

# Fracture Liaison Services (FLS): a Review

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## ABSTRACT

Fragility fractures, namely fractures from low-energy mechanisms that would not produce fracture in a healthy bone, are most commonly caused by osteoporosis, and constitute a major financial burden worldwide. The effectiveness of systems for the prevention of fragility fractures, also known as fracture liaison services (FLS) has been investigated by numerous programs. The FLS is a coordinated care paradigm where several providers work together to help the patient manage their osteoporosis following a fragility fracture in order to help prevent subsequent fractures. FLS offers a thorough method for not only identifying individuals who are at risk for secondary fracture but also for putting into practice evidence-based therapies to stop further fractures. For the FLS to be successful, doctors, nurses, administration and national healthcare systems must work together toward the common objective of protecting patients aged 50 and older from fragility fractures. This review article discusses the current FLS programs, their pros and cons, and emphasizes on the Greek FLS model.

**KEYWORDS:** Osteoporosis; Fragility fractures; Fracture liaison services

### Introduction

Fragility fractures, namely fractures from low-energy mechanisms that would not produce fracture in a healthy bone, are most commonly caused by osteoporosis. Nearly 9 million of these fractures occur each year due to osteoporosis worldwide (1). Fragility fracture rates will probably continue to rise as osteoporosis prevalence rises with aging and our population gets older, resulting in a lower quality of life and increased mortality; 24% of hip fracture patients who are

fifty years of age or older pass away within a year of the fracture (2). Additionally, fragility fractures have significant economic expenses in addition to their immediate impact on the patient. The cost of osteoporosis-related fractures in the US in 2005 was estimated at \$19 billion. These expenses are expected to increase to almost \$25.3 billion by 2025 (2,3). A patient's risk of subsequent fracture increases by approximately two fold after suffering a vertebral fracture, and by three fold after suffering a subsequent hip fracture (4). Due

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to the severity of these effects, prevention of a secondary fracture is considered of great importance, both from a patient-care and social perspective.

The effectiveness of systems for the prevention of secondary fractures, also known as fracture liaison services (FLS) has been investigated by numerous programs (5–17). The FLS is a coordinated care paradigm where several providers work together to help the patient manage their osteoporosis following a fragility fracture in order to help prevent subsequent fractures. This review article discusses the current FLS programs, their pros and cons, and emphasizes on the Greek FLS model.

### Prediction of secondary fractures

A bone mineral density (BMD) T-score of  $-2.5$  or lower was the operational definition of osteoporosis provided by the World Health Organization in 1994 (18), and this criterion has since been adopted as the diagnostic standard. Although there is a 1.5–2.5 fold increase in fracture risk with each standard deviation decrease in BMD, the sensitivity of BMD alone to identify people at risk for a fracture is  $<50\%$  (19,20), and many patients experience fractures with a T score  $> -2.5$ . For this reason, techniques for predicting fractures have been created to help identify people who are “at risk.” The Fracture Risk Assessment Tool (FRAX) was created by conducting a thorough meta-analysis of the primary data from nine geographically dispersed cohort studies. It was then verified in an additional eleven cohorts, and it was published in 2008 (21).

Age, sex, weight, height, previous fracture, parent’s hip fracture, current smoking, use of glucocorticoids, rheumatoid arthritis, secondary causes of osteoporosis, alcohol use, and BMD (although this can be disregarded in resource-constrained situations where BMD assessment is not possible) are the parameters used in FRAX. The results include the 10-year likelihood of a major osteoporotic fracture (clinical spine, proximal humerus, distal forearm, or hip fracture), as well as the 10-year likelihood of hip fracture. Globally, fracture incidence varies by geography, and FRAX is calibrated to offer nation-specific models (22).

Thresholds for therapeutic intervention can be

determined using these percentage risks. Over 80 guidelines from around the world include FRAX (22). In general, patients who are at risk for primary and secondary fractures can be identified with the help of population screening techniques, BMD measurements (if available), and fracture prediction algorithms such as FRAX. Nevertheless, using an FLS is another way to spot and assist those who are “at risk” for fractures.

### Prevention of secondary fractures - FLS programs

FLS is a specialized program created to recognize, investigate, and facilitate the initiation of the right treatment for individuals who have poor bone health and are at high risk for secondary fractures. When a patient suffers a fragility fracture, he/she is considered as having poor bone quality and thus susceptible to more fractures. The FLS model of care automatically enlists those patients for the medically necessary assessment of their risk for a secondary fracture, offers treatment recommendations, and may initiate treatment as needed. The FLS model results in higher rates of diagnosis and therapy and less attrition in the post-fracture phase of care as compared to other osteoporosis management methods, such as referral letters to primary care physicians or endocrinologists following fracture.

