, should also be encouraged. Referral pathways should be set up to ensure all the patients receive appropriate bone healthcare provided by the FLS.

Out of the Hospital FLS Setup

An out-of-hospital FLS requires another setup that relies mainly on reporting from fracture clinic accident and emergency department as well as radiology departments. This mandates close liaison with local secondary care center(s) to enable seamless, continuous capture of all relevant cases. Similar approach should be followed regarding in-patients where coordination with orthopedic department, orthogeriatrics, as well as radiology department should be implemented to identify patients who may get admitted with fractures or sustain a fracture during their hospital admission.

It is, however, improbable that any single approach will identify all patients with a new fracture and the FLS coordinator will customize screening methods as per local systems. Therefore, it is recommended that multiple strategies are used for identification to maximize the yield.

Investigate

A comprehensive multifactorial assessment should be carried out targeting the group of people who need it. Prompt assessment and intervention is highly required as the risk of having a subsequent fracture is high particularly in the first year following an index fracture. Therefore, investigations should start as soon as feasible after the fracture so that interventions are not delayed. These include:

Fracture Risk Assessment

There are several fracture risk assessment tools. The commonest in use is FRAX which is endorsed by the International Osteoporosis Foundation and National Osteoporosis Foundation. Q-fracture has been recommended for use mainly in the UK. Guidelines and treatment recommendations regarding how to implement FRAX or Q-fracture in fracture risk assessment should be followed to develop local protocols. However, users need to be aware of key limitations of these risk tools to understand how to handle the calculated fracture risk scores. These limitations include differences in one fracture risk by differences in fracture site, number of fractures and recency of fracture, as well as prevalence of other medical conditions such as diabetes mellitus or drug therapies such as androgen deprivation therapy.

DXA Scans

BMD measurement is an important part of clinical decision-making. It quantifies 16 the severity of osteoporosis, serves as a means to quantify fracture risk, is an important part of clinical as well as therapeutic decision-making, and also establishes a baseline for future evaluation of treatment performance. Therefore, it is recommended to have a BMD measurement before commencing osteoporosis drug therapy wherever feasible.

Vertebral Fracture Assessment (VFA)

In addition to BMD measurement, DXA can be used to assess for prevalent vertebral fractures. Quick and cheap to perform and with minimal additional X-ray exposure, VFA not only precludes the substantially higher cost and radiation exposure of conventional plain spine radiology but

also can reliably identify the presence of vertebral fractures and semi-quantitatively assess the degree of the vertebral fracture. Guidelines produced by the International Society for Clinical Densitometry [20] can be used to develop local protocols.

Trabecular Bone Score (TBS)

The trabecular bone score is a measure of bone texture correlated with bone microarchitecture and a marker for the risk of osteoporosis. Introduced in 2008 [22], its main projected use is alongside measures of bone density in better predicting fracture risk in people with metabolic bone problems. The trabecular bone score is a textural parameter that can be applied to DEXA, which quantifies the local variations in gray level. TBS is derived from the evaluation of the experimental variogram, obtained from the grayscale DEXA.

It was reported that TBS is a reflection of the structural condition of the bone microarchitecture. TBS is strongly correlated with the number of trabeculae and their connectivity and negatively with the space between trabeculae [23, 24]. That is to say that a high TBS value means that microarchitecture bone is dense, well connected with little spaces between trabeculae. Conversely, a low TBS value means that the microarchitecture of bone is incomplete and poorly connected with wide spaces between trabeculae [25]. FRAX scores can be adjusted for TBS. An algorithm derived from WHO FRAX calculation tool (available online https://www.sheffield.ac.uk/TBS/) has been developed to adjust: probability of fracture from clinical risk factors and BMD to account for TBS. The calculated probabilities of fracture have been shown to be more accurate when computed including TBS.

