Joint Bone Spine 90 (2023) 105574

Contents lists available at ScienceDirect

Joint Bone Spine

journal homepage: www.elsevier.com

Review

Effectiveness of fracture liaison services in osteoporosis

Julien Paccou [a,*], Cécile Philippoteaux [b], Bernard Cortet [a], Patrice Fardellone [c]

[a] Department of Rheumatology, MABlab ULR 4490, Université de Lille, CHU de Lille, 59000 Lille, France
[b] Department of Rheumatology, CHU de Lille, 59000 Lille, France
[c] Department of Rheumatology, CHU d'Amiens, Unité EA MP3CV, Amiens, France

ARTICLE INFO

Article history:
Accepted 3 April 2023
Available online 18 April 2023

Keywords:
Fracture liaison service
Post-fracture care
Digital health

ABSTRACT

Background: In response to the gradual decline in the number of prescriptions for anti-osteoporosis medication (AOM) following fragility fractures, fracture liaison services (FLSs) have been set up around the world with the aim of filling this treatment gap. Several studies have already reported the benefits of such organizations, particularly in reducing fracture risk, mortality rates and healthcare costs, and literature on FLSs has increased at a steady pace over time.
Methods: A narrative review was conducted on the latest available findings on the effectiveness of FLSs. Various approaches to implementing an effective FLS program are discussed.
Results: FLS programs have enhanced the management of osteoporosis-related fractures. However, several studies have highlighted that not all FLSs are necessarily effective in reducing subsequent fracture risk and mortality. Long-term AOM persistence and monitoring are another critical issue in FLS programs. A few studies have reported that FLSs are associated with an improvement in AOM persistence, regardless of the type of AOM. Practitioners in the FLS setting need to be aware of the impact of recency of fracture and fracture recurrence rates, and the need for timely interventions. The administration of zoledronic acid in an in-patient setting may improve AOM treatment rates in patients, who often encounter obstacles to outpatient follow-up. Introducing 'vertebral fracture identification services' in FLS programs is also an option. However, doing so leads to an increase in workload and this would need to be considered by any FLS that is considering introducing such a service. Evidence suggests that digital technologies can support (i) multidisciplinary teams in providing the best possible patient care based on current evidence, and (ii) patient self-management. However, as the methodological quality of many of the studies evaluating these technologies was poor, their validity of their results is limited.
Conclusion: Further research should focus on the optimal implementation of post-fracture care using automated systems, and standardized reporting of patient's characteristics and outcome measures using key performance indicators.

1. Introduction

A fragility fracture is a significant event for patients and their relatives, and can lead to substantial changes in quality of life (QoL), disability, higher morbidity, and even higher mortality [1–3]. Despite effective treatments to reduce fracture risk, there has been a gradual decline in the number of prescriptions for anti-osteoporosis medication (AOM) over the last decades [4–6]. The most important reason for this gap is fear of rare side effects (e.g., atypical femur fractures and osteonecrosis of the jaw) and concerns regarding the long-term efficacy of the AOM both in osteoporosis patients and general practitioners. In response to this global phenomenon, fracture liaison services (FLS) have been set up around the world with the aim of filling this treatment gap [7–9]. The concept of the "FLS" – as a service led by an interdisciplinary team with a coordinator at its head – was specifically developed for the secondary prevention of fractures (Fig. 1). The first FLSs were set up in the 1990s [10] for the purpose of identifying patients with recent fractures, performing diagnostic workups [DXA scans, vertebral fracture (VF) identification, blood tests, etc.], and initiating treatment and sometimes follow-up with the aim of reducing subsequent fracture risk.

Several hybrid service solutions, such as orthogeriatric units, have since emerged and qualify as post-fracture care (PFC) services,

* Corresponding author.
E-mail address: julien.paccou@chru-lille.fr (J. Paccou).

https://doi.org/10.1016/j.jbspin.2023.105574
1297-319X/

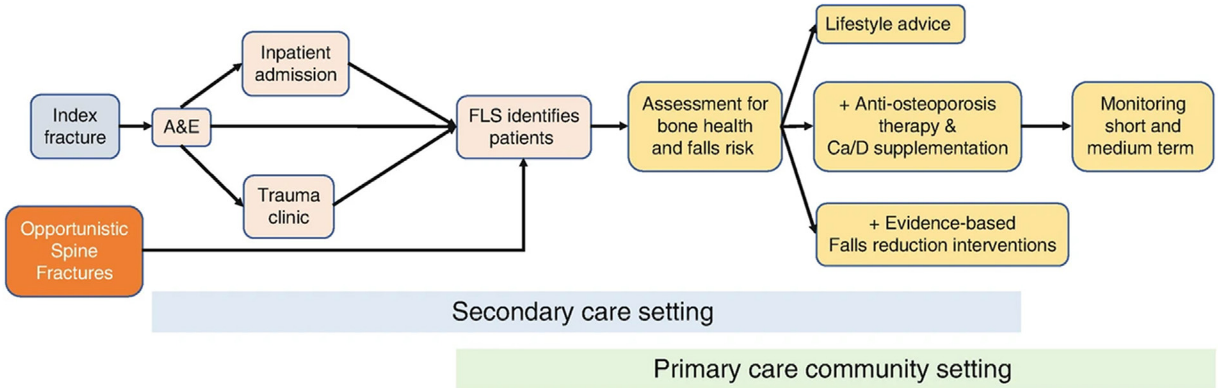

Fig. 1. An example of a fracture liaison service model in the United Kingdom. [This figure is reuse from https://www.researchgate.net/figure/An-example-of-a-Fracture-Liaison-Service-model-in-the-United-Kingdom_fig2_343795362. This work is licensed under a Creative Commons Attribution 4.0 International License (https://creativecommons.org/licenses/by/4.0/)].

