Does Fracture Liaison Service Improves Fracture Risk Assessment among Patients with Fragility Fractures? A Systematic Review

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Protocol

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Abstract

Background:

The fragility fractures can cause substantial pain, disability, reduced quality of life and mortality. The probability of sustaining subsequent fractures increases up to five times after an initial fragility fracture. The Fracture Liaison Service is a coordinated model of care that aims to bridge the post-fracture care gap by improving subsequent fracture risk assessment and post-fracture management. However, there are very few studies that included fracture risk assessment as a significant outcome of an FLS program. This systematic review aims to evaluate the available evidence on the effect of FLS in improving fracture risk assessment among fragility fracture patients

Method:

A systematic literature search will be carried out on the major electronic databases including PubMed, Embase, CINAHL Plus, and Cochrane to identify the outcomes of Fracture Liaison Service. The literature search will not be restricted to the context and year of publication. Two researchers will independently conduct the databases search. We will pilot the search strategy to ensure sufficient sensitivity and specificity. The JBI critical appraisal tools will be used to assess methodological quality of all the included studies.

Discussion:

This review will highlight an urgent need for more studies from different geographical areas to determine best practices for implementing fracture risk assessment globally and guiding clinical decision making for osteoporosis management. The findings of this systematic review will highlight the importance of including fracture risk assessment as a significant parameter to evaluate FLS programs implemented across the globe.

Conclusion:

This systematic review will provide more information about fracture risk assessments and its reporting. It will also highlight the variations in the methods of performing a fracture risk assessment with and without BMD testing and the impact of the FLS program in improving fracture risk assessment.

Introduction:

Fragility fractures are associated with substantial pain, disability, reduced quality of life, and decreased life expectancy [1]. One in five men and nearly one in three women aged 50 years and above will sustain a significant fragility fracture during their lives [2]. The probability of sustaining subsequent fractures

increases up to five times after an initial fragility fracture [3]. The subsequent risk is 200% more if a patient has sustained a vertebral fracture, and the risk of subsequent hip fracture increases up to 300% [4]. Despite the availability of effective pharmacological treatments and clinical guidelines for bone health management after a fragility fracture, approximately 80% of the patients presenting with fractures are not offered screening for subsequent fracture risk and/or treatment with bone strengthening medication worldwide [5].

In the last decade, many advances are achieved in the understanding and management of musculoskeletal disorders around the world. One of the most significant contributions is in achieving clarity and consensus about how best to deliver secondary prevention to patients who have already sustained a fragility fracture. The significance of this increases progressively as the population tends to drive the occurrence of fragility fractures upwards [6]. The healthcare cost of fragility fractures is significant predominantly in European countries like the UK and is expected to grow as the population ages from £1.8 billion to approximately £2.2 billion by 2025 [7]. In a growing number of countries throughout the world including Australia, Canada, the United Kingdom, the USA, and England, secondary prevention programs targeted to prevent fragility fractures are proving to be a highly cost-effective strategy [8]

Several programs have examined the usefulness of systems for the prevention of subsequent fractures, often denoted as Fracture Liaison Services (FLS). A Fracture Liaison Service is a cost-effective systematic model of care that aims to bridge the post-fracture care gap. An FLS ensures that fracture patients are identified and receive treatment to prevent subsequent fractures [9]. Many studies have shown promising results whereby FLS programs improve the management of fragility fractures. A study conducted in France showed that approximately 95% of the patients in a hospital-based FLS program were prescribed bone active medication while without FLS, only 25% of the patients received pharmacological management [10]. A prospective study conducted in British Columbia, Canada demonstrated that the provision of an FSL program increased the bone mineral density testing rates as well as medication initiation rates [11].

FLS programs are designed to cover all components of secondary fracture prevention from the identification of patients, future fracture risk evaluation, treatment, and monitoring. There is increasing evidence to indicate that the FLS model of care is effective across most of the aspects of secondary fracture prevention such as reducing re-fracture rates, improving treatment initiation rates, and decreasing the risk of mortality [12]. However, there is no direct evidence indicating that FLS improves fracture risk evaluation. A fracture risk assessment helps clinicians to classify high-risk patient populations not only at the health system and demographic level, encouraging financial resources to be allocated to those who are most at risk, but also at the individual level, allowing the patient to participate in joint decision-making mechanisms for care.