Falls Risk Assessment

All people aged 65 years and older checked be checked for whether they have fallen in the past year and about the frequency, context, and characteristics of their fall/s. Older people reporting a fall or considered at risk of falling should be observed for balance and gait deficits and considered for their ability to benefit from interventions to improve strength and balance. This may also be appropriate in people aged 50–64 seen by the FLS who have risk factors for falls. FLS coordinators will need adequate training and expertise in these initial assessment techniques.

An FLS will engage closely with local falls services, to determine access to appropriate pathways to ensure early falls risk assessment and intervention post-fracture. Several tools to assess for falls risk are available which can be implemented in standard practice [26–30]. While the responsibility for any subsequent multifactorial falls assessment and targeted intervention will lie primarily with local falls services, measures to protect the patients from sustaining another fracture should be tackled by the FLS team. Therefore, there must be clear and timely linkage to the necessary intervention pathways.

Other Investigations

Patients believed to be at increased risk of fracture should be also medically assessed for:

(a) Osteosarcopenia as this makes the subject prone to falling over and sustain low-trauma fractures.
(b) Underlying secondary causes of osteoporosis/high fracture risk including exclusion of diseases that can present with osteoporosis and vertebral fracture (such as multiple myeloma or malignancies/metastasis).

Laboratory tests should be carried out to guide treatment selection and ensure treatment safety. Blood tests for bone profile and kidney functions should be carried out from point of view of safe prescribing, whenever a bisphosphonate treatment is advised. Vitamin D assessment would help in the assessment of osteosarcopenia.

Other procedures may be appropriate for individual patients depending on the clinical presentation and local protocols. These may include [31]:

- Full blood count (FBC).
- Erythrocyte sedimentation rate (ESR).

- C-reactive protein.
- Liver function tests (LFTs).
- Thyroid function tests (TFTs).
- Serum protein immunoelectrophoresis, serum free light chains, and urinary Bence-Jones protein.
- Plasma parathyroid hormone particularly in patients with hypercalcemia.
- Serum prolactin.
- Serum testosterone, sex hormone-binding globulin, follicle stimulating hormone, luteinizing hormone (in males).
- 24-hour urinary free cortisol/overnight dexamethasone suppression test
- Endomysial and/or tissue transglutaminase antibodies.
- Biomarkers of bone turnover.
- Urinary calcium excretion.

Inform

Patient education is an important component of an FLS. By adopting the patient-centered care of management style, this will ensure giving sufficient time within the patients' appointment to encourage them to raise their queries, discuss their management options and available medications, provide information about other services they may be referred to (such as falls prevention, physiotherapy, pain clinics, orthopedic surgery, etc.), and explain the next steps in their care. The priorities are to cover simple key points and back this up with information resources in appropriate formats. Information should cover:

- Osteoporosis and risk factors for fracture.
- Lifestyle interventions aimed at reducing fracture risk including nutrition and exercise.
- Coping with pain and any disability associated with their fracture.
- Drug treatment options for osteoporosis management—including information on benefits and possible side effects.
- Reducing falls risk.
- Next steps in their care plan and follow-up appointments.
- People may feel overwhelmed when they are given a diagnosis. Feeling concerned and worried about themselves may make them not able to absorb or understand all the information given to them in the standard clinic setting. Information leaflets summarizing the key information in an appropriate format can give them extra information outside the clinic setting after their FLS appointment. Ways to contact the FLS staff or through an information helpline by organization bodies such as Royal Osteoporosis Society in the UK should be provided. Patients groups also are helpful in spreading the word and sharing experiences. All written communications and materials need to be in layman's terms and easily understood by the person who has had a fracture. It is good practice to ensure the person receives a copy of reports and clinic letters from the FLS appointments to facilitate their ongoing care.

Intervention

Intervention following FLS assessment will comprise a package of care tailored to the individual patient's needs. This should address all the modifiable fracture risk factors that have been identified for the individual person. In general treatment strategy should handle three main pillars:

- People at high risk of fragility fracture should start an appropriate osteoporosis therapy.
- People at high risk of falling should be referred to falls prevention services and offered interventions such as balance exercise and measures to improve sarcopenia to keep them strong, steady, and independent.
- People who are start interventions to reduce risk of fracture should be monitored by the FLS team.