Box 1: Capture the fracture best practice framework

The 13 Capture the Fracture Best Practice Standards are:

1. Patient identification standard
2. Patient evaluation standard
3. Post-fracture assessment timing standard
4. Vertebral fracture standard
5. Assessment guidelines standard
6. Secondary causes of osteoporosis standard
7. Falls prevention services standard
8. Multifaceted health and lifestyle risk-factor assessment standard
9. Medication initiation standard
10. Medication review standard
11. Communication strategy standard
12. Long-term management standard
13. Database standard

of which FLSs are an example. FLS implementation has been supported by the International Osteoporosis Foundation (IOF) through its secondary prevention program called Capture the Fracture (CTF), which was launched in 2012 [11]. Through this program, FLSs can be mapped (already 800 FLSs in 51 countries), and the Best Practices Framework (BPF) serves as the IOF's measurement tool for awarding 'CTF Best Practice Recognition' based on 13 globally endorsed criteria ranging from 'patient identification' to 'database' (Box 1). It has been a positive step towards standardizing FLS processes and outcomes.

While it is acknowledged that FLS programs share common features, there are also many differences among them. As such, each FLS is unique in terms of how it is organized and its relationship with local stakeholders. In a systematic review conducted in 2013, the authors divided interventions into four care models based on 'intervention intensity', ranging from A (identification, assessment, treatment initiation) to D (education of patient only). It was demonstrated that more intensive care models exhibit better outcomes [12]. To summarize, the most effective FLS programs implement the '5 I' approach (identify, inform, investigate, initiate AOM, and iterate).

Notwithstanding the heterogeneous nature of FLS programs, several studies have already reported the benefits of such organizations, particularly in reducing fracture risk, mortality rates and healthcare costs [13–15]. Literature on FLSs has increased at a steady pace over time and this review focuses on the latest available findings on the effectiveness of FLSs, and discusses various approaches to implementing an effective FLS program.

2. Methods

A systematic search of the literature published in the English Language between January 1, 2021, and November 30, 2022, was conducted. The search term was 'fracture liaison service'. The initial search returned 146 articles. All relevant studies, including editorials, observational studies, randomized and non-randomized trials and existing systematic and narrative reviews were included. Case reports and conference proceedings were excluded. Ultimately, 26 articles were selected for this review.

3. Fracture liaison services as clinically- and cost-effective initiatives

3.1. *Effectiveness in reducing subsequent fracture risk and mortality*

Overall, FLSs were found to improve DXA scanning rates and the number of prescriptions for AOM, while at the same time reducing the rates of new fractures and mortality. The effectiveness of FLSs in reducing the number of subsequent fractures and mortality rates has been summarized in several reviews, albeit with variable impacts on these two outcomes [16–18].

However, studies on the effectiveness of FLSs in reducing subsequent fracture risk are heterogeneous in terms of length of follow-up, study design, study population, and the classifications of groups of fractures. Moreover, most previous studies did not apply a competing mortality risk analysis when analyzing subsequent fracture risk [19].

In a systematic literature review (conducted between January 1, 2010, and April 30, 2020) and meta-analysis, Li et al. evaluated the impact of FLSs on subsequent fractures and mortality [20–22]. Twelve studies compared outcomes before (pre-FLS) and after (post-FLS) FLS implementation, 2 studies compared outcomes between hospitals with and without FLS, and a further 2 studies performed both comparisons. Follow-up times ranged from 6 months to 4 years. The meta-analysis of 9 comparisons (in 8 papers) revealed that FLS care was associated with a significantly lower probability of subsequent fractures (odds ratio [OR] 0.70; 95% confidence interval [CI]: 0.52–0.93). No significant differences in the odds of mortality were observed (OR: 0.73, 95% CI: 0.49–1.09, $P = 0.12$) in the meta-analysis of 8 comparisons (in 7 papers).

In a recently published study (comparing post-FLS and pre-FLS outcomes), Vranken et al. [23] investigated whether FLS care was associated with a reduction in subsequent fracture and mortality risk within 3 years of a major/hip (pelvis, proximal humerus or tibia, vertebral, multiple ribs, distal femur) or non-major/non-hip index fracture. The pre-FLS group consisted of 2530 patients (72% women), of whom 1188 (46.9%) had major/hip index fractures. The post-FLS group consisted of 6152 patients (69% women), of whom 2973 (48.3%) had major/hip index fractures. The authors found that FLS care was associated with lower mortality risk within the first 3 years (HR: 0.84; 95% CI: 0.73–0.96) and lower subsequent major/hip fracture risk within the first year (subdistribution hazard [SHR] approach 0.67; 95% CI: 0.52–0.87) in patients with a major/hip index fracture, but not in patients with a non-major/non-hip fracture (all other fractures) [23].

