Fracture Unit: a model of continuity of treatment in fragility fractures

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ABSTRACT

Fragility fractures result from a progressive depletion of bone tissue, mainly caused by aging and menopause. Due to the increased aging population, fragility fractures are currently placing a considerable economic burden on national health systems. Despite the present awareness regarding osteoporotic fractures, many patients are not yet appropriately treated or do not carry out the treatment on a continuous basis. As a result, osteoporosis remains an undertreated and underdiagnosed pathology that increases the patient's fracture risk 2-3 fold. Fracture Units (FUs) are tertiary prevention models whose main aim is to direct patients to programs to avoid subsequent fractures. FUs address patients who have suffered a fragility fracture through a complete multidisciplinary diagnostic approach that is started at hospital admission and should be followed by regular check-ups after discharge: long-term personalized therapeutic programs are tailored to each patient's intrinsic fracture risk and comorbidities. FUs make use of local hospital-based resources with nurses playing a decisive role as intermediary figures between doctors and patients, taking care of the latter at follow-ups.The potential benefits of FUs include: (1) reduction of present fracture complications, (2) reduction of subsequent fracture risk by promoting diagnostic tests (e.g. DXA scans or spinal X-rays), (3) greater percentages of patients discharged with optimal anti-osteoporosis therapy, and (4) reduction of healthcare costs associated with osteoporosis. The main goal of this review is to illustrate and describe economic and clinical outcomes using the FU model of care with reference to other, different types of service models.

KEYWORDS

Fragility fracture, fracture liaison service, fracture unit, osteoporosis, hip fracture, prevention.

Introduction

According to the Italian National Institute for Statistics (ISTAT), Italy has one of the world's highest life expectancies, with an estimated current life expectancy of 78.4 years for men and 87.4 years for women. Rising life expectancy is associated with a higher prevalence of chronic and degenerative diseases, including osteoporosis [1].

Osteoporosis is a chronic condition characterized by reduced bone mineral density (BMD) and microarchitectural deterioration of bone tissue, which together increase bone fragility and fracture risk [2,3]. The World Health Organization has estimated that there are over 200 million people affected by osteoporosis in the world, this total making osteoporosis the most frequent critical health issue after cardiovascular diseases [4]. In Italy, 5 million people are estimated to have osteoporosis (80% of whom are post-menopausal women), yet this pathology often remains undiagnosed until a low-energy fragility fracture occurs.

If left untreated, osteoporosis increases an individual's fragility fracture risk [5]. Only 26% of fragility fracture patients have a previous diagnosis of osteoporosis; moreover, just 64.3% of patients with a claims-documented diagnosis of osteoporosis received some form of pharmacological therapy 1 year after diagnosis [6]. Providing treatment is promptly started, an investigation approach in the high-risk population lowers the subsequent fracture rate by 51%, while optimal treatment reduces it by 39.5% [7]. Several studies have shown that fragility fracture incidence increases with age, peaking at 65 years of age, and that this inevitably leads to a rise in the yearly incidence of fragility fracture in patients >75 years old [8].

Fragility fractures are a major risk factor for the occurrence of a subsequent fracture, being associated with a 2- to 5-fold increased risk of a further fracture [9]: studies show that almost 50% of women admitted for a fragility fracture have a positive past medical history of fragility fracture.

Fragility fracture patients suffer pain, disability and death [10]; osteoporotic fractures (mainly hip and vertebral, but also rib, radial, tibial and tarsal fractures) must be treated with the

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necessary precautions to reduce the risk of bone synthesis failure, impaired fracture healing, consolidation delay and non-union. During surgical planning, the orthopedic surgeon must choose appropriate fixation devices as well as osteoinductive and osteoconductive bone substitutes, and opt for a minimally invasive surgery to preserve tissue vascularization and morphology. Hip fractures are the most catastrophic complication of osteoporosis, resulting in a mortality rate of 5% at 1 month and 20% at 1 year; furthermore, 30% of hip fractured patients are estimated to become permanently disabled, 40% lose the ability to walk independently, and 80% become unable to perform daily activities independently [11].

In Italy, 94,525 femoral neck fractures in people >65 years old were recorded in 2014, of which about 84.9% were suffered by patients aged ≥75 years [12]. Fracture Units (FUs) or Fracture Liaison Services (FLSs) have been proposed as a means to reduce this risk by acting as proactive care models to address the gap in tertiary prevention and help to prevent subsequent fractures. The osteoporosis treatment gap is a worldwide phenomenon, which hinges on suboptimal diagnosis and poor treatment adherence [1,13,14].

Only 9-50% of fractured patients go on to have a bone health assessment and only 56% of at-risk patients are discharged with an anti-osteoporosis treatment [15].

FUs can minimize the debilitating consequences of subsequent fractures and the associated economic burden on healthcare systems.

The Fracture Unit: a model concept

Reducing the risk of future fractures is the primary goal of any FU model, and it is achieved by proactively identifying at-risk patients and initiating bone health assessments [16]. Specifically, the main aims of an FU are: (1) to identify fragility fracture patients, (2) to perform future fracture risk assessment, and (3) to initiate appropriate anti-osteoporosis treatment [17]. In clinical practice, at-risk patients are identified by assessing patients over the age of 50 years presenting with a fragility fracture (e.g. after a fall from a standing height), although some centers also include women as young as 40 years old [18].