Prior to the implementation of secondary fracture prevention initiatives, 2% to 25% of people worldwide received evidence-based osteoporosis treatment following a known fragility fracture (23). These figures suggest that doctors are not greatly involved in their patients’ secondary fracture prevention. With a marked growth in the use of post-fracture care, national healthcare systems and regional centers in many nations have begun to build their own FLS-type systems (5–13,24,25). Additionally, as a result of these programs’ longevity, numerous studies have demonstrated an increase in the number of treatments started and a lengthened period of treatment adherence (7,9,10). Additional analysis revealed that these programs over time reduced the incidence of secondary fractures and even mortality (10,14,15,25–27).

FLS has also been demonstrated to be a cost-effective approach in numerous studies (6,15,16,28–33).

Particularly, cost savings are driven not just by lower osteoporosis management costs but also by a rise in quality-adjusted life years and a decline in fracture rates.

### FLS implementation

A clear road map is essential to guarantee that everyone involved in the FLS implementation has the same understanding of the program's goals and objectives. An FLS coordinator or practitioner, a nurse navigator, and a leading physician can be the founding members of the FLS program while the team can be expanded as necessary in the future. According to previous research less success has been reported with an FLS core made up of primary care physicians, rheumatologists, or endocrinologists (34,35), rather than with orthopaedic surgeons and this is mainly due to: when treating a fracture, the orthopaedic surgeon is already familiar with the patient and family, and he or she is the one who establishes a connection between the fracture and osteoporosis; patients frequently wait until fracture healing before visiting their primary care physician, which creates the misconception that no further treatment is necessary.

The FLS program coordinator is often a nurse practitioner or physician assistant with a focus on secondary fracture prevention (5,26,36,37). This provider needs to be proficient in many different areas such as being able to involve patients and their families in their care, have a thorough understanding of the most recent treatment algorithms and osteoporosis standards, while being capable to establish connections with other specialties and services within the institution. In order to ensure that patients keep their appointments and receive care as needed, this practitioner should collaborate closely with the leading physician and is frequently housed in the same office. To allow for simultaneous care from both physicians, this practitioner could also practice separately. Depending on the advanced practice practitioner's license, the FLS coordinator may also run a clinic independently from the leading physician. The FLS coordinator should regularly update practice patterns based on national recommendations and stay up to speed with national quality metrics (37).

To ensure that all eligible patients are engaged in the FLS program and to promote communication within

the care team, the FLS coordinator needs nursing support (37,38). A "nurse navigator" is necessary in this position to help with osteoporosis education, medicine administration and training, and prescription insurance verifications. Additionally, a nurse navigator is used to find patients who should be referred to FLS by looking at inpatient censuses, emergency room discharges, and outpatient referral trends. The navigator may serve as the FLS program's first point of contact, arranging outpatient referrals and scheduling with the FLS while also offering instructional sessions for inpatients that may include handouts or films. To ensure that all patients who may potentially benefit from the FLS are enrolled, the nurse navigator should build cooperative partnerships with services other than orthopaedic surgery. Other services in the FLS coordination include the departments of radiology, neurosurgery, general practice, women's health, hospital medicine, and so forth because these specialties can also recognize and treat individuals with fragility fractures who do not need orthopaedic care (26). Patients may also be identified as FLS candidates using the electronic health record based on diagnostic or procedural coding.

It has been shown that preventing subsequent fractures lowers overall healthcare costs (23,39). It is recommended that the hospital administration pay for start-up costs as a part of a quality initiative associated with a musculoskeletal service line (40). A business plan can show cost savings from secondary fracture readmissions that are avoidable, and reportable metrics like readmission rates can support program implementation. To include volume predictions of office visits and related ancillary revenue directly related to the FLS service, the program is later integrated into the departmental or service line budget (such as bone densitometry, anabolic or antiresorptive medications, and laboratory studies). For better secondary fracture prevention and to show compliance with osteoporosis measures, data collection is crucial. There are typically two or three exam rooms in an office setting. To strengthen the care team for the disease condition and increase patient access and compliance, it is advised that the office location mirrors that of the leading - physician (40). Currently, billing is distinct from the overall duration of fracture care due to the FLS's

specialized knowledge in a fee-for-service paradigm; however, shifting to value-based healthcare systems will probably alter this practice.

To enhance the reporting of claims data and patient outcomes, segregating the FLS in the electronic health record seems to be efficient. Additionally, templates and order sets created specifically for osteoporosis aid in gathering information about patients' vulnerability to fragility fractures. To improve patient access and compliance, it is best to have laboratory and imaging services in the same place. Cost-effective ordering is also guaranteed when laboratory test orders are standardized and entered into the electronic health record using best-practice principles. Radiographs and bone densitometry should be included in imaging modalities. Insurance agencies frequently demand bone densitometry before beginning pharmacologic treatment, even when the patient has a known fragility fracture with poor bone quality (26).