A prospective observational cohort study was conducted on patients over 60 years of age who sustained a hip fracture within 3 consecutive years, before and after the implementation of an FLS ($n = 357$ before, and $n = 744$ after) [24]. In patients included after the implementation of the FLS protocol, compared with those included before the implementation of the FLS protocol, the Cox proportional hazard model showed that the adjusted 1-year and 2-year HRs for all-cause mortality were 0.76 (95% CI: 0.58–0.98) and 0.87 (95% CI: 0.69–1.09), respectively. In total, 336 patients (30.5%) died during the 2-year follow-up period: 114 patients (31.9%) before and 222 patients (29.8%) after FLS implementation ($P = 0.44$). Moreover, implementing the FLS protocol did not affect the risk of sustaining a second major osteoporotic fracture (i.e., contralateral hip, distal radius, proximal humerus, and vertebral fractures). The lower mortality rate in the first year could be related to the type of intervention, such as fall-risk interventions and stimulating a healthy lifestyle, whereas a lack of adherence to AOM could explain the absence of a favorable effect on mortality in the second year (only 30.5% of patients adhered to AOM after the introduction of the FLS protocol) [24].

FLS programs have enhanced the management of osteoporosis-related fractures, have shown their clinical effectiveness, and have minimized the burden of this disease. However, several studies have highlighted that not all FLSs are necessarily effective in reducing subsequent fracture risk and mortality.

3.2. Effectiveness in improving AOM persistence

Medication persistence is the interval of time from initiation to discontinuation of therapy, as measured by a time metric. Medication compliance (also known as adherence) refers to the proportion of prescribed medication taken within a specific time interval. A commonly used measure of adherence is the mean medication possession ratio (MPR) [25].

Persistence with AOM is known to be poor in osteoporosis patients, and persistence rates have been reported to decline to less than 50% over a 12-month period [26,27]. A retrospective cohort study (FRACTOS) using the French national healthcare database showed that treatment persistence following an index severe osteoporotic fracture was 49.0% at 12 months, 31.7% at 2 years, and 12.9% at 3 years [27]. Several studies have sought to evaluate the impact of FLSs on persistence, and the results are unequivocal: FLSs are associated with a marked improvement in persistence [28,29].

In a recently published prospective study ($n = 888$; mean age: 75 years; women: 83%; mean follow-up: 56 months), Naranjo et al. concluded that AOM persistence in their FLS after a mean follow-up of 5 years was around 46.5%, i.e., double what has been observed in non-FLS studies [30,31]. In that study, the patients were mainly treated with oral bisphosphonates (62.2%). However, oral bisphosphonates are the main treatment prescribed in most FLSs, and data were lacking on long-term persistence with injectable osteoporosis treatments (zoledronic acid, teriparatide and denosumab). In a study conducted by Delbar et al., treatment persistence (any class) was estimated at 84.1% (95% CI: 79.1% to 88.1%) at 12-month follow-up, and dropped to 70.3% (95% CI: 63.7% to 75.9%) at 24 months [32]. When drug-specific analyses were performed, persistence rates were found to be higher with denosumab than with any other treatment: 97.1% (95% CI: 81.4% to 99.6%) and 91.1% (95% CI: 74.8% to 97.0%) for denosumab at 12 and 24 months, respectively [32].

Long-term AOM persistence and monitoring are another critical issue in FLS programs. FLSs are associated with an improvement in persistence, regardless of the type of AOM.

3.3. Effectiveness in improving health-related QoL

Morbidity and mortality following a fracture are important clinical considerations, as is the substantial loss of patients' QoL. Health state utility value (HSUV) measures are a specific set of health-related QoL instruments. In fracture research, many studies have investigated HSUVs in patients. For example, the large ICUROS study reported that fractures resulted in substantial QoL loss immediately after fracture, and that QoL improved after 4 months but did not return to pre-fracture levels [33]. In 2014, a meta-analysis identified 62 studies that reported HSUVs after hip, vertebral, or distal forearm fractures [34]. Until now, very few studies have investigated QoL in patients with fractures attending an FLS [35,36], especially the course of HSUVs in the long-term.

In a recent study [37], the authors investigated the course of HSUVs in 499 patients (mean age: 64.6 ± 8.6 years; females: 71.3%) with a recent fracture – 26.7% had at least one vertebral fracture (VF) – presenting at an FLS in the Netherlands. Health state utility value was measured over a 3-year follow-up using two generic preference-based instruments: the EuroQol (EQ-5D-5L) and the Short Form Health Survey (SF-36). When EQ-5D data were considered, no significant changes were observed over 3 years, although a small but statistically significant improvement was observed at 6 and 12 months compared to baseline HSUV. The lack of patients' QoL data immediately after fracture was a main limitation of this study. Additionally, patients attended the FLS on average 107 days after their index fracture, which is quite late.

