



A Second Fragility Fracture Before Any Bone Health Assessment: A Narrative Review of Fracture Liaison Services and the Care Gap They Exist to Close

Andreas Lang^{1*}, Marija Tomic² and Helen Ashcroft³

¹Department of Orthogeriatrics, Salzach Institute of Clinical Medicine, Salzburg, Austria

²Department of Rheumatology, Kvarner Medical Centre, Rijeka, Croatia

³Department of Orthopaedics, Pennine Institute of Clinical Sciences, Leeds, United Kingdom

***Correspondence to:** Andreas Lang, Department of Orthogeriatrics, Salzach Institute of Clinical Medicine, Salzburg, Austria

Received: 2 May 2023; **Accepted:** 9 September 2023; **Published:** 15 December 2023

Copyright: © 2023 AL, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

A fragility fracture is the clearest warning a skeleton can give. It is also, routinely, the one nobody acts on. Most patients who break a bone after a fall from standing height leave hospital with the fracture treated and the osteoporosis behind it neither investigated nor named.

Objectives: *To review the published evidence on secondary fracture prevention: how large the treatment gap is, why a first fracture so often passes without assessment, what fracture liaison services change, and what the evidence for them does and does not establish.*

Material and Methods: *Narrative review of meta-analyses, cohort studies, population registries, national audits, randomised trials of anti-osteoporosis therapy and society guidance indexed in PubMed and the major bone, rheumatology and orthopaedic journals. No new patient data were generated; every estimate quoted is one published by the original investigators.*

Results: *A prior fracture carried a relative risk of any subsequent fracture of 1.86 across 11 cohorts followed for 250,000 person-years, and the excess risk is concentrated in the first two years. Across 29 European countries in 2019, 71 per cent of women eligible for treatment received none, leaving 14.0 million untreated; the gap was 55 per cent in 2010, so it has widened. Pooled against usual care, fracture liaison services increased bone density testing by 24 percentage points, treatment initiation by 20 and adherence by 22, and reduced absolute re-fracture risk by 5 percentage points and mortality by 3.*

Conclusion: *The drugs work, the risk is quantified, and the patient is already in the building with a broken bone. What is missing is a person whose job it is to notice. Fracture liaison services supply exactly that, and the evidence for them is consistent in direction while resting almost entirely on before-and-after and cohort designs rather than randomised comparison.*

Abbreviations: BMD – Bone Mineral Density, DXA – Dual-Energy X-Ray Absorptiometry, FLS – Fracture Liaison Service, FRAX – Fracture Risk Assessment Tool, IOF – International Osteoporosis Foundation, RR – Relative Risk.

Keywords: Osteoporosis; Fragility Fracture; Secondary Fracture Prevention; Fracture Liaison Service; Treatment Gap

Introduction

Osteoporosis is silent until it is not. Its first clinical expression is usually a fracture sustained in a fall that would not have broken a healthy bone, and worldwide such fractures number in the millions each year [1,2]. In Europe alone, 4.3 million fragility fractures were recorded in 2019 at a cost exceeding 56 billion euros, of which only 3 per cent was spent on the drugs that prevent them [3,4].

What makes this a tractable problem rather than merely a large one is that the first fracture identifies the patients who will have the second. Prior fracture is among the strongest and best-quantified risk factors in clinical medicine [5,6], the risk is highest in the months immediately afterwards [7,8], and effective treatments exist [9,10,11,12]. Every element of a prevention strategy is therefore available at the moment a patient arrives in an emergency department with a broken wrist.

It is mostly not used. The dominant finding of two decades of audit is that the majority of patients presenting with a fragility fracture are never assessed for osteoporosis and never started on treatment [4,13]. This review sets out the size of that gap, what explains it, and what the evidence says about fracture liaison services, the organisational response designed to close it.

Material and Methods

Search strategy: PubMed and the archives of the major bone, rheumatology, orthopaedic and geriatric medicine journals were searched for studies of secondary fracture prevention. Search terms combined fragility fracture, osteoporosis and refracture with fracture liaison service, secondary prevention, treatment gap, care gap, coordinator, imminent risk and models of care. Reference lists of society guidance and best-practice frameworks [14,15,16] were screened by hand for primary sources.