Prior to the implementation of FLS (5), the leading physician, FLS coordinator, nurse navigator, referring providers, and administrative stakeholders must establish shared objectives to guarantee that everyone involved has the same vision. With a targeted FLS deployment for patients with low-energy hip fractures, a new program may be successful. The program can subsequently be expanded to encompass all low energy fractures in patients who are older than forty-nine years old after confirming the correctness of the referral procedure and data reporting. Data reporting is crucial and should cover the ratio of referrals to eligible patients, the rate of missed appointments, treatment compliance, and mortality and secondary fracture rates (41–46). This data can assist in reevaluating FLS resources and predicting the program's future requirements.

A specific FLS should work to address the problem of fragility fractures in their specific region; of course, there will be differences in the patient population's demographics and the healthcare facilities that are available. The resources needed to implement FLS are, however, actually quite meager. The only technological requirements are a DXA scanner and a computer, and in low-resource settings, paper copies of the FRAX® tool are available for use and treatment decisions can be made without bone mineral density in-

formation. While FLS is typically reserved for patients with less severe fractures or abnormal laboratory results, in some regions the orthopaedic team will initiate a single dose of zoledronate in patients with hip fractures and normal laboratory results with calcium and vitamin D supplementation.

### Potential benefits

FLS offers a base to benefit from both recent and anticipated improvements in health-care reform (39). Organizations in the healthcare industry can benefit from FLS as they make the switch from volume to quality payment. The current system of reimbursement is fee-for-service driven and not often connected to the overall quality of care. Regardless of the standard of care delivered or the results for patients, providers are paid equally for treatments. Another paradigm may switch to remuneration based on quality-of-care standards and patient outcomes as the system transitions to value-based or quality-based payments. A health care system will need to implement quality-care initiatives and provide evidence of better patient outcomes in order to reap the rewards of these new incentives. The FLS model of care is an illustration of a strategy that can enhance results in the treatment of patients with fragility fractures and lower secondary fracture rates.

### Potential pitfalls and solutions

Certain barriers occasionally prevent the initiation of FLS (47). One such situation involves insufficient funding to hire an FLS nurse specialist; one possible option is to hire (or re-deploy) a member of the secretarial staff to do the administrative responsibilities that are a part of the FLS nurse specialist function. Language can be a barrier to using international resources although the Best Practice Framework (BPF) document is currently available in 12 major languages. All FLS registering for the Capture the Fracture (CTF) program must complete it. Lack of prior FLS management expertise may cause a lack of trust and the suspension of an FLS initiative. Through the use of instructional resources and personal mentoring from skilled FLS providers, this can be solved. Since 2015, webinars have been held as a part of the CTF Educational Program with the goal of interacting with the FLS community of the CTF and disseminating parti-

ment information about FLS and secondary fracture prevention.

With the help of the CTF mentorship program, organizations interested in launching a new FLS can interact with eminent FLS professionals. The initiative establishes a forum for the exchange of crucial knowledge and abilities between FLS champions and FLS in the early stages of development, locally and regionally. The mentorship program has been in operation since its launch in 2016, giving a combination of on-site training and FLS seminars to provide advice on FLS implementation. During the on-site training, a FLS champion (mentor) hosts a FLS candidate (mentee) and spends a day teaching them how to implement a FLS and apply to CTF by completing the BPF questionnaire. The content is customized to match the mentee's specific needs because the training is conducted one-on-one. Conversely, FLS workshops draw in a bigger crowd, frequently more than 15 FLS applicants from the same nation.

### Measuring the effectiveness of FLS

Eleven patient-level key performance indicators (KPIs) for FLS have been developed by the IOF CTF® Campaign in collaboration with the Fragility Fracture Network (FFN) and National Osteoporosis Foundation (NOF) to help guide quality improvement. These 11 FLS KPIs that have been suggested, give a comprehensive picture of how the FLS delivers secondary fracture prevention at the patient level. The degrees of achievement correspond to those that economic models employ to show the anticipated advantages of secondary fracture prevention in the local context. For an FLS to realize its predicted ability to lower re-fracture rates through secondary fracture prevention, it must reach a green level of accomplishment across all KPIs. Up until this point, FLS should actively pursue quality improvement. In some regions, meeting these KPIs may rely on modifying local healthcare systems outside the purview of the FLS. These KPIs should be viewed as instruments for enhancing service provision while utilizing already available resources. They should also be used to communicate to payers the precise service gaps that exist and suggested targets for development. The reduction of secondary fracture rates is the ultimate objective of FLS (5).

The majority of individuals with reportedly fractured spines do not require secondary fracture prevention (48). Improved techniques for identifying people with spine fractures are being developed. Text analysis of radiological reports or medical records may be required (49). Although these techniques are precise, they might not be sensitive since they rely on radiologists, whose reporting of spine fractures is notoriously inaccurate (48).