Data on QoL improvement in patients attending an FLS are scarce, and further studies on this outcome are needed to draw definitive conclusions.

3.4. Cost-effectiveness of FLS programs

A significant body of evidence collected over time has shown that FLS programs are effective in reducing healthcare costs. Due to restrictions on the length of the manuscript and reference list, the reader is also referred to the recent publications on the cost-effectiveness of FLS programs [38–41].

4. Approaches to implementing an effective FLS program

4.1. Prompt initiation of AOM to reduce imminent fracture risk

After a sentinel fracture, the risk of re-fracture is high, and up to 50% of the 10-year risk is compressed into the first two years post-fracture. Hence the term, "imminent fracture risk" [42]. Practitioners in the FLS setting need to be aware of the impact of recency of fracture and fracture recurrence rates, and the need for timely interventions. The ability to stratify risk and enable treatment decisions without BMD measurement in some very high-risk patients could become a standard practice in FLSs. Tracking the interval of time from sentinel fracture to initiation of AOM is within the control of FLS, and from a system-related perspective, the goal is to minimize the number of steps that high fracture risk patients need to negotiate before receiving AOM [42].

In a recently published study, Fan et al. concluded that integrating FLS and orthopedic services with in-patient zoledronic acid (ZA) administration improved AOM prescription rates in patients with fragility fractures, who often encounter obstacles to out-patient follow-up [43]. The authors included 1240 FLS in-patients seen between February 1, 2016, and December 30, 2019. Hip fractures occurred in 739 of the 1240 patients (60%). Of the 114 patients who received in-patient AOM, 108 were given ZA. In-patient ZA administration affected neither the average length of stay, nor the 30-day readmission rate. The infusion of ZA during hospitalization for the index fracture led to a 70% increase in treatment rate, compared to a baseline rate of 8% to 11% [43].

4.2. Integration of vertebral fracture identification in FLS programs

Integrating VF identification in FLS programs is another challenge. Two different aspects have been recently addressed in the literature: (i) the use of DXA vertebral fracture assessment (VFA) in all FLS patients with non-vertebral fractures [44,45], and (ii) the use of routine clinical computed tomography (CT) imaging to screen for VFs, with the aim of including these patients in the FLS [46,47].

In a position paper published by the IOF Fracture Working Group, Lems et al. advocated that DXA-VFA be performed in all FLS patients [44]:

- to detect subclinical VFs, which may lead to a change in risk category, and thus initiation or type and duration of AOM, depending on age and local criteria for intervention;
- to provide a baseline assessment, which can be used to discriminate between later incident VFs and prevalent VFs, which is critical to optimal treatment monitoring.

Only a small number of studies have been conducted on the added value of VFA in patients with a non-vertebral fracture and a DXA-measurement. Two FLS studies have already shown that VFs can be detected in around 20% of patients, and that VF detection impacts treatment in around 10% of patients [48,49].

In a recent (non-FLS) registry-based cohort study conducted in Manitoba, Canada from 2010 to 2018 [45], DXA-VFA was performed in patients with T-scores below −1.5, aged 70+ years (or younger with height loss or glucocorticoid use). The cohort consisted of 12,756 patients (women: 94.4%; mean age: 75.9 years) and VFs were identified in 1925 patients (15.1%) overall. The VFA was positive for undiagnosed VFs in 20.2% of the patients with a prior fracture ($n = 3729$), as opposed to 13.0% in those without fracture ($n = 9027$). Prior hip, humerus, pelvis, forearm, and other fractures, but not ankle fractures, were associated with a greater likelihood of previously undetected VFs [45].

Studies have shown that introducing DXA-VFA in FLS programs is feasible. However, it still remains to be determined whether DXA-VFA should be routinely performed in all FLS patients with non-vertebral fractures, or limited to patients fulfilling current International Society for Clinical Densitometry (ISCD), National Osteoporosis Foundation (NOF) and IOF indication criteria.

Several other techniques exist that might be usefully incorporated into a comprehensive strategy for VF detection in FLS programs. One technique that could be used for VF case detection is computed tomography (CT). While CT scans of the thorax, pelvis and abdomen often include spinal elements, VFs may be present without being identified or reported. Indeed, it has been estimated that only 13–16% of retrospectively confirmed VFs on CT scans are reported, probably because they are incidental findings and not the primary purpose for the investigation.

In a quality improvement project, a VF identification service (Optasia Medical, OM) was incorporated with routine CT scans performed in a UK teaching hospital as part of its FLS [46]. Vertebral fractures were prospectively identified using OM's machine learning algorithm and crosschecked by the OM radiologist. In total, 4461 patients with CT scans were assessed over a 3-month period. VFs were identified in 850 patients (19.1%). The average number of patients per week with identified VFs was 61 (range: 19–95). Vertebral fractures were reported in only 416 patients (48.9%). The median (IQR) number of identified VFs was 2.