Eligibility: Studies were included if they quantified subsequent fracture risk after an index fragility fracture, measured investigation or treatment rates after fracture, or evaluated a service model intended to improve them. Randomised trials of anti-osteoporosis drugs are cited to establish that effective treatment exists, not as evidence about service delivery, and are identified as such.

Data extraction and handling: Design, setting, sample size, comparator and the reported estimate were extracted as published. Whether a comparison was randomised, concurrently controlled or before-and-after is reported alongside every figure, because that distinction carries most of the uncertainty in this literature. No pooling or re-analysis was performed. Figures 1 to 4 and Tables 1 and 2 reproduce published values only. This is a narrative synthesis and was not registered as a systematic review.

Results

The risk a first fracture announces: An international meta-analysis of 11 cohorts comprising 15,259 men and 44,902 women, followed for 250,000 person-years, found that a previous fracture carried a relative risk of any subsequent fracture of 1.86 (95% CI 1.75 to 1.98) (Figure 4) [5]. A later analysis extended this to 64 cohorts in 32 countries and 19.5 million person-years for use in FRAX, confirming the association and its dependence on time since the index event [6]. That time dependence matters clinically: subsequent fractures cluster in the period immediately following the first [7,8,17], which is precisely the period in which the patient is under orthopaedic care and therefore reachable.

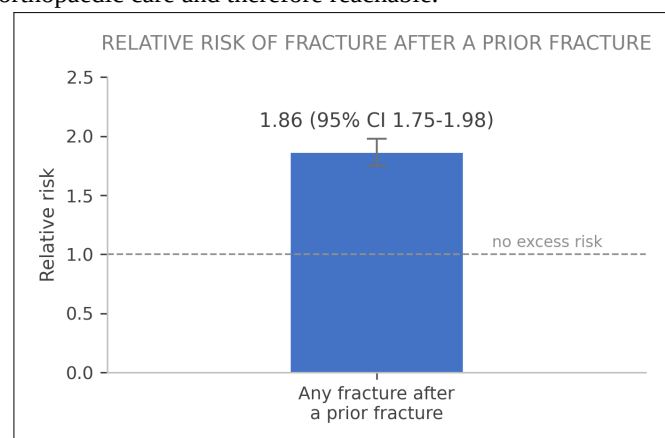


Figure 4: Relative risk of any subsequent fracture in patients with a previous fracture, pooled across 11 cohorts [5]

What a fracture costs beyond the bone: The consequences are not confined to the skeleton. Excess mortality following osteoporotic fracture is well documented [18], and a subsequent fracture carries further excess mortality on top of that of the index event [19]. The economic burden follows the clinical one, and its distribution is instructive: the overwhelming majority of the European spend goes on treating fractures rather than preventing them [3,20].

The size of the treatment gap: The most systematic European estimate comes from the SCOPE 2021 scorecard, covering the 27 European Union member states plus the United Kingdom and Switzerland. On average, 71 per cent of women who exceeded the intervention threshold received no osteoporosis treatment, leaving 14.0 million women untreated. The gap varied more than twofold between countries, from 32 per cent in Ireland to 87 per cent in Bulgaria (Figure 1) [4,13].

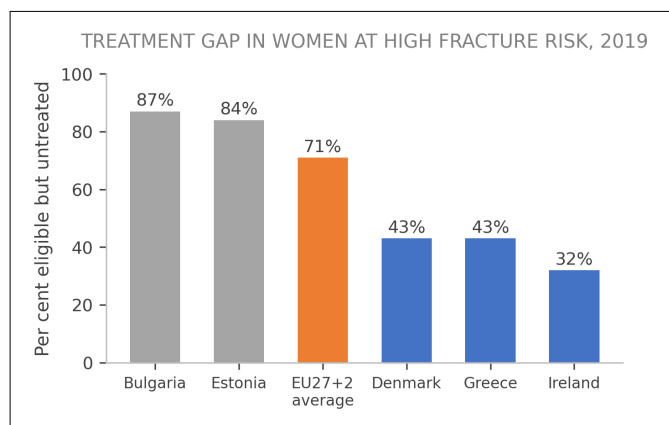


Figure 1: Proportion of women above the intervention threshold receiving no osteoporosis treatment, selected European countries and the EU27+2 average [4,13]

The gap is widening: The same exercise conducted in 2010 found an average treatment gap of 55 per cent, with 10.6 million women untreated. Nine years later the gap had risen to 71 per cent and the number untreated to 14.0 million (Figure 2) [13]. Some of this reflects a growing and ageing eligible population rather than deteriorating practice, but the direction is unambiguous, and it runs opposite to the direction of the evidence base. In the United States, osteoporosis medication use after hip fracture declined over roughly the same period [21].