Patients who are evaluated by the FLS after having fractured during therapy frequently need a different approach to treatment (50,51). Testing for specialized laboratory tests is another potential KPI. This is relevant given that laboratory testing has detected secondary causes in up to 35% of FLS patients with osteoporosis (52). Several national guidelines for the prevention of secondary fractures recommend a variety of laboratory testing, although there is little agreement among them. Testing for vitamin D is one instance. Given the effectiveness of regular supplementation (53) and the difficulty in interpreting results due to seasonal variation and changes brought on by acute inflammation, some guidelines pragmatically advise high-dose empirical supplementation over systematic testing for the majority of patients following a fragility fracture if oral AOMs are advised. However, some investigations have called into doubt the effectiveness and security of greater vitamin D doses (54), emphasizing the requirement to assess vitamin D status in many individuals. Nearly all clinical guidelines state that patients in need of AOM should receive calcium and vitamin D replenishment; however, calcium replenishment can be easily obtained by diet, over-the-counter supplements, or prescribed medications, making calcium replenishment measurement difficult. Additionally, clinical investigations have shown that calcium and vitamin D supplementation alone is ineffective in the post-fracture scenario to lower the risk of re-fracture (55,56).

### The Hellenic experience

There are two reports of FLS implementation in Greece. The first one was conducted at the 251 Hellenic Air Force and VA General Hospital of Athens (17) and the second was a multicenter study involving four orthopaedic departments across the country (66). The recruitment efficacy was very low (29.3%), significant-

ly lower than the first FLS Greek report (54.5%) (17), or other national programs, such as those in The Netherlands, Spain, and UK (5,9,10), despite the fact that a large number of patients were deemed eligible to participate in the program. The majority of eligible patients who volunteered to participate in this FLS had a hip fracture. Nevertheless, despite the surprisingly low recruitment rate, 99% of those who were recruited completed the study and showed up for the 12-month follow-up appointment (66). This is in contrast to the first FLS Greek report, which was conducted in a single hospital and found that the completion rate was <20% (17), but it is consistent with other studies that found that between 65% and 80% of patients adhered to their treatment plans and scheduled follow-up visits (7,9,10). This startling discrepancy in the two FLS structures can be explained by variances in the recruitment rate and the percentage of patients who ultimately completed the follow-up visits. In the first FLS program (17), the registered nurse who was explicitly tasked with this work and as a result was both motivated and committed, conducted the screening and recruitment of eligible patients. The treating physicians were required to be active in the recruitment of the eligible patients during their usual clinical work at the hospital in the current trial, in which Orthopaedic Departments were involved rather than hospitals, and this may have influenced the outcome. In other words, in addition to their often busy schedules, the orthopedic surgeons had the extra responsibility of patient recruiting. The relatively high percentage of patients (57.3%) receiving treatment for osteoporosis may have been another likely factor in the high percentage of uncooperative individuals. As a result, patients probably chose to be monitored by their own doctor rather than in a FLS environment. Furthermore, this large proportion of patients who had previously had osteoporosis follow-up could be a sign of population selection bias in the study. A likely yet not solid explanation for this would be the urban and rather central location of these University Departments, which is likely to make them easily accessible to patients with unrestricted access to health services and thus make them adequately treated for a variety of medical conditions. A patient in Greece can typically choose among the hospitals of his or her residential area. However, despite the low

recruitment rate of eligible patients, the treating physician's contribution to the recruited patients' completion rate turned out to be crucial, as almost all of them followed through with the follow-up appointments for up to one year. These adherent individuals lacked any distinctive traits that could pinpoint, and neither their treatment within the FLS nor outside of it differed from other patients. Additionally, as this was a general finding across all four locations, it is not possible to be attributed to the FLS staff members' unique communication skills. Therefore, it makes sense to draw the conclusion that the patient remains under medical care anytime the treating physician is active in the process of recruiting and motivation.

The allocated personnel's commitment to spending time outlining the hazards of osteoporosis and the advantage of therapy appears to be a key factor in whether osteoporotic patients are successfully recruited. Similar studies (11,17) have demonstrated that FLS workers are typically not employed exclusively; rather, the task is performed in conjunction with the rest of their duties and is primarily voluntary. However, it is evident from the experience gained in Greece that even when a program as complex and time-consuming as an FLS is run by committed and motivated staff who are willing and able to thoroughly explain the risks of osteoporosis to patients and persuade them of the immediate need for treatment, the results are, on the whole, highly satisfactory and successful. Specific guidelines (57,58), unambiguous FRAX cutoffs for cost-effective treatment (59,60), and convenient access to BMD testing with adequate reimbursement promote osteoporosis management in Greece. The national registration and audit FLS programs, however, will perform poorly anytime there is a paucity of funding, at least in terms of disease awareness.