In another study, the prevalence of VFs in CT scans of patients aged 45 years and older with long-term hospital records (at least 5 years) was investigated (between September 2008 and May 2017) [47]. Vertebral fractures were retrospectively identified by 2 radiologists. The study population consisted of 718 patients (228 women and 490 men; mean age 69.3 ± 10.1 years) and the overall prevalence of VFs was 30.5%. Scan reports mentioned a VF in only 24.7% of patients with a prevalent VF.

Integrating a 'vertebral fracture identification service' in a FLS program is possible. Approximately one in five CT scans detect an individual with a fracture. However, this increase in workload needs to be considered by any FLS considering introducing such a service.

4.3. Delegating denosumab adherence management to pharmacists

Poor adherence to AOM is a major concern, particularly with denosumab. In a recent retrospective study, the authors compared 2 models of adherence to 6-monthly at-home denosumab injections. The only difference between the two models was that, in the 1st model, ultimate responsibility for adherence lay with the prescriber, whereas in the second model, ultimate responsibility lay with the pharmacist. It was possible to achieve 94% adherence for denosumab injections [time limit $\leq$ 30 days; mean number of injections = 1.8 (1.0)] just by transferring the complete supply chain to one pharmacy-initiated homecare provider after AOM initiation [50].

4.4. Digital health

While FLS have been proven to significantly enhance osteoporosis care, such programs might benefit from digital technologies that enhance automation. In a rapid review of evidence from the Technology Working Group of the Royal Osteoporosis Society and Bone Research Academy, Gupta et al. explored potential uses of digital technologies in the general management of osteoporosis, and more specifically in the context of FLSs [51]. In the field of osteoporosis care, such technologies – referred to collectively as 'digital health' technologies – encompass the following:

- electronic patient records;
- clinical decision support systems (CDSSs);
- decision aids for patients;
- digital health-supported patient communication;
- electronic mobile applications;
- E-Triage;
- E-Consult systems;
- digitally delivered osteoporosis education for clinicians;
- information for patients;
- artificial intelligence (AI) approaches to case findings and image analysis.

While the FRAX online calculator is the most obvious osteoporosis-specific application of digital health, tools such as the FLS Database (FLS-DB), comprising reminders, risk assessments, and educational material, are good examples of digital health technologies used to support PFC. Moreover, FLS-DB is used to measure the volume and quality of care in secondary fracture prevention delivery across England and Wales using 11 key performance indicators (KPIs) [52].

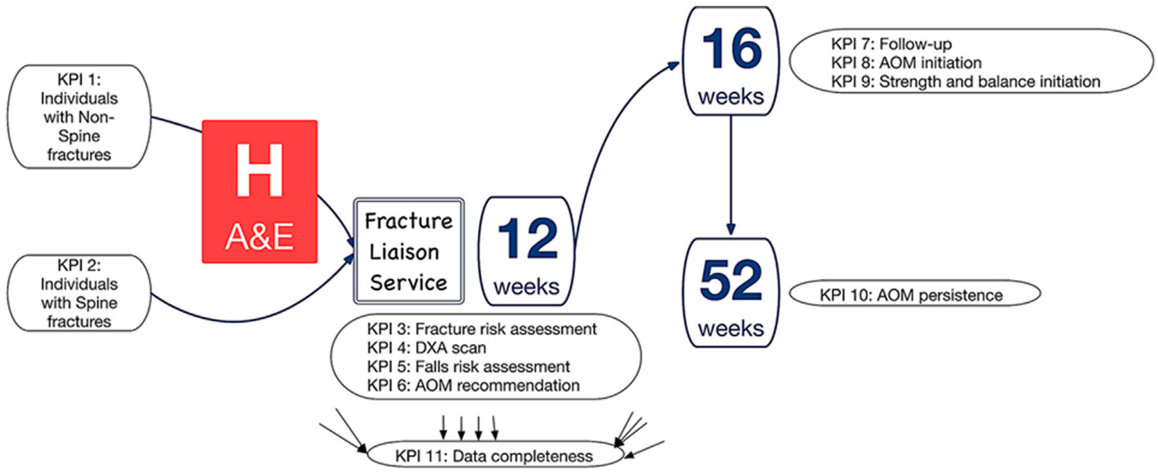

Fig. 2. International Osteoporosis Foundation (IOF)/Fragility Fracture Network (FFN)/National Osteoporosis Foundation (NOF) indicator set. This figure is reuse from [56], with permission (We thank Springer Nature for this permission).

Furthermore, automated software could assist FLS programs in detecting more at-risk people than traditional case finding. Two electronic search tools – automated electronic search (AES) and the X-ray Artificial Intelligence Tool (XRAIT) – that screen medical records and/or radiology reports for documented fractures were assessed to determine their effectiveness in detecting patients with fragility fracture [53]. Each tool was used for 6 months at two tertiary hospitals in Sydney, Australia. A random sample of patients detected using the search tools was then manually analyzed by researchers. At the two centers, AES detected 872 and 1364 cases with fractures, respectively, whereas XRAIT detected 1414 and 2180 patients with fractures, respectively. Both tools captured a large volume of patients with "any fracture". However, the positive predictive value in detecting fragility fractures differed between AES and XRAIT, and subsets of patients with a known fragility fracture were missed by both tools. In a previous publication [54], XTRAIT was compared with a traditional FLS identification strategy. Over a 3-month period, XTRAIT detected three times more fractures (421 fractures/339 individuals) than manual case finding (98 individuals).