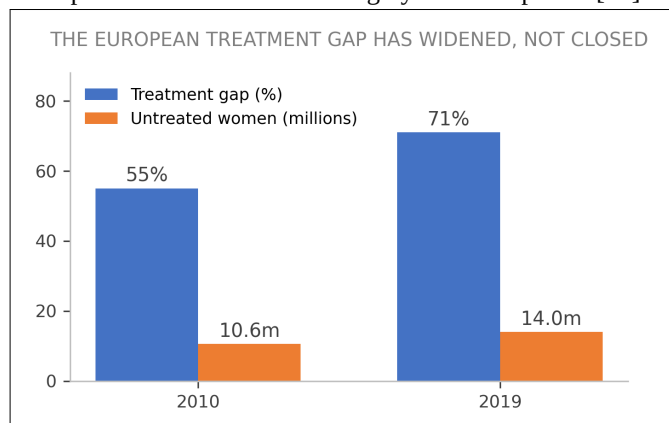


Figure 2: European treatment gap and the number of untreated women at high risk, 2010 against 2019 [13]

Study	Design and cohort	Principal reported finding
Kanis et al. 2004 [5]	Meta-analysis, 11 cohorts, 250,000 person-years	Prior fracture: RR 1.86 (95% CI 1.75-1.98) for any fracture
Kanis et al. 2023 [6]	Meta-analysis, 64 cohorts, 19.5m person-years	Confirms association; risk varies with time since index fracture
SCOPE 2021 [4,13]	Scorecard, EU27 plus UK and Switzerland	71% treatment gap in 2019; 14.0m women untreated; 55% in 2010
Ganda et al. 2013 [22]	Systematic review and meta-analysis of care models	Intensity of the model predicts investigation and treatment rates
Wu et al. 2018 [23]	Systematic review and meta-analysis of FLS	BMD testing +24pp, treatment +20pp, re-fracture -5pp, mortality -3pp
Li et al. 2021 [24]	Systematic review and meta-analysis, 16 studies	Lower subsequent fracture and mortality with FLS
Axelsson et al. 2020 [25]	Cohort, four Swedish hospitals	Recurrent fracture risk fell after FLS implementation

Table 1: Principal studies reviewed, with the finding as reported by the original investigators

Why the fracture passes unremarked: The explanation is structural rather than clinical. A fragility fracture presents to orthopaedics, whose task is the bone in front of them and whose follow-up ends when it has healed. Osteoporosis belongs to no single specialty, the assessment requires a separate investigation on a separate pathway, and responsibility for arranging it is diffuse enough that it frequently falls to nobody [15,16,26]. Even where treatment is started, persistence is poor, and poor adherence measurably erodes the fracture reduction achieved [27,28].

What a fracture liaison service is: The model originates in Glasgow, where a dedicated coordinator systematically identified patients presenting with fragility fracture, assessed them and arranged treatment [29]. The essential feature is a named person with responsibility for case-finding, not a new investigation. The approach was formalised as coordinator-based secondary prevention [15] and subsequently as the International Osteoporosis Foundation's Best Practice Framework, which sets out standards against which services can be benchmarked [16,30].

What the evidence shows: A systematic review and meta-analysis comparing services against no service found bone density testing increased by 24 percentage points (95% CI 18 to 29), treatment initiation by 20 (16 to 25) and adherence by 22 (13 to 31), with absolute re-fracture risk reduced by 5 percentage points (3 to 8) and mortality by 3 (1 to 5) (Figure 3) [23]. A later meta-analysis of 16 studies reached compatible conclusions on subsequent fracture and mortality [24]. Individual services report the same direction: reduced re-fracture in Australia [31,32], reduced subsequent non-vertebral fracture and mortality in the Netherlands [33], and reduced recurrent fracture risk across four Swedish hospitals [25]. Economic evaluations generally find the model cost-effective and often cost-saving [34].