Osteoporosis requires preventative and ongoing therapy to lower the risk of future problems, just like other silent and asymptomatic chronic diseases like diabetes and hypertension. However, for a variety of reasons, treatment compliance is currently very low (61,62). According to a recent study, only 19% of patients with hip fractures were receiving therapy for bone-active osteoporosis prior to the fracture, and this number barely changed after the fracture, climbing to 21% (63). Given that there are effective medi-

cines to prevent future fractures, this type of diagnostic gap is too great, which highlights the need for a more concentrated public health strategy (64,65). Hip fractures made up more than 50% of the eligible and ultimately included cases in this study, which may indicate a selection bias. This is explained by the fact that in Greece almost all hip fractures result in admission to an orthopaedic department, while less serious fractures may be treated in outpatient facilities that are either public or private. Therefore, a large proportion of hip fractures will be present in any Greek FLS that occurs in an orthopaedic department that receives trauma cases. The first Greek study revealed that a male relative younger in age with a single NVF other than the hip fit the description of osteoporotic patients reluctant to take part in an FLS program. Patients with a hip fracture and several comorbidities who were older than 75 also seemed to be more likely to give up on the endeavor. These are the patients who don't stick to therapy as well because they either don't understand how serious fractures are or have a tough time getting to an outpatient clinic due to a bad transportation system. Greece lacks a public non-emergency transportation facility that is patient-centered, which is essential for elderly patients, especially those who live alone. The ability to confirm whether the aforementioned characteristics applied to the included subjects was limited by the fact that pertinent data on the patients who rejected to participate or who were lost to follow-up were missing from this study. Finally, of the 392 patients who finished the latest Greek project, 12 additional fragility fractures developed during the follow-up visits of our current study (66). The numbers were too small to draw any firm conclusions, and the treatment duration was too brief to significantly affect the re-fracture rates, despite the fact that all of these fractures were documented in patients who had rejected or stopped anti-osteoporotic medication. This

finding suggests a chance occurrence more than an occurrence directly linked to or motivated by the absence of anti-osteoporotic therapy.

Based on the knowledge gained from the FLS implementation in Greece, it is necessary to significantly enhance recruitment rates. The treating physician must be well-educated, driven, and capable of devoting the necessary time to persuading patients to enroll in order to increase both the recruitment and completion rates. Additionally, certain target populations require special consideration, including young people and older adults with comorbidities and/or polypharmacy. Additionally, there is an urgent need for a national fracture database, and HSSBM is working with the ministry of health and other medical societies to achieve this objective. All FLS activities will undoubtedly benefit from this, particularly at the national level. The operational structure of the FLS, which is a very labor-intensive and time-consuming effort, should be adequately and consistently supported by the national healthcare system for a vital role in the final outcome.

### Conclusion

Fragility fracture care includes more than just stabilizing a shattered bone through surgery. Osteoporosis, the underlying condition that led to the fracture, needs to be actively managed as a disease. The majority of healthcare professionals do not thoroughly assess this underlying medical state and then develop a treatment plan for it, and this lack of action could have long-term financial repercussions. FLS offers a thorough method for not only identifying individuals who are at risk for secondary fracture but also for putting into practice evidence-based therapies to stop further fractures. For the FLS to be successful, doctors, nurses, administration and national healthcare systems must work together toward the common objective of protecting patients aged 50 and older from fragility fractures. 

## REFERENCES

1. Johnell O, Kanis JA. An estimate of the worldwide prevalence and disability associated with osteoporotic fractures. *Osteoporos Int.* 2006 Dec;17(12):1726–33.
2. Autier P, Haentjens P, Bontin J, Baillon JM, Grivegnée AR, Closon MC, et al. Costs induced by hip fractures: a prospective controlled study in Belgium. *Belgian Hip Fracture Study Group. Osteoporos Int.* 2000;11(5):373–80.
3. Burge R, Dawson-Hughes B, Solomon DH, Wong JB,