Artificial intelligence methods for image analysis were not addressed in the review of evidence from the Technology Working Group of the Royal Osteoporosis Society and Bone Research Academy [51]. However, large-scale screening for VFs using dedicated automated software during opportunistic screening seems feasible [46,55].

Evidence suggests that digital technologies can support (i) multidisciplinary teams in providing the best possible patient care based on current evidence, and (ii) patients in self-management. However, as the methodological quality of many of the studies evaluating these technologies was poor, their validity is limited.

The digital modification of healthcare has featured several challenges that affect especially medical professionals and patients. Challenges relate to concerns ranging from data interoperability to issues related to data access, storage, ownership and sharing. These concerns raise also security and privacy questions. Moreover, the evidence regarding the cost-effectiveness of digital tools in health remains scarce and limited.

4.5. Quality improvement process

The IOF Capture the Fracture® Campaign, conducted with the Fragility Fracture Network (FFN) and the NOF, has developed 11 patient-level KPIs for FLSs to track quality improvement (Fig. 2) [56]. The 11 KPIs are an adaptation of an existing KPI set from the UK-based FLS-DB Audit [51]. Using the IOF-FFN-NOF KPI set, FLS should be able to improve clinical outcomes for their local populations. To illustrate the usefulness of the IOF-FFN-NOF KPI set, a new registry (REFRA-FLS) was created in Spain to monitor the performance of different types of FLSs [57]. The results of the study highlight the benefits of establishing a nationwide computerized registry – such as the REFRA-FLS registry – to monitor the performance of different types of FLSs.

LYOSIS® is a new digital tool that has been endorsed by the IOF. This bone KPI capture and monitoring tool is now available and should help FLSs improve the effectiveness of their programs.

5. Conclusions

FLSs are the most effective secondary fracture prevention model of care for managing osteoporosis following fragility fractures. Overall, FLSs have demonstrated their ability to reduce the incidence of new fractures with a favorable cost-effectiveness ratio. However, several studies have highlighted that not all FLSs are necessarily effective, and studies on the effectiveness of FLS programs are heterogeneous in design and study population. Furthermore, we have to keep in mind that each FLS is unique and the heterogeneous nature of FLS programs makes difficult the conduction of meta-analysis.

Instead of focusing efforts on building randomized controlled studies to determine the efficacy of FLS protocols, further research should focus on the optimal implementation of PFC using automated systems, and standardized reporting of patient's characteristics and outcome measures, as described in the IOF Capture the Fracture KPI set.

Disclosure of interest

Prof. Julien Paccou received research funding from MSD and honoraria for lectures from Amgen, UCB, Sandoz, Novartis, Theramex and Eli Lilly.

Dr. Cécile Philippoteaux declares that she has no competing interest.

Prof. Bernard Cortet received honoraria for lectures from Amgen, Lilly, Viatris, MSD, Novartis, Theramex, UCB, Alexion and Kyowa-Kirin.

Prof. Patrice Fardellone received honoraria for lectures from Amgen, Expanscience, Lilly, Viatris, Theramex and UCB.