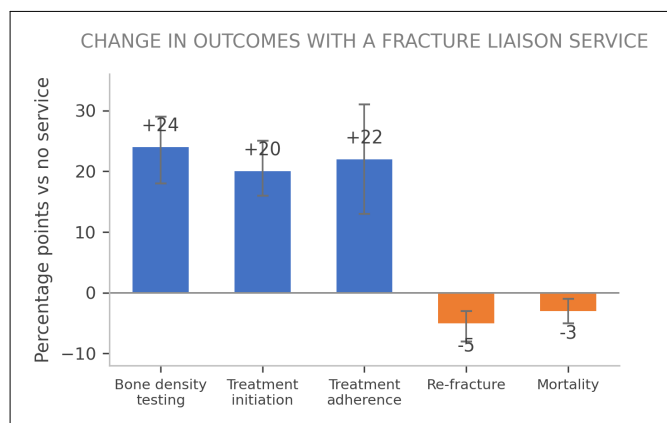


Figure 3: Change in outcomes with a fracture liaison service compared with no service, in percentage points with 95% confidence intervals [23]

Element	What it addresses	Evidence
Systematic case-finding	Patients never identified as having osteoporosis	Defining feature of the original model [29]
A named coordinator	Diffuse responsibility between specialties	Coordinator-based models outperform alerts alone [15,22]
Model intensity	Whether assessment is arranged or merely recommended	Higher-intensity models achieve higher rates [22]
Benchmarked standards	Wide variation in what a service does	IOF Best Practice Framework [16,30]
Adherence follow-up	Treatment started but not continued	Poor persistence erodes fracture reduction [27,28]
Cost-effectiveness	Whether services survive budget scrutiny	Generally cost-effective or cost-saving [34]

Table 2: Components of a fracture liaison service and the failure each is intended to correct

Discussion

The gap between what is known and what is done is unusually wide here, and unusually well documented. Prior fracture has been an established risk factor since 2004 [5], effective drugs have been licensed for longer [9,10,11,12], and yet the proportion of eligible European women left untreated rose from 55 to 71 per cent across the decade in which that evidence matured [13]. Whatever is failing is not the science.

What fracture liaison services do is supply an owner. The intervention is administrative in form and clinical only in consequence: someone reviews the fracture lists, contacts the patient, arranges the scan, starts the treatment and checks that it continues. The pooled effects are correspondingly modest in absolute terms, five percentage points off re-fracture and three off mortality, but they apply to a very large population who are currently receiving nothing [23,24].

The evidence deserves an honest description. Almost none of it is randomised. The pooled estimates combine before-and-after comparisons, concurrent cohorts and historical controls, designs in which secular improvement in fracture care is difficult to separate from the effect of the service itself [22,23,24]. Services that publish tend to be services that work,

and the units that establish them are plausibly the units already interested in bone health. Both would inflate the apparent effect. The mortality finding in particular should be read with caution, since it is not obvious by what mechanism a coordinator reduces death within the follow-up periods reported [24].

Two things nonetheless favour the conclusion. The direction is consistent across countries, health systems and service designs [25,31,32,33]. And the intermediate outcomes, on which the evidence is strongest, are exactly the ones the model is designed to change: investigation, initiation and adherence [23]. A service that reliably moves those three, in a population whose risk is quantified and whose treatment is proven, does not require a separate trial to be worth having.

Study limitations

The limitations belong to the underlying literature. The absence of randomised comparison is the central one, and it will not be remedied, since withholding a service believed to work is not straightforwardly justifiable [22,23]. Definitions vary: services described as fracture liaison services range from a letter to a general practitioner to a fully staffed clinic with follow-up, and pooling them assumes an equivalence that does not exist [30,35]. Treatment gap estimates depend on the intervention threshold chosen and on the completeness of prescribing data, both of which differ between the countries compared [4,13]. Vertebral fractures, which are frequently asymptomatic, are systematically under-counted in every dataset cited here [1,17]. Follow-up in most service evaluations is one to three years, shorter than the horizon over which secondary prevention pays off [24,25]. And the evidence is drawn almost entirely from high-income settings [3,36].