Osteoporosis Therapy

There are a range of effective drug treatments for osteoporosis [32, 33]. Treatment decisions should adopt shared decision-making approach taking into account the patient's medical status, the

patient's preference, and an analysis of benefit versus risk (side effects). An optimal treatment choice should be supported by a strong evidence base and should have demonstrated benefits in terms of reducing vertebral and nonvertebral (including hip) fracture risk [31].

Falls Management

Many fragility fractures occur as a result of a fall, and many of the falls contributing risk factors are modifiable with appropriate interventions. Though clinical trials of falls interventions have not to date demonstrated an effect upon fracture risk reduction, common sense should be adopted in promoting these proven interventions to reduce future falls risk [34, 35]. Exercise can also reduce fear of falling and improve confidence [29]. It may help to promote bone strength as well as help with the symptoms caused by vertebral fractures especially postural changes and back pain [36].

In most cases, the development of an individualized multifactorial intervention will be undertaken by the falls prevention service which may comprise:

- Strength and balance training.
- Home hazard assessment and intervention.
- Vision assessment and referral.
- Medication review with modification/withdrawal.

Regular balance exercises are recommended for anyone who is unsteady or older 48 than 65 years and not doing regular active leisure or sports [37].

Improving Adherence

Commonly reported barriers to osteoporosis treatment adherence include actual and perceived side effects, dosing complexity, medication costs, lack of perceived need for therapy, poor perceptions regarding treatment effectiveness, poor patient-provider relationship, little patient involvement in treatment decision-making, and lack of treatment follow-up [38–42]. Evidence suggests that patients regularly reassess their perceived need for treatment against barriers to continued therapy [42, 43]. Strategies that enhance patient-provider communication and treatment follow-up may thus help to improve treatment adherence [44].

First, patients who feel comfortable with their physicians are more likely to trust the diagnosis, accept a prescribed treatment, and return to their doctor to discuss medication problems [40, 44]. Healthcare providers play a key role in shaping perceptions of fracture risk and osteoporosis drug effectiveness [40, 45, 46]. However, many patients fail to associate fracture with a diagnosis of osteoporosis [45, 46], and patients underestimate the extent of bone loss identified by bone mineral density testing [47]. Improved patient understanding of bone quality and need for pharmacotherapy is therefore critical [39, 41, 43]. Second, early treatment follow-up facilitates adherence by addressing adverse drug effects and problems with dosing complexity [40]. In fact, drug switching, between drugs or drug regimens, improves compliance to osteoporosis pharmacotherapy [48, 49].

Potential strategies to improve adherence to osteoporosis pharmacotherapy include improving patient-provider relationships and increased treatment monitoring through regular follow-up, clinical testing, and reminder systems [50, 51]. Providing patients with educational material alone does not improve treatment adherence [50, 52]. Instead, multifaceted and individualized approaches with regular follow-up are needed [44, 51]. An intensive intervention involving patient education and ten scheduled motivational interviews over a 12-month period has shown promising outcomes with positive impact on treatment adherence [53].

Integrate

An FLS can be based in hospital or in the community. Regardless, in order to be effective, the FLS will be integrated with other services and the wider fracture prevention care pathway. This

enables an FLS to maximize case-finding, refer to appropriate services to meet a patient's needs, and ensure transfer of care to facilitate long-term management of osteoporosis. Osteoporosis drug treatments need to be taken correctly for long periods in order to gain maximum benefit. Ensuring good communication among health professionals delivering fracture preventative care enables long-term support for patients to maximize treatment adherence and benefits.