- King A, Tosteson A. Incidence and economic burden of osteoporosis-related fractures in the United States, 2005-2025. *J Bone Miner Res.* 2007 Mar;22(3):465-75.
4. Black DM, Arden NK, Palermo L, Pearson J, Cummings SR. Prevalent vertebral deformities predict hip fractures and new vertebral deformities but not wrist fractures. Study of Osteoporotic Fractures Research Group. *J Bone Miner Res.* 1999 Dec;14(5):821-8.
  5. McLellan AR, Gallacher SJ, Fraser M, McQuillan C. The fracture liaison service: success of a program for the evaluation and management of patients with osteoporotic fracture. *Osteoporos Int.* 2003 Dec;14(12):1028-34.
  6. Ahmed M, Durcan L, O'Beirne J, Quinlan J, Pillay I. Fracture liaison service in a non-regional orthopaedic clinic—a cost-effective service. *Ir Med J.* 2012 Jan;105(1):24, 26-7.
  7. Boudou L, Gerbay B, Chopin F, Ollagnier E, Collet P, Thomas T. Management of osteoporosis in fracture liaison service associated with long-term adherence to treatment. *Osteoporos Int.* 2011 Jul;22(7):2099-106.
  8. Chandran M, Tan MZW, Cheen M, Tan SB, Leong M, Lau TC. Secondary prevention of osteoporotic fractures—an “OPTIMAL” model of care from Singapore. *Osteoporos Int.* 2013 Nov;24(11):2809-17.
  9. Dehamchia-Rehailia N, Ursu D, Henry-Desailly I, Fardelone P, Paccou J. Secondary prevention of osteoporotic fractures: evaluation of the Amiens University Hospital's fracture liaison service between January 2010 and December 2011. *Osteoporos Int.* 2014 Oct;25(10):2409-16.
  10. Eekman DA, van Helden SH, Huisman AM, Verhaar HJJ, Bultink IEM, Geusens PP, et al. Optimizing fracture prevention: the fracture liaison service, an observational study. *Osteoporos Int.* 2014 Feb;25(2):701-9.
  11. Huntjens KMB, van Geel TACM, Blonk MC, Hegeman JH, van der Elst M, Willems P, et al. Implementation of osteoporosis guidelines: a survey of five large fracture liaison services in the Netherlands. *Osteoporos Int.* 2011;22(7):2129-35.
  12. Vaile JH, Sullivan L, Connor D, Bleasel JF. A Year of Fractures: a snapshot analysis of the logistics, problems and outcomes of a hospital-based fracture liaison service. *Osteoporos Int.* 2013 Oct;24(10):2619-25.
  13. Wallace I, Callachand F, Elliott J, Gardiner P. An evaluation of an enhanced fracture liaison service as the optimal model for secondary prevention of osteoporosis. *JRSM Short Rep.* 2011 Feb 10;2(2):8.
  14. Fraser M, McLellan AR. A fracture liaison service for patients with osteoporotic fractures. *Prof Nurse.* 2004 Jan;19(5):286-90.
  15. Mitchell PJ. Best practices in secondary fracture prevention: fracture liaison services. *Curr Osteoporos Rep.* 2013 Mar;11(1):52-60.
  16. McLellan AR, Wolowacz SE, Zimovetz EA, Beard SM, Lock S, McCrink L, et al. Fracture liaison services for the evaluation and management of patients with osteoporotic fracture: a cost-effectiveness evaluation based on data collected over 8 years of service provision. *Osteoporos Int.* 2011 Jul;22(7):2083-98.
  17. Makras P, Panagoulia M, Mari A, Rizou S, Lyritis GP. Evaluation of the first fracture liaison service in the Greek healthcare setting. *Arch Osteoporos.* 2017 Dec;12(1):3.
  18. World Health Organization. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis : report of a WHO study group [meeting held in Rome from 22 to 25 June 1992] [Internet]. World Health Organization; 1994 [cited 2022 Dec 11]. Available from: <https://apps.who.int/iris/handle/10665/39142>
  19. Schuit SCE, van der Klift M, Weel AE a. M, de Laet CEDH, Burger H, Seeman E, et al. Fracture incidence and association with bone mineral density in elderly men and women: the Rotterdam Study. *Bone.* 2004 Jan;34(1):195-202.
  20. Wainwright SA, Marshall LM, Ensrud KE, Cauley JA, Black DM, Hillier TA, et al. Hip fracture in women without osteoporosis. *J Clin Endocrinol Metab.* 2005 Dec;90(5):2787-93.
  21. Kanis JA, McCloskey EV, Johansson H, Strom O, Borgstrom F, Oden A, et al. Case finding for the management of osteoporosis with FRAX—assessment and intervention thresholds for the UK. *Osteoporos Int.* 2008 Oct;19(10):1395-408.
  22. Kanis JA, Harvey NC, Cooper C, Johansson H, Odén A, McCloskey EV, et al. A systematic review of intervention thresholds based on FRAX: A report prepared for the National Osteoporosis Guideline Group and the International Osteoporosis Foundation. *Arch Osteoporos.* 2016 Dec;11(1):25.
  23. Akesson K, Marsh D, Mitchell PJ, McLellan AR, Stenmark J, Pierroz DD, et al. Capture the Fracture: a Best Practice Framework and global campaign to break the fragility fracture cycle. *Osteoporos Int.* 2013 Aug;24(8):2135-52.
  24. Murray AW, McQuillan C, Kennon B, Gallacher SJ. Oste-