Conclusion

A second fragility fracture in a patient who was never assessed after the first is a system failure with a known cause and a known remedy. The risk conferred by an index fracture has been quantified across millions of person-years, the treatments that reduce it are licensed and inexpensive, and the patient is physically present in a hospital at the moment the opportunity arises. Fracture liaison services close the gap by assigning responsibility for that moment to a named person, and every reported series points the same way even though the designs are weak. The finding that should provoke most discomfort is not any single effect estimate but the trajectory: across the decade in which this evidence accumulated, the proportion of eligible European women receiving no treatment went up.

Acknowledgements

The authors thank the investigators whose cohorts, registries and service evaluations are drawn together in this article, and the coordinators who collect the data on which secondary prevention audit depends.

Funding

No dedicated funding from public, commercial or charitable sources supported the preparation of this review.

Conflict of Interest

The authors declare no competing interests.

Ethics Statement

This article reviews previously published studies only. No new patient data were collected and no participants were recruited, so ethical approval was not required.

References

1. Johnell O, Kanis JA. "An estimate of the worldwide prevalence and disability associated with osteoporotic fractures". *Osteoporos Int* 17(2006):1726-1733.
2. Compston JE, McClung MR, Leslie WD. "Osteoporosis". *Lancet* 393(2019):364-376.
3. Borgstrom F, Karlsson L, Orsater G, Norton N, Halbout P, Cooper C, et al. "Fragility fractures in Europe: burden, management and opportunities". *Arch Osteoporos* 15(2020):59.
4. Kanis JA, Norton N, Harvey NC, Jacobson T, Johansson H, Lorentzon M, et al. "SCOPE 2021: a new scorecard for osteoporosis in Europe". *Arch Osteoporos* 16(2021):82.
5. 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* 35(2004):375-382.
6. Kanis JA, Johansson H, McCloskey EV, Liu E, Akesson KE, Anderson FA, et al. "Previous fracture and subsequent fracture risk: a meta-analysis to update FRAX". *Osteoporos Int* 34(2023):2027-2045.
7. Johansson H, Siggeirsdottir K, Harvey NC, Oden A, Gudnason V, McCloskey E, et al. "Imminent risk of fracture after fracture". *Osteoporos Int* 28(2017):775-780.
8. van Geel TA, van Helden S, Geusens PP, Winkens B, Dinant GJ. "Clinical subsequent fractures cluster in time after first fractures". *Ann Rheum Dis* 68(2009):99-102.
9. Black DM, Delmas PD, Eastell R, Reid IR, Boonen S, Cauley JA, et al. "Once-yearly zoledronic acid for treatment of postmenopausal osteoporosis". *N Engl J Med* 356(2007):1809-1822.
10. Lyles KW, Colon-Emeric CS, Magaziner JS, Adachi JD, Pieper CF, Mautalen C, et al. "Zoledronic acid and clinical fractures and mortality after hip fracture". *N Engl J Med* 357(2007):1799-1809.
11. Cummings SR, San Martin J, McClung MR, Siris ES, Eastell R, Reid IR, et al. "Denosumab for prevention of fractures in postmenopausal women with osteoporosis". *N Engl J Med* 361(2009):756-765.
12. Saag KG, Petersen J, Brandi ML, Karaplis AC, Lorentzon M, Thomas T, et al. "Romosozumab or alendronate for fracture prevention in women with osteoporosis". *N Engl J Med* 377(2017):1417-1427.
13. Willers C, Norton N, Harvey NC, Jacobson T, Johansson H, Lorentzon M, et al. "Osteoporosis in Europe: a compendium of country-specific reports". *Arch Osteoporos* 17(2022):23.
14. Kanis JA, Cooper C, Rizzoli R, Reginster JY. "European guidance for the diagnosis and management of osteoporosis in postmenopausal women". *Osteoporos Int* 30(2019):3-44.
15. 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* 22(2011):2051-2065.
16. 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* 24(2013):2135-2152.
17. Balasubramanian A, Zhang J, Chen L, Wenkert D, Daigle SG, Grauer A, et al. "Risk of subsequent fracture after prior fracture among older women". *Osteoporos Int* 30(2019):79-92.
18. Cooper C, Atkinson EJ, Jacobsen SJ, O'Fallon WM, Melton LJ. "Population-based study of survival after osteoporotic fractures". *Am J Epidemiol* 137(1993):1001-1005.
19. Bliuc D, Nguyen ND, Milch VE, Nguyen TV, Eisman JA, Center JR. "Mortality risk associated with low-trauma osteoporotic fracture and subsequent fracture in men and women". *JAMA* 301(2009):513-521.
20. Hernlund E, Svedbom A, Ivergard M, Compston J, Cooper C, Stenmark J, et al. "Osteoporosis in the European Union: medical management, epidemiology and economic burden". *Arch Osteoporos* 8(2013):136.
21. Solomon DH, Johnston SS, Boytsov NN, McMorro D, Lane JM, Krohn KD. "Osteoporosis medication use after hip fracture in U.S. patients between 2002 and 2011". *J Bone Miner Res* 29(2014):1929-1937.
22. Ganda K, Puech M, Chen JS, Speerin R, Bleasel J, Center JR, et al. "Models of care for the secondary prevention of osteoporotic fractures: a systematic review and meta-analysis". *Osteoporos Int* 24(2013):393-406.
23. Wu CH, Tu ST, Chang YF, Chan DC, Chien JT, Lin CH, et al. "Fracture liaison services improve outcomes of patients with osteoporosis-related fractures: a systematic literature review and meta-analysis". *Bone* 111(2018):92-100.