Management Plan

Long-term treatment of osteoporosis will be managed by the GP. Clear management plans from the FLS will outline the recommendations for treatment and review timescales. The FLS report will support transfer of care and long-term management of osteoporosis by the patient's primary care team. A report template will be created with input from GPs and patients, and feedback should be invited to ensure the report meets their needs. Inclusion of the following information is recommended:

- Patient demographics and unique identifier.
- Details of fragility fracture(s).
- Current osteoporosis treatment.
- Results of assessments including fracture risk assessment, BMD results, and laboratory tests.
- Management recommendations including treatment changes, recommended review dates, and circumstances for re-referral.
- Appropriate primary care codes including the fracture site and type of fracture (e.g., osteoporotic).

FLS should carry out initial follow-up contact by 16 weeks and at 52 weeks, to follow up regarding the individual patient's management. Later further annual reviews should be completed outside of the FLS. In day-to-day practice, this can be set up subject to the local capability and capacity. Examples include via a GP or another member of the primary care team or a community pharmacist.

A reassessment of fracture risk should be carried out by the GP at 3 years (for intravenous zoledronic acid) or 5 years (for oral bisphosphonate) to determine whether it is appropriate to continue drug treatment or take a "drug holiday." Denosumab treatment should only be discontinued after advice from a specialist in bone metabolism [ROS report].

Quality

Leadership, governance, professional accountability, and staff development are essential to providing an efficient, coordinated, and consistent service that meets the needs and expectations of its patients. In order to deliver high-quality care, staff will demonstrate the necessary professional competencies and will participate in CPD to maintain their knowledge.

Service improvement involves individual staff, work teams, and organizations looking at how making changes to the way they work can help improve patient care by making services better. Auditing and peer support help to share experience and learn from each other challenges.

Clear lines of responsibility ensure that complex healthcare systems work most effectively for the benefit of patients. Within the FLS, there are some criteria that help to keep the service provided to the optimum. These include:

- A designated lead clinician accountable for all components of the service.
- The FLS is developed in line with a local fracture prevention strategy.
- Core clinical data from people identified by the FLS is recorded on an operational database. – A quality assurance framework is in place which includes:
  (a) An ongoing program of service/quality improvement including regular audit.
  (b) Participation in national audits.
  (c) Peer review.
  (d) Patient and carer experience measures.
- Staff are active participants in a regional clinical or professional network.

FLS Outcomes

Future Fracture Risk Reduction

The golden outcome of FLS is to reduce the risk of developing a subsequent fracture. Most of the studies carried out to assess for the outcomes of FLSs were studies evaluating FLS models. These research works proactively identified at-risk patients and initiated bone health assessments on them according to specific FLS protocols. Comparing the results of these studies to either primary care follow-up or a comparable hospital without an FLS program revealed a significant reduction in subsequent fractures over 2–4 years following the index fracture in the FLS group [16, 54–65].

In one of the studies carried out at the Concord facility in Sydney, Australia, patients who were followed up in the primary care by their GP had a markedly increased risk of subsequent fracture (hazard ratio [HR] 5.63, 95% confidence interval [95% CI] 2.73–11.6, P 0.01) after adjustments for other predictive factors, i.e., age and weight, compared to those assessed by their Type A FLS over 2–4 years follow-up [59]. In another study based in Newcastle, Australia, patients who were managed by their Type A FLS had a lower rate of re-fracture, 5.1%, compared to those not included in their assessment group, 16.4% ($P < 0.001$) after 2 years [60]. This same service was then compared with a comparable cohort from another hospital that does not have an FLS. It demonstrated that over 3 years there was a 30–40% reduction in re-fracture rate among FLS patients (all fractures: HR 0.67, 95% CI 0.47–0.95, $P = 0.025$; major fractures – hip, spine, femur, pelvis, humerus: HR 0.59, 95% CI 0.39–0.90, $P = 0.013$) [65]. Similarly, in the Netherlands, when a hospital with an FLS program was compared against one without, the FLS center had a reduced re-fracture rate, in a time-dependent fashion: after 1 year of follow-up, there was a non-significant 16% reduction (HR 0.84, 95% CI 0.64–1.10), but after 2 years of follow-up, there was a significant 56% reduction (HR 0.44, 95% CI 0.25–0.79) [66].