There are very few studies that included fracture risk assessment as a significant outcome of an FLS program. Furthermore, fracture risk assessments are often reported as part of a bone mineral density

(BMD) test but not all fracture risk assessments require BMD testing [13]. Variations in the methods of performing a fracture risk assessment with and without BMD testing have produced inconclusive results about the impact of the FLS program in improving fracture risk assessment. Hence, it is important to determine whether an FLS improves fracture risk assessment and what fracture prediction tools are used to predict subsequent fracture risk with and without BMD testing. The present systematic review aimed to critically evaluate the available evidence on the effect of FLS in improving fracture risk assessment among fragility fracture patients. The findings of this systematic review will highlight the importance of including fracture risk assessment as a significant parameter to evaluate FLS programs implemented across the globe. It will also highlight the different fracture risk tools used by health care providers to predict subsequent fracture risk.

Methods:

This systematic review will be reported according to the recommended items in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) checklist [14]. This protocol for this systematic review is registered with International Prospective Register for Systematic Reviews (PROSPERO) database (Registration Number: CRD42021245075).

Eligibility Criteria:

Studies will be included in the systematic review according to the following PICO criteria: participants (population), intervention, comparison, outcome(s) of interest, and study design.

Participants (Population):

Studies involving patients aged ≥ 50 years (regardless of sex), with any type of fragility or osteoporotic fracture will be included in the systematic review. The reason for the inclusion of a specific age group is that, by definition, an FLS targets this age group [15]. We will exclude studies involving patients with fractures associated with trauma or road traffic accidents. Studies involving other bone-associated diseases such as osteomyelitis, tumors, and gout will be excluded.

Intervention:

The systematic review will examine studies that evaluated the Fracture Liaison Service program/secondary fracture prevention program implemented at any healthcare setting (hospitals and/or community). We will also include studies that implemented FLS/secondary fracture prevention programs as digital health or telemedicine intervention. In addition, FLS with geriatric assessment programs will also be included in the current systematic review. However, studies involving geriatric assessment programs alone and trauma care programs will be excluded from the review.

Comparison:

The comparison group is usual care (non-FLS care) for fragility fracture patients practiced in any healthcare setting.

Outcome(s) of Interest:

The primary outcome will be the proportion of fragility fracture patients evaluated for subsequent fracture risk. This is often indicated by the number of fracture patients that were assessed for future fracture risk divided by the total number of fracture patients recruited in the study. Measurement of proportion of fracture risk assessment in study arms (FLS vs. non-FLS care) is also reported using crude and adjusted prevalence ratios, odds ratios, and relative risk based on study design. Secondary outcomes will be types of fracture risk prediction tools used to predict subsequent fracture risk. Potential fracture risk assessment tools may include the following: FRAX tool, QFracture, DeFRA, or Garvan. Another secondary outcome will be rates of bone mineral density (BMD) testing (a radiological test to measure bone density and predict the risk of bone fracture) performed as a part of fracture risk assessment protocol within the FLS program.

Study design:

Eligible studies will be randomized controlled trials and non-randomized experimental study design (quasi-experimental, pre-post designs, time-series analysis) reporting on the outcomes of the FLS program. Observational studies with a control group (case-control, prospective, and retrospective cohort) will also be included to determine the proportion of fragility fracture patients assessed for subsequent fracture risk. We will exclude qualitative studies, scoping reviews, narrative reviews, editorials, protocols, case reports, case series, cross-sectional studies, conference abstract, opinion articles, systematic reviews, and meta-analyses. Studies published in languages other than English will also be excluded. The literature search will not be restricted to the context and year of publication.