- oporosis risk assessment and treatment intervention after hip or shoulder fracture. A comparison of two centres in the United Kingdom. *Injury*. 2005 Sep;36(9):1080-4.
25. Van der Kallen J, Giles M, Cooper K, Gill K, Parker V, Tembo A, et al. A fracture prevention service reduces further fractures two years after incident minimal trauma fracture. *Int J Rheum Dis*. 2014 Feb;17(2):195-203.
  26. Gallacher SJ. Setting up an osteoporosis fracture liaison service: background and potential outcomes. *Best Pract Res Clin Rheumatol*. 2005 Dec;19(6):1081-94.
  27. Langridge CR, McQuillian C, Watson WS, Walker B, Mitchell L, Gallacher SJ. Refracture following fracture liaison service assessment illustrates the requirement for integrated falls and fracture services. *Calcif Tissue Int*. 2007 Aug;81(2):85-91.
  28. Seibel MJ. No more excuses: fracture liaison services work and are cost-effective. *Med J Aust* [Internet]. 2011 Nov 21 [cited 2022 Dec 2];195(10). Available from: <https://www.mja.com.au/journal/2011/195/10/no-more-excuses-fracture-liaison-services-work-and-are-cost-effective>
  29. Cooper MS, Palmer AJ, Seibel MJ. Cost-effectiveness of the Concord Minimal Trauma Fracture Liaison service, a prospective, controlled fracture prevention study. *Osteoporos Int*. 2012 Jan;23(1):97-107.
  30. Mitchell PJ. Fracture Liaison Services: the UK experience. *Osteoporos Int*. 2011 Aug;22 Suppl 3:487-94.
  31. Spencer D, Howe G, Manolios N. No more excuses: fracture liaison services work and are cost-effective. *Med J Aust*. 2012 Apr 2;196(6):384.
  32. Solomon DH, Patrick AR, Schousboe J, Losina E. The potential economic benefits of improved postfracture care: a cost-effectiveness analysis of a fracture liaison service in the US health-care system. *J Bone Miner Res*. 2014 Jul;29(7):1667-74.
  33. Bogduk N. No more excuses: fracture liaison services work and are cost-effective. *Med J Aust*. 2012 Aug 6;197(3):147.
  34. Kaufman JD, Bolander ME, Bunta AD, Edwards BJ, Fitzpatrick LA, Simonelli C. Barriers and solutions to osteoporosis care in patients with a hip fracture. *J Bone Joint Surg Am*. 2003 Sep;85(9):1837-43.
  35. Jaglal SB, Hawker G, Bansod V, Salbach NM, Zwarenstein M, Carroll J, et al. A demonstration project of a multi-component educational intervention to improve integrated post-fracture osteoporosis care in five rural communities in Ontario, Canada. *Osteoporos Int*. 2009 Feb;20(2):265-74.
  36. Bogoch ER, Elliot-Gibson V, Wang RYC, Josse RG. Secondary causes of osteoporosis in fracture patients. *J Orthop Trauma*. 2012 Sep;26(9):e145-152.
  37. Marsh D, Akesson K, Beaton DE, Bogoch ER, Boonen S, Brandi ML, et al. Coordinator-based systems for secondary prevention in fragility fracture patients. *Osteoporos Int*. 2011 Jul;22(7):2051-65.
  38. Tosi LL, Gliklich R, Kannan K, Koval KJ. The American Orthopaedic Association's "own the bone" initiative to prevent secondary fractures. *J Bone Joint Surg Am*. 2008 Jan;90(1):163-73.
  39. Lee D, Filler B, Twetten M. Enhancing fracture and osteoporosis care: implementing a fracture liaison service can improve outcomes, reduce costs. *AAOS Now*. 2013 Jan 1;30-1.
  40. Miller AN, Lake AF, Emory CL. Establishing a fracture liaison service: an orthopaedic approach. *J Bone Joint Surg Am*. 2015 Apr 15;97(8):675-81.
  41. Kanis JA, Johnell O, De Laet C, Johansson H, Oden A, Delmas P, et al. A meta-analysis of previous fracture and subsequent fracture risk. *Bone*. 2004 Aug;35(2):375-82.
  42. Feldstein A, Elmer PJ, Smith DH, Herson M, Orwoll E, Chen C, et al. Electronic medical record reminder improves osteoporosis management after a fracture: a randomized, controlled trial. *J Am Geriatr Soc*. 2006 Mar;54(3):450-7.
  43. Huntjens KMB, Kosar S, van Geel T a. CM, Geusens PP, Willems P, Kessels A, et al. Risk of subsequent fracture and mortality within 5 years after a non-vertebral fracture. *Osteoporos Int*. 2010 Dec;21(12):2075-82.
  44. Huntjens KMB, van Geel TACM, van den Bergh JPW, van Helden S, Willems P, Winkens B, et al. Fracture liaison service: impact on subsequent nonvertebral fracture incidence and mortality. *J Bone Joint Surg Am*. 2014 Feb 19;96(4):e29.
  45. van Helden S, Cals J, Kessels F, Brink P, Dinant GJ, Geusens P. Risk of new clinical fractures within 2 years following a fracture. *Osteoporos Int*. 2006;17(3):348-54.
  46. van den Bergh JP, van Geel TA, Geusens PP. Osteoporosis, frailty and fracture: implications for case finding and therapy. *Nat Rev Rheumatol*. 2012 Jan 17;8(3):163-72.
  47. Fuggle NR, Kassim Javaid M, Fujita M, Halbout P, Dawson-Hughes B, Rizzoli R, et al. Fracture Risk Assessment and How to Implement a Fracture Liaison Service. In: Falaschi P, Marsh D, editors. *Orthogeriatrics: The Management of Older Patients with Fragility Fractures* [In-