The Kaiser Permanente Southern California Healthy Bones Program, adopting a Type A service, the FLS reported itself to be very successful and has been highly commended by the International Osteoporosis Foundation (IOF) Capture the Fracture initiative [67]. They have published their outcomes from their collection of 11 medical centers, with an average reduction in re-fracture rate of 37.2% (range 23.1–60.7%) over the first 4 years [63, 64]. Subsequent analysis revealed a 38.1% reduction in expected hip fractures [54]. A cohort study conducted in Sweden analyzing patients in the year before and after the implementation of a Type B FLS program demonstrated a reduction in re-fracture rate of 42% in the FLS group (HR 0.58, 95% CI 0.40–0.87) after 6 years [67].

Less intense models focusing on improving patient and physician knowledge of bone health have not demonstrated any improvement on re-fracture rates. A randomized trial that allocated at-risk patients to four different arms, physician education, patient education, patient and physician education, and standard care, demonstrated no significant difference in re-fracture rates [68].

Vertebral Fragility Fractures

Big percentage of the FLS studies focus on the patients who sustained hip fractures, as these are generally associated with the greatest morbidity and mortality, and appendicular fractures, as these fractures seek medical attention allowing a good capture rate. In contrast, in standard practice, there is another important cohort of osteoporotic fragility fractures who are usually missed. These are those who develop vertebral fractures. Most vertebral fractures are asymptomatic, and only one-third present to medical attention. Symptomatic and asymptomatic vertebral fractures are associated with significant frailty, morbidity, and mortality [70–73]. In hospital, rate of vertebral fractures detection is poor and, even when detected, generally does not lead to initiation of any bone health assessment or treatment

[74]. A key area for improvement is how the secondary prevention care is delivered. The FLS program pays full attention as it has been specifically developed to identify such silent vertebral fragility fractures as well as those admitted to hospital. Earlier study revealed a threefold increase in the referral rate for BMD assessment for patients with silent vertebral fractures [75].

Mortality

Few studies have been published discussing mortality as an outcome associated with FLS programs. In the study carried out by Huntjens and colleagues, adopting a Type A FLS, the patients were followed up for 2-years duration. Outcomes revealed a 35% reduction in mortality following a fragility fracture compared with a comparable cohort not assessed by FLS (HR 0.65, 95% CI 0.53–0.79) [66]. In another large cohort study carried out in the UK by Hawley et al., using hospital admission data from 11 hospitals also reported a reduction in 30-day mortality by 20% (HR 0.80, 95% CI 0.71–0.91) and 1-year mortality by 16% (HR 0.84, 95% CI 0.77–0.93) in patients admitted to hospital after a hip fracture [76]. This data set included hospitals with a newly implemented orthogeriatric service and an FLS program.

Bone Health and Bone Mineral Density Assessment

There is overwhelming evidence that FLS is associated with an increased number of patients referred for DXA scanning. Compared to either usual care or a specified period pre-FLS, there was almost a 2- to 18-fold increase in DXA referrals. Comparison of the different FLS models revealed that a more involved FLS program, such as a Type A model, was more likely to lead to higher referral rates compared to a less intensive model (Table 14.3).

A Scottish study compared two hospitals, one with a Type A FLS and one with usual care, and found that rates of offering DXA scans were significantly higher at the FLS center (85% vs 6% for humeral fractures, 20% vs 9.7% for hip fractures) [77]. Another study based in Edmonton, Canada, which randomly assigned patients with hip fracture to either an FLS or usual care, also reported a significant increase in BMD testing in the FLS group (80% vs 29%, adjusted odds ratio [OR] 11.6, 95% CI 5.8–23.5, P 0.01) [78]. The same department subsequently evaluated this same model in patients with wrist fractures, and

Table 14.3 FLS models of care and their impact on the patients' management in terms of BMD testing as well as receiving osteoporosis treatment