24. Li N, Hilgsmann M, Boonen A, van Oostwaard MM, de Bot RTAL, Wyers CE, et al. "The impact of fracture liaison services on subsequent fractures and mortality: a systematic literature review and meta-analysis". *Osteoporos Int* 32(2021):1517-1530.
25. Axelsson KF, Johansson H, Lundh D, Moller M, Lorentzon M. "Association between recurrent fracture risk and implementation of fracture liaison services in four Swedish hospitals: a cohort study". *J Bone Miner Res* 35(2020):1216-1223.
26. Chesser TJS, Javaid MK, Mohsin Z, Pari C, Belluati A, Contini A, et al. "Overview of fracture liaison services in the UK and Europe: standards, model of care, funding, and challenges". *OTA Int* 5(2022):e198.
27. Imaz I, Zegarra P, Gonzalez-Enriquez J, Rubio B, Alcazar R, Amate JM. "Poor bisphosphonate adherence for treatment of osteoporosis increases fracture risk: systematic review and meta-analysis". *Osteoporos Int* 21(2010):1943-1951.
28. Siris ES, Selby PL, Saag KG, Borgstrom F, Herings RM, Silverman SL. "Impact of osteoporosis treatment adherence on fracture rates in North America and Europe". *Am J Med* 122(2009):S3-S13.
29. 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* 14(2003):1028-1034.
30. Javaid MK, Kyer C, Mitchell PJ, Chana J, Moss C, Edwards MH, et al. "Effective secondary fracture prevention: implementation of a global benchmarking of clinical quality using the IOF Capture the Fracture Best Practice Framework tool". *Osteoporos Int* 26(2015):2573-2578.
31. Lih A, Nandapalan H, Kim M, Yap C, Lee P, Ganda K, et al. "Targeted intervention reduces refracture rates in patients with incident non-vertebral osteoporotic fractures: a 4-year prospective controlled study". *Osteoporos Int* 22(2011):849-858.
32. Nakayama A, Major G, Holliday E, Attia J, Bogduk N. "Evidence of effectiveness of a fracture liaison service to reduce the re-fracture rate". *Osteoporos Int* 27(2016):873-879.
33. Huntjens KM, van Geel TA, van den Bergh JP, 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* 96(2014):e29.
34. Wu CH, Kao IJ, Hung WC, Lin SC, Liu HC, Hsieh MH, et al. "Economic impact and cost-effectiveness of fracture liaison services: a systematic review of the literature". *Osteoporos Int* 29(2018):1227-1242.
35. Wu CH, Chen CH, Chen PH, Yang JJ, Chang PC, Huang TC, et al. "Identifying characteristics of an effective fracture liaison service: systematic literature review". *Osteoporos Int* 29(2018):1023-1047.
36. Walters S, Khan T, Ong T, Sahota O. "Fracture liaison services: improving outcomes for patients with osteoporosis". *Clin Interv Aging* 12(2017):117-127.

Citation: Lang A, Tomic M, Ashcroft H. "A Second Fragility Fracture Before Any Bone Health Assessment: A Narrative Review of Fracture Liaison Services and the Care Gap They Exist to Close." *J Clin Case Stud* (2023): 001-006 doi: 10.5281/zenodo.22227636