Information sources and search strategy:

A systematic electronic literature search will be conducted to assess the effect of FLS in improving fracture risk assessment among fragility fracture patients. We will search four major electronic databases including PubMed, Cochrane Library, EBSCO CINAHL Plus, and Embase. Non-published gray literature (conference papers, student thesis, and public repositories) will also be explored to extract relevant literature. We will also appraise the reference list of included studies to identify potentially relevant articles. A detailed search strategy will be used to explore these databases. The search strategy will be designed and carried out by both the reviewers with the help of an information scientist at Gerstein Library. The key search terms will be clustered into four categories of interest: Population (Patients aged ≥ 50 years with fragility fractures), intervention (Fracture Liaison Service or secondary fracture prevention Program), comparison (non-FLS or standard care), and outcome (a measurement of the proportion of fracture risk assessment performed and BMD testing). Additionally, we will use indexed keywords in Medical Subject Headings (MeSH) to ensure uniformity of search terms (Appendix 1). Appendix 2 illustrates the preliminary search strategy carried out on Embase.

Selection of studies:

All the articles extracted from the electronic databases will be uploaded into Endnote [14]. The references from Endnote will then be imported into Covidence software to streamline the process of the systematic review. The articles will be screened by two reviewers (A.A and J.S) independently. In the first step, the articles will be screened by study titles using the Covidence software. Then, the abstract of shortlisted studies will be screened. In the second step, full texts of selected articles will be retrieved and examined against the eligibility criteria. At last, the references of selected studies will be hand-searched to extract any potentially relevant studies missed in the initial searched strategy. A pre-structured screening form will be designed, and pilot tested to ensure the uniformity and reliability of screened studies among two reviewers. Both reviewers will define the intervention and outcomes of interest after screening the articles to verify the relevance of the studies. Each reviewer will provide a strong justification for excluding full-text articles. The disagreement between the two reviewers will be resolved by negotiation and discussion in a consensus meeting. The selection process of studies will be reported using a PRISMA flow diagram (Appendix 3).

Data Collection process:

Data extraction will be performed onto a customized excel sheet by two reviewers (A.A and J.S) independently. The data extraction tables completed by both the reviewers will be matched to confirm that the main findings are documented. A third reviewer in the data extraction process will be involved if any discordant information is witnessed. The preliminary table for data extraction is illustrated in Appendix 4. The table includes the title of the study, primary author, date of publication, date of extraction, country of study, reviewer name, the objective of the study, study population, type of fracture prevention program, study outcomes (proportions, prevalence ratios, odds ratios, and relative risks for improvement in fracture risk assessment and BMD testing), eligibility criteria, reasons for exclusion, and quality appraisal of selected studies. The data extraction tables will also provide a summary of all the included studies. A preliminary data extraction table is presented in Appendix 3.

Quality Assessment:

The quality of the selected studies will be assessed by standardized quality assessment tools which will be performed by the two reviewers (A.A and J.S) independently. The JBI critical appraisal tools will be used to assess methodological quality of all the included studies [16]. We selected JBI because the tool has a separate checklist for different study designs and assesses multiple aspects of methodological quality such as eligibility criteria, study subjects and setting, the validity of outcome measurement, confounding factors and strategies to account for confounding, and appropriateness of statistical analysis. Each component of the checklist is judged as either the information is present in sufficient detail or not and classified as “yes”, “no”, “Unclear”, and “not applicable”. The reviewer will assign a score of 1 for “yes”. The sum of scores for each “yes” in the checklist will be used to judge the risk of bias. We will not exclude any study with a high risk of bias (low “yes” counts); instead, we will report methodological quality for each included study in the review.

Synthesis of included studies:

In the first step, a brief quantitative summary of demographic variables such as year of publication, study setting, study design, sample size, types of FLS program, and fracture risk assessment tools will also be performed. These findings will be presented in the descriptive table of the result section. Later, the rates of BMD testing will be reported. The meta-analysis will be carried out if ≥ 2 studies can be pooled, with consideration of statistical and clinical heterogeneity. All the meta-analyses will be performed in Review Manager Software [17]. The studies included in the systematic review will be reviewed for inclusion in the meta-analysis. Studies with no denominator data or control group or pre-post experimental design will be excluded from the meta-analysis. Since heterogeneity in the data is expected a priori, we will use the random effects model to estimate the pooled effects. Forest plots will be utilized to demonstrate the extent of heterogeneity among selected studies. Statistical heterogeneity will be quantified by estimating I^2 statistic. Also, potential sources of heterogeneity will be investigated further by subgroup analyses according to type of FLS model and baseline characteristics. In the second step, the findings from the articles will be synthesized descriptively to report on common results among the selected articles including types of secondary fracture prevention programs, qualitative and quantitative tools used for fracture risk assessment, and types of healthcare settings implementing FLS.