Model	Description	% receiving BMD testing	% receiving osteoporosis treatment
Status quo	Manitoba statistics for major osteoporotic fractures (2007/2008)	13%	8%
Type D (zero model)	Only provides osteoporosis education to the fracture patient. Primary care provider (PCP) is not alerted or educated	No study on BMD testing	8%
Type C (1 "I" model)	1. Identification the PCP is alerted that a fracture has occurred and further assessment is needed. Leaves the investigation and initiation of treatment to the PCP	43%	23%
Type B (2 "I" model)	1. Identification 2. Investigation leaves the initiation of treatment for fragility fracture patients to the PCP	60%	41%
Type A (3 "I" model)	1. Identification 2. Investigation 3. Initiation of osteoporosis treatment where appropriate	79%	46%

it also showed increased BMD testing in the FLS group (52% vs 18%, relative risk [RR] 2.8, 95% CI 1.9–4.2, $P < 0.01$) [79]. Even in studies where the comparison was made with a period pre-FLS, a significant increase in DXA referral was noted. An Italian study reported that their Type A inpatient FLS model of patients over 65 years with a proximal femoral fracture increased BMD testing by over threefold, from 14.5% to 47.6% ($P < 0.01$) [80]. A similar finding was reported in another study based in America where the initiation of an FLS during hip fracture rehabilitation increased BMD testing from 35% to 65% [57]. The Kaiser Permanente FLS have published multiple reports addressing the issue of osteoporosis investigation since their establishment in 2002. They reported a 247% increase in total annual DXA scans over the first 4 years [63] and a 263% increase over the first 6 years [54]. In concordance, visual data showed further increase in annual DXA scans in their seventh and eighth years [64].

On the other hand, findings from less intensive services have not been as robust. An education-based Type C service reported that patients followed up 3 months after their index fracture via a phone call were more likely to have been recommended a DXA scan (OR 5.22, $P < 0.01$) compared to a control group that received no contact [81]. Yet, it was not reported how many of these recommendations translated into referrals. Another study employing an educational program (Types C and D) reported no significant difference in BMD assessment between the different groups, suggesting that the less intensive services may be less effective [68]. Hence, being able to initiate bone health assessment as part of an FLS program appears crucial in ensuring that a BMD assessment is done. This was demonstrated when a Type D service (education in the form of a letter) was compared with the same service with an additional offer for a free BMD assessment. The group offered the BMD assessment showed a significantly higher rate of investigation for osteoporosis (38% vs 7%, $P < 0.01$) [82]. The same department later compared an outpatient Type B service with the aforementioned Type D service, showing more BMD testing with the more involved Type B intervention (83% vs 26%) [58]. Again, this reaffirms that a more intensive model is more efficient in initiating bone health assessment.

Referring a patient for BMD assessment with DXA is not a thorough assessment of fracture risk. Besides BMD measurement, a comprehensive bone health assessment includes assessment of other risks for future fractures. A two-center comparison study (Type B vs standard service), comparing the practices in postmenopausal women with hip fractures, found much improved investigative work in terms of documentation of osteoporosis risk factors at the FLS center (83% vs 7%) [83]. A Type A FLS from Sydney, Australia, reported that a total of 84% of patients identified by their service had a comprehensive assessment that also included a DXA scan [84].

Overall, referrals for DXA from an FLS program range from 67.4% to 73.4% in Scotland [13] and 83.0% to 99.6% in the Netherlands [85]. Using an automated referral system has been reported to increase referral to 100% [86]. However, as many as 45% of those referred would either decline or not attend [13, 87].

Osteoporosis Treatment Initiation and Adherence

As an outcome of BMD assessment and considering the other risk factors, once the diagnosis of osteoporosis or high fracture risk probability is made, this would mandate starting osteoporosis therapy. This is supported by the results of earlier studies in which osteoporosis treatment was shown to be effective in reducing subsequent fracture risk. Oral bisphosphonates are the most prescribed pharmacological agent. However, adherence to oral bisphosphonate has been reported to be poor with only a third continues taking the medication at 1 year [88]. Therefore, osteoporosis treatment outcomes can be splitted into the rate of initiation of therapy and the level of adherence to therapy treatment at later point of time.