References

[1] Bliuc D, Nguyen ND, Milch VE, et al. Mortality risk associated with low-trauma osteoporotic fracture and subsequent fracture in men and women. JAMA 2009;301:513–21.
[2] Cooper C. The crippling consequences of fractures and their impact on quality of life. Am J Med 1997;103:S12–9.
[3] Haleem S, Lutchman L, Mayahi R, et al. Mortality following hip fracture: trends and geographical variations over the last 40 years. Injury 2008;39:1157–63.
[4] Klop C, Gibson-Smith D, Elders PJ, et al. Anti-osteoporosis drug prescribing after hip fracture in the UK: 2000–2010. Osteoporos Int 2015;26:1919–28.
[5] Solomon DH, Johnston SS, Boytsov NN, et al. Osteoporosis medication use after hip fracture in US patients between 2002 and 2011. J Bone Miner Res 2014;29:1929–37.
[6] Skjødt MK, Khalid S, Ernst M, et al. Secular trends in the initiation of therapy in secondary fracture prevention in Europe: a multi-national cohort study including data from Denmark, Catalonia, and the United Kingdom. Osteoporos Int 2020;31:1535–44.
[7] Naranjo A, Ojeda-Bruno S, Bilbao-Cantarero A, et al. Two-year adherence to treatment and associated factors in a fracture liaison service in Spain. Osteoporos Int 2015;26:2579–85.
[8] Boudou L, Gerbay B, Chopin F, et al. Management of osteoporosis in fracture liaison service associated with long-term adherence to treatment. Osteoporos Int 2011;22:2099–106.
[9] Dehamchia-Rehailia N, Ursu D, Henry-Desailly I, et al. Secondary prevention of osteoporotic fractures: evaluation of the Amiens University Hospital's fracture liaison service between January 2010 and December 2011. Osteoporos Int 2014;25:2409–16.
[10] Gallacher SJ. Setting up an osteoporosis fracture liaison service: background and potential outcomes. Best Pract Res Clin Rheumatol 2005;19:1081–94.
[11] A°kesson K, Marsh D, Mitchell PJ, et al. Capture the Fracture: a Best Practice Framework and global campaign to break the fragility fracture cycle. Osteoporos Int 2013;24:2135–52.
[12] Ganda K, Puech M, Chen JS, et al. Models of care for the secondary prevention of osteoporotic fractures: a systematic review and meta-analysis. Osteoporos Int 2013;24:393–406.
[13] Axelsson KF, Johansson H, Lundh D, et al. Association between recurrent fracture risk and implementation of fracture liaison services in four Swedish hospitals – A cohort study. J Bone Miner Res 2020;35:1216–23.
[14] Nakayama A, Major G, Holliday E, et al. Evidence of effectiveness of a fracture liaison service to reduce the re-fracture rate. Osteoporos Int 2016;27: 873–9.
[15] Wu CH, Tu ST, Chang YF, et al. Fracture liaison services improve outcomes of patients with osteoporosis-related fractures: a systematic literature review and meta-analysis. Bone 2018;111:92–100.
[16] Sanli I, van Helden SH, Ten Broeke RHM, et al. The role of the fracture liaison service (FLS) in subsequent fracture prevention in the extreme elderly. Aging Clin Exp Res 2019;31:1105–11.
[17] Beaton DE, Mamdani M, Zheng H, et al. Improvements in osteoporosis testing and care are found following the wide scale implementation of the Ontario fracture clinic screening program: an interrupted time series analysis. Medicine 2017;96:e9012.
[18] Breuil V. Making sure the first osteoporotic fracture is also the last. Joint Bone Spine 2020;87:9–11.
[19] Javaid K. Efficacy and efficiency of fracture liaison services to reduce the risk of recurrent osteoporotic fractures. Aging Clin Exp Res 2021;33:2061–7.
[20] Li N, Hiligsmann M, Boonen A, et al. The impact of fracture liaison services on subsequent fractures and mortality: a systematic literature review and meta-analysis. Osteoporos Int 2021;32:1517–30.
[21] Ganda K. Fracture liaison services: past, present and future: Editorial relating to: the impact of Fracture Liaison Services on subsequent fractures and mortality: a systematic literature review and meta-analysis. Osteoporos Int 2021;32:1461–4.
[22] Lems WF, van den Bergh JP, Geusens PPMM. The fracture liaison service, a step forward not only in fracture reduction, but also in mortality reduction. Osteoporos Int 2022;33:1639–40.
[23] Vranken L, de Bruin IJA, Driessen AHM, et al. Decreased mortality and subsequent fracture risk in patients with a major and hip fracture after the introduction of a fracture liaison service: a 3-year follow-up survey. J Bone Miner Res 2022;37:2025–32.
[24] González-Quevedo D, Pérez-Del-Río V, Moriel-Garceso D, et al. A 2-year follow-up of a novel Fracture Liaison Service: can we reduce the mortality in elderly hip fracture patients? A prospective cohort study. Osteoporos Int 2022;33:1695–702.
[25] https://www.ispor.org/member-groups/special-interest-groups/medication-adherence-and-persistence.
[26] Durden E, Pinto L, Lopez-Gonzalez L, et al. Two-year persistence and compliance with osteoporosis therapies among postmenopausal women in a commercially insured population in the United States. Arch Osteoporos 2017;12:22.
[27] Roux C, Thomas T, Paccou J, et al. Refracture and mortality following hospitalization for severe osteoporotic fractures: the Fractos Study. JBMR Plus 2021;5:e10507.
[28] Eekman DA, van Helden SH, Huisman AM, et al. Optimizing fracture prevention: the Fracture Liaison Service, an observational study. Osteoporos Int 2014;25:701–9.
[29] Majumdar SR, Johnson JA, Lier DA, et al. Persistence, reproducibility, and cost-effectiveness of an intervention to improve the quality of osteoporosis care after a fracture of the wrist: results of a controlled trial. Osteoporos Int 2007;18:261–70.