Discussion:

This systematic review will be conducted to quantify contemporary data from existing literature on the impact of FLS in improving fracture risk assessment following a fragility fracture. The evidence from the review will highlight the importance of implementing secondary fracture prevention programs globally and the status of fracture risk assessment practices within existing secondary fracture prevention programs. This review will highlight an urgent need for more studies from different geographical areas to determine best practices for implementing fracture risk assessment globally and guiding clinical decision making for osteoporosis management. The results of the systematic review will be disseminated through publications in peer-reviewed journals and presenting at national and international conferences in the form of oral and poster presentations. Any modifications made to this protocol when conducting the review will be outlined and reported in the final manuscript.

Declarations

Ethics approval and consent to participate:

Not Applicable

Consent for publication:

Not Applicable

Availability of data and materials:

All the articles that will be generated or analyzed during this systematic review will included in this published article as a supplementary information

Competing interests

The authors declare that they have no competing interests

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The study is not funded

Authors' contributions

ASP—Study design, formulation of research question, literature review, database searching, articles review, manuscript writing, and reviewing. SN—study design, FLS expertise, manuscript writing and review. JS—formulation of research question, literature search, second reviewer, systematic review expert input in the manuscript, manuscript writing and reviewing.

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Not Applicable

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Appendix

Appendix 1: Key Search Terms

Population	Human [MeSH], aged [MeSH], middle-aged, fracture* [MeSH], Fragility fracture [MeSH], osteoporotic fracture*, Bone [MeSH], Low energy fracture*, Low trauma fracture*, postmenopausal osteoporosis [MeSH], Post-Menopausal Bone Loss, Bone Fracture
Intervention	health care facilities, services, health service, health care delivery, health services research, health care organization, preventive health service, health care system, health care utilization, health care management, health care quality, health, health care, health promotion [MeSH], Prevention [MeSH], fracture liaison service*, secondary fracture prevention program*
Fracture risk assessment	Fracture risk assessment [MeSH], risk assessment [MeSH], FRAX, Qfracture, bone fragility risk,
BMD testing	Bone densitometry [MeSH], dual energy x ray absorptiometry [MeSH], DEXA Scan, Bone density [MeSH], bone risk, bone mineral density, BMD test,

Appendix 2: Search Strategy (Medline)

S#	SEARCHES	RESULTS
1	exp Fractures, Bone/	188111
2	Geriatric Assessment/	28750
3	health services for the aged/ or exp preventive health services/ or exp rehabilitation/	919558
4	2 or 3	938018
5	1 and 4	8439
6	limit 5 to ("middle aged (45 plus years)" or "all aged (65 and over)" or "aged (80 and over)")	5229
7	Frail Elderly/	12184
8	1 and 7	490
9	6 or 8	5526
10	cohort studies/ or longitudinal studies/ or follow-up studies/ or prospective studies/	1438304
11	case-control studies/ or retrospective studies/ or cross-sectional studies/	1466673
12	observational study.pt. or observational study as topic/	99935
13	Registries/	94045
14	seer program/ [****US Cancer registry****]	8174
15	or/10-14 [***Cohort study terms****]	2675080
16	odds ratio/ or risk/ or risk assessment/ or risk factors/	1205573
17	causality/ or precipitating factors/ or risk factors/	867943
18	Poisson Distribution/ or Logistic Models/ or Multivariate Analysis/	251989
19	Asymptomatic Diseases/	6451
20	(risk: or cause or causal or causation or relative risk).mp.	3698875
21	or/16-20 [****Risk terms****]	3839505
22	15 and 21 [****MEDLINE Specific Risk filter****]	990917
23	9 and 15	2612
24	21 and 23	1185
25	(fracture adj2 liaison adj2 (service* or program*)).ti,ab,kf,in.	332

26	24 not 25	1154

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Appendix3.png](#)
- [Appendix4.png](#)