There is overwhelming evidence that FLS increases initiation of osteoporosis treatment.

The Type A services reported treatment initiation by an RR 1.50–4 [89], with data gathered up to 2 years after joining an FLS program [55, 60, 77, 78, 80, 90]. The Edmonton series described treatment as an outcome measure in their trials. Results of the study revealed that comparing the FLS cohort outcome to the standard service revealed higher number of bisphosphonates prescription in the FLS group at 6 months after hip fracture (51% vs 22%, adjusted OR 4.7, 95% CI 2.4–8.9, $P < 0.01$) and wrist fracture (22% vs 7%, adjusted RR 2.6, 95% CI 1.3–5.1, $P = 0.008$) [78, 79]. They also described more patients receiving "appropriate care," i.e., their overall treatment was concordant with guidelines, in the FLS group [78, 79]. The comparative study of the Fracture Prevention Clinic in Newcastle, Australia (Type A FLS vs standard service), also demonstrated increased treatment rates in the FLS group after an average of 2 years of follow-up (81.3% vs 54.1%, $P < 0.01$) [60].

Even when recommendations for osteoporosis therapy were made by the FLS but initiated in the primary care by the GP, there was an increase in treatment rate after fracture from 12.6% to 31.8%, after 1 year of follow-up in the study carried out by Axelsson and co-authors [91]. Another study that looked at a cohort of older women with hip fractures showed that more patients for who the FLS had recommended osteoporosis treatment were prescribed treatment compared to standard care (90.5% vs 60.9%, P 0.01) [83]. However, when no treatment recommendations were made (Type C or D model – educational programs), it made no difference to treatment initiation rates [68].

Analysis of the adherence to osteoporosis treatment revealed that there was wide variation, particularly for bisphosphonates, both in reported adherence and also when adherence was measured. Overall, adherence at 1 year has been reported to range from 44% to 80% [80, 91–93]. The Geisinger Medical Center High-Risk Osteoporosis Clinic (HiROC), Pennsylvania, USA, which includes monitoring osteoporosis patients at 3 months (via phone) and a follow-up visit at 1 year, reported that adherence to oral bisphosphonates was 80.7% at 3 months and 67.7% at 12 months. In another study, although adherence at 1 year improved since the start of a dedicated hip fracture FLS program compared to a pre-FLS period (44.07% vs 14.04%, $P < 0.01$), it demonstrated a significantly low proportion of patients on treatment [80]. A Spanish study which included patient education and telephone follow-up at 3, 6, 12, and 24 months recorded adherence rates to treatment of 72% at 1 year and 73% at 2 years, with significantly better adherence among women and those who had previously been treated with a similar drug [92]. Among patients initiated treatment in a French hospital, adherence was recorded as 80% after 1 year and 67.7% at final follow-up (mean 27.4 [11.7] months) [93].

Cost-Effectiveness of an FLS

In addition to clinical effectiveness, commissioning of an FLS needs to also weigh up the cost-effectiveness of such an intervention. A number of FLSs have conducted formal cost analysis of their existing FLSs, most of them using decision analysis models. Analyses conducted alongside a randomized trial of an FLS for hip fracture and wrist fracture patients with usual care reported that for every 100 patients managed, they would prevent 6 fractures (4 hips) and 3 fractures (1 hip), respectively [8]. This would result in a saving of over US$250,000 to the healthcare system and up to 4 quality-adjusted life years (QALY) gained [94, 95]. Analysis from another Canadian center, the Osteoporosis Exemplary Care Program in Toronto, showed that assessing 500 patients per year would prevent three hip fractures, saving CA$48,950 per year [96]. They also calculated that the employment of an FLS coordinator would still be a cost-effective measure even if they managed as few as 350 patients per year [97]. In the USA, a model based on a Type A FLS in Boston calculated that for every 10,000 patients managed, 153 fractures (109 hip) would be prevented, which equated to an overall saving of US$66,879, and there would be an increase in quality-adjusted life expectancy (QALE) of 37.4 years [98]. The Glasgow, UK, FLS devel-

oped a cost-effectiveness and budget-impact model, based on their internal data. They calculated that for 1000 patients managed in their FLS program, which identifies, investigates, and initiates treatment costing £290,000, they prevented 18 fractures (11 hips), leading to an overall saving of £21,000 [99].