[30] Naranjo A, Molina A, Quevedo A, et al. Fracture liaison service model: treatment persistence 5 years later. Arch Osteoporos 2021;16:60.
[31] Naranjo A, Molina A, Quevedo A, et al. Long-term persistence of treatment after hip fracture in a fracture liaison service. Sci Rep 2022;12:9373.
[32] Delbar A, Pflimlin A, Delabrière I, et al. Persistence with osteoporosis treatment in patients from the Lille University Hospital Fracture Liaison Service. Bone 2021;144:115838.
[33] Svedbom A, Borgström F, Hernlund E, et al. Quality of life after hip, vertebral, and distal forearm fragility fractures measured using the EQ-5D-3L, EQ-VAS, and time-trade-off: results from the ICUROS. Qual Life Res 2018;27:707–16.
[34] Si L, Winzenberg TM, De Graaff B, et al. A systematic review and meta-analysis of utility-based quality of life for osteoporosis-related conditions. Osteoporos Int 2014;25:1987–97.
[35] Singh S, Whitehurst DG, Funnell L, et al. Breaking the cycle of recurrent fracture: implementing the first fracture liaison service (FLS) in British Columbia, Canada. Arch Osteoporos 2019;14:116.
[36] Inderjeeth CA, Raymond WD, Briggs AM, et al. Implementation of the Western Australian Osteoporosis Model of Care: a fracture liaison service utilising emergency department information systems to identify patients with fragility fracture to improve current practice and reduce re-fracture rates: a 12-month analysis. Osteoporos Int 2018;29:1759–70.
[37] Li N, van Oostwaard M, van den Bergh JP, et al. Health-related quality of life of patients with a recent fracture attending a fracture liaison service: a 3-year follow-up study. Osteoporos Int 2022;33:577–88.
[38] Lüthje P, Nurmi-Lüthje I, Tavast N, et al. Evaluation of minimal fracture liaison service resource: costs and survival in secondary fracture prevention-a prospective one-year study in South-Finland. Aging Clin Exp Res 2021;33:3015–27.
[39] Senay A, Fernandes JC, Delisle J, et al. Patient healthcare trajectory and its impact on the cost-effectiveness of fracture liaison services. J Bone Miner Res 2021;36:459–68.
[40] Nayak S, Singer A, Greenspan SL. Cost-effectiveness of secondary fracture prevention intervention for Medicare beneficiaries. J Am Geriatr Soc 2021;69:3435–44.
[41] Saunders H, Sujic R, Bogoch ER, et al. Cost-utility analysis of the Ontario fracture screening and prevention program. J Bone Joint Surg Am 2021;103:1175–83.
[42] Javaid MK, Harvey NC, McCloskey EV, et al. Assessment and management of imminent fracture risk in the setting of the fracture liaison service. Osteoporos Int 2022;33:1185–9.
[43] Fan W, Machado M, Leder BZ, et al. Inpatient zoledronic acid and integrated orthopedic and fracture liaison services improve osteoporosis treatment rates. J Clin Endocrinol Metab 2022;108:191–7.
[44] Lems WF, Paccou J, Zhang J, et al. Vertebral fracture: epidemiology, impact, and use of DXA vertebral fracture assessment in fracture liaison services. Osteoporos Int 2021;32:399–411.
[45] Binkley N, Schousboe JT, Lix LM, et al. Should vertebral fracture assessment be performed in Fracture Liaison Service patients with non-vertebral fracture? Osteoporos Int 2023;34:129–35.
[46] Ong T, Copeland R, Thiam CN, et al. Integration of a vertebral fracture identification service into a fracture liaison service: a quality improvement project. Osteoporos Int 2021;32:921–6.
[47] Löffler MT, Kallweit M, Niederreiter E, et al. Epidemiology and reporting of osteoporotic vertebral fractures in patients with long-term hospital records based on routine clinical CT imaging. Osteoporos Int 2022;33:685–94.
[48] Gallacher SJ, Gallagher AP, McQuillian C, et al. The prevalence of vertebral fracture amongst patients presenting with non-vertebral fractures. Osteoporos Int 2007;18:185–92.
[49] Aboudiab M, Grados F, Batteux B, et al. Vertebral fracture assessment (VFA) in patients over 50 years of age with a non-severe peripheral fracture. Osteoporos Int 2020;31:1477–86.
[50] van den Berg P, Sluiter E, Oosterveld MH, et al. Single pharmacy governed denosumab home administration: optimal adherence by means of a fracture liaison service (FLS) and home care collaboration. Osteoporos Int 2022;33:881–7.
[51] Gupta A, Maslen C, Vindlacheruvu M, et al. Digital health interventions for osteoporosis and post-fragility fracture care. Ther Adv Musculoskelet Dis 2022;14 [1759720X221083523].
[52] https://www.rcplondon.ac.uk/projects/outputs/fls-db-methodology.
[53] Blaker K, Wijewardene A, White E, et al. Electronic search programs are effective in identifying patients with minimal trauma fractures. Osteoporos Int 2022;33:435–41.
[54] Kolanu N, Brown AS, Beech A, et al. Natural language processing of radiology reports for the identification of patients with fracture. Arch Osteoporos 2021;16:6.
[55] Roux C, Rozes A, Reizine D, et al. Fully automated opportunistic screening of vertebral fractures and osteoporosis on more than 150,000 routine computed tomography scans. Rheumatology (Oxford) 2022;61:3269–78.
[56] Javaid MK, Sami A, Lems W, et al. A patient-level key performance indicator set to measure the effectiveness of fracture liaison services and guide quality improvement: a position paper of the IOF Capture the Fracture Working Group, National Osteoporosis Foundation and Fragility Fracture Network. Osteoporos Int 2020;31:1193–204.
[57] Montoya-Garcia MJ, Carbonell-Abella C, Cancio-Trujillo JM, et al. Spanish National Registry of Major Osteoporotic Fractures (REFRA) seen at Fracture Liaison Services (FLS): objectives and quality standards. Arch Osteoporos 2022;17:138.