- ternet]. 2nd ed. Cham (CH): Springer; 2021 [cited 2022 Dec 11]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK565570/>
48. Mitchell RM, Jewell P, Javaid MK, McKean D, Ostlere SJ. Reporting of vertebral fragility fractures: can radiologists help reduce the number of hip fractures? *Arch Osteoporos.* 2017;12(1):71.
  49. Pandya J, Ganda K, Ridley L, Seibel MJ. Identification of Patients with Osteoporotic Vertebral Fractures via Simple Text Search of Routine Radiology Reports. *Calcif Tissue Int.* 2019 Aug;105(2):156–60.
  50. Vaculík J, Stepan JJ, Dungal P, Majerniček M, Čelko A, Džupa V. Secondary fracture prevention in hip fracture patients requires cooperation from general practitioners. *Arch Osteoporos.* 2017 Dec 18;12(1):49.
  51. Sherrington C, Fairhall NJ, Wallbank GK, Tiedemann A, Michaleff ZA, Howard K, et al. Exercise for preventing falls in older people living in the community. *Cochrane Database Syst Rev.* 2019 Jan 31;1(1):CD012424.
  52. Malgo F, Appelman-Dijkstra NM, Termaat MF, van der Heide HJL, Schipper IB, Rabelink TJ, et al. High prevalence of secondary factors for bone fragility in patients with a recent fracture independently of BMD. *Arch Osteoporos.* 2016;11(1):12.
  53. Gallagher JC, Sai A, Templin T, Smith L. Dose response to vitamin D supplementation in postmenopausal women: a randomized trial. *Ann Intern Med.* 2012 Mar 20;156(6):425–37.
  54. Burt LA, Billington EO, Rose MS, Raymond DA, Hanley DA, Boyd SK. Effect of High-Dose Vitamin D Supplementation on Volumetric Bone Density and Bone Strength: A Randomized Clinical Trial. *JAMA.* 2019 Aug 27;322(8):736–45.
  55. Brandrud AS, Nyen B, Hjortdahl P, Sandvik L, Helljesen Haldorsen GS, Bergli M, et al. Domains associated with successful quality improvement in healthcare – a nationwide case study. *BMC Health Services Research.* 2017 Sep 13;17(1):648.
  56. Mitchell PJ, Cooper C, Fujita M, Halbout P, Åkesson K, Costa M, et al. Quality Improvement Initiatives in Fragility Fracture Care and Prevention. *Curr Osteoporos Rep.* 2019 Dec;17(6):510–20.
  57. Makras P, Anastasilakis AD, Antypas G, Chronopoulos E, Kaskani EG, Matsouka A, et al. The 2018 Guidelines for the diagnosis and treatment of osteoporosis in Greece. *Arch Osteoporos.* 2019 Mar 15;14(1):39.
  58. Makras P, Vaiopoulos G, Lyritis GP, Greek National Medicine Agency. 2011 guidelines for the diagnosis and treatment of osteoporosis in Greece. *J Musculoskelet Neuronal Interact.* 2012 Mar;12(1):38–42.
  59. Makras P, Athanasakis K, Boubouchairopoulou N, Rizou S, Anastasilakis AD, Kyriopoulos J, et al. Cost-effective osteoporosis treatment thresholds in Greece. *Osteoporos Int.* 2015 Jul;26(7):1949–57.
  60. Makras P, Boubouchairopoulou N, Katsarolis I, Athanasakis K. Cost-effective osteoporosis treatment thresholds for people living with HIV infection in Greece. *J Musculoskelet Neuronal Interact.* 2017 Dec 1;17(4):292–8.
  61. Peacock E, Krousel-Wood M. Adherence to Antihypertensive Therapy. *Med Clin North Am.* 2017 Jan;101(1):229–45.
  62. Polonsky WH, Henry RR. Poor medication adherence in type 2 diabetes: recognizing the scope of the problem and its key contributors. *Patient Prefer Adherence.* 2016;10:1299–307.
  63. Munson JC, Bynum JPW, Bell JE, Cantu R, McDonough C, Wang Q, et al. Patterns of Prescription Drug Use Before and After Fragility Fracture. *JAMA Intern Med.* 2016 Oct 1;176(10):1531–8.
  64. Kanis JA, Svedbom A, Harvey N, McCloskey EV. The osteoporosis treatment gap. *J Bone Miner Res.* 2014 Sep;29(9):1926–8.
  65. The Lancet Diabetes Endocrinology null. Osteoporosis: a roadmap to close the treatment gap. *Lancet Diabetes Endocrinol.* 2018 Nov;6(11):833.
  66. Makras P, Babis GC, Chronopoulos E, Karachalios T, Kazakos K, Paridis D, Potoupnis M, Tzavellas AN, Valkanis C, Kosmidis C. Experience gained from the implementation of the fracture liaison service in Greece. *Arch Osteoporos.* 2020 Jan 3;15(1):12.