In a separate study also based in Ontario, Canada, cost-effectiveness was compared between a less intense Type C model and a Type A model. For the Ontario Fracture Clinic Screening Program (Type C FLS), 4.3 quality-adjusted life years (QALYs) were gained, and an extra CA$83,000 was spent per 1000 patients, equating to a cost of CA$19,132 per QALY gained. Their subsequent enhanced FLS called the Bone Mineral Density Fast Track program (Type A FLS) was reported to be even more cost-effective at CA$5720 per QALY gained [100]. Hence, this almost fourfold difference in cost-effectiveness suggests that a more intense model may deliver better outcomes.

These studies demonstrate that FLSs are not only cost-effective but also cost-saving. Investment in FLS will reduce future fractures, which ultimately translates into lower overall healthcare cost. However, the cost-effectiveness of each FLS very much depends on the structure of each individual FLS in the context of the healthcare model of that respective geographical region.

Best Practice Framework for Fracture Liaison Services

The IOF released a landmark document entitled Capture the Fracture in 20,127 and went on to publish their Best Practice Framework (BPF) (https://www.capturethefracture.org/), in order to provide guidance for institutions in the process of implementing an FLS and to allow evaluation of services using pre-determined outcome measures. It included 13 key domains—patient identification, patient evaluation, post-fracture assessment timing, identifying vertebral fragility fractures, adherence to local/regional/national guidelines, evaluating secondary cause of osteoporosis, access to falls prevention services, lifestyle risk assessment, initiation of treatment, review of treatment, communication between primary and secondary care, plan for long-term management (>12 months), and all fragility fractures being recorded on a database [101].

Similarly, the UK Royal Osteoporosis Society (ROS) have also published their FLS clinical standards (https://theros.org.uk/healthcare-professionals/tools-and-resources/clinical-guidance/documents/clinical-standards-for-fracture-liaison-services/) based on a 5IQ process of identifying those at risk, investigating bone health and falls risk, informing patients about their condition and management plan, intervening with bone protection and falls intervention, integrating patient care between primary and secondary care, and maintaining quality of the service via database collection, audit, and professional development.

Recently, the International Osteoporosis Foundation launched a new FLS program "Getting to Gold." This new initiative provides effective long-term support for FLS that were established with the help of the Capture the Fracture mentorship program (FLS workshops and onsite trainings). Getting to Gold helps to ensure that a developed FLS can improve and sustain itself in the long run. While the standard FLS workshops and onsite trainings focus more on the early stages of development and building business cases, Getting to Gold focuses on making sure FLS grow in number and quality and are sustainable locally. The first step of the program is the development of a team of key national FLS mentors. The local mentors will be trained through a series of online and in-person sessions. Once evaluated and certified by the IOF, they will support local service development as well as help local FLSs become efficient, sustainable, and able to offer a good patient experience.

In conclusion, the fracture liaison service model appears to address many of the historic shortcomings in traditional management of fragility fractures. It has proven to improve diagnosis and long-term treatment and to decrease morbidity in these patients. It also takes away

ambiguity regarding which specialty manages the disease and allows for efficient communication between multiple specialties and reduces the chance a patient may get lost while navigating the current healthcare system. As the population continues to age, managing and preventing life-altering fractures will become an increasingly important issue. Given that the sentinel sign of osteoporosis is fracture, and the increasing interest in several organization bodies as well as the documented cost-effectiveness of the project, the role played by FLS is expected to grow over time in a trial to comply with the initiative of "Capture the Fracture" launched by the International Osteoporosis Foundation.

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