These actions establish a tertiary prevention model that operates according to a global patient-specific approach and using hospital-based resources (i.e. existing structures). One of the first published articles on FU models concerned a program implemented in 1999 across two collaborating National Health Service Trusts in Glasgow, Scotland, that coined the term "Fracture Liaison Service" [19]. In the years since then, similar services have been set up in many countries worldwide, trying out various types of FU models.

Fracture Unit models

In 2011, Marsh and Akesson reported 12 different secondary fracture prevention models that have been described in the scientific literature. These range from programs aimed solely at increasing awareness of osteoporosis to more intensive ones focusing on treatment planning, some delivered within an FU and others involving only the primary care provider (i.e. general practitioner, GP). In every model, the FU is coordinated by a designated healthcare chief, who is in charge of case-finding patients and following prescribed protocols, providing assistance and referral access to specialist physicians. Accordingly, FUs are characterized three interventions, which are often summarized as the "3Is" [20]:

1. **Identification** (of patients at risk of subsequent fracture);
2. **Investigation** (for bone fragility);
3. **Initiation** (of treatment for subsequent fracture prevention).

Ganda *et al*. provides a useful system [21] in which FU models are classified into 4 groups, named A to D according to their intensity level (i.e. strictly speaking, the number of "Is" involved), with Type A being the most intensive and Type D the least. The Type A model features all three aforementioned "Is" while Type B includes only two, leaving treatment initiation to the GP. Type C models identify patients at risk and provide education on osteoporosis, giving lifestyle advice on fall prevention, but do not undertake any assessment or treatment initiation. A key feature of Type C models is the recommendation for further assessment, with notification of the GP. Services organized according to the Type D model only identify at-risk patients and educate them, but take no further steps in alerting a responsible third party (Tables I, II).

Table I FU models.

Type A model	"3 Is" model	Identifies, Investigates and Initiates treatment
Type B model	"2 Is" model	Identifies and Investigates but leaves the initiation of treatment to the primary care provider.
Type C model	"1 I" model	Fracture patients receive education about osteoporosis and receive lifestyle advice including advice on fall prevention; GPs are alerted.
Type D model	**"zero Is" model**	Only provides osteoporosis education to the fracture patient

The "4Is" model

The Lucky Bone™ FLS program in Canada [22] proposed an additional FU model providing "4Is" management, with the fourth "I" representing Integrative follow-ups to ensure treatment persistence, compliance and safety. The same study also demonstrated that a high (95%) level of decision-making consensus between physicians and specialist nurses is possible: nurses were empowered by a system that let them manage patients, suggesting that FUs can be run safely and efficiently with minimal physician supervision. Incidentally, optimal communication between hospital physicians and GPs, often responsible for continuous patient assessment and adherence monitoring, is needed to pursue FU outcomes [23].

Table II Different FU models and their effect on BMD testing and treatment.

MODEL	DESCRIPTION	PROPORTION RECEIVING BMD TESTING	PROPORTION RECEIVING OSTEOPOROSIS TREATMENT
Status Quo	Manitoba statistics for the major osteoporotic fractures (2007/2008)	13%	8%
Type D	Only provides osteoporosis education to the fracture patient. Primary care provider (PCP) is not alerted or educated	No study on BMD testing	8%
Type C ("1 I" model)	The PCP is alerted that a fracture has occurred and further assessment is needed. This model leaves the investigation and initiation of treatment to the PCP.	43%	23%
Type B ("2 Is" model)	1. Identification 2. Investigation	60%	41%
Type A ("3 Is" model)	1. Identification 2. Investigation 3. Initiation of osteoporosis treatment where appropriate	79%	46%

FU outcomes

We evaluated the following FU outcomes:

A. **Subsequent fracture risk reduction;**
B. **Time to subsequent fracture;**
C. **Treatment rate;**
D. **Mortality;**
E. **Bone health assessment;**
F. **Osteoporosis treatment initiation and adherence;**
G. **Cost effectiveness;**

A. **Subsequent fracture risk reduction**. Compared both with primary care follow-up and follow-up by healthcare facilities without an FU program, an FU-targeted group showed a significant reduction in the subsequent-fracture index over the following 2–4years [24]. An Australian study reported that patients who were followed-up by their GP had an increased risk of subsequent fracture compared with those assisted by a Type A FU over 2–4 years of follow-up (p<0.01) [25]. Another Australian study reported that Type A FU patients had a lower rate of subsequent fractures compared with patients not followed by an FU (5.1% *vs* 16.4% at two years, p<0.001) [26]. This same Type A service was then compared with a comparable cohort from another hospital not providing any FU service; this comparison showed a 30%–40% reduction in subsequent fracture in FU-followed patients over a 3-year observation period [27]. The International Osteoporosis Foundation (IOF) took action with the "Capture the Fracture" initiative, a Kaiser Permanente Southern California Healthy Bones Type A service, collecting outcomes from 11 medical centers and demonstrating an average reduction in subsequent fracture rate of 37.2% over the first 4 years of observation [24].

B. **Subsequent fracture time span**. Our research found only one study, by Axelsson *et al*. [28], that reported the time elapsing before a subsequent fracture (estimated to be 294 days in treated patients versus 185 days in untreated patients, p<0.001). This time was not significantly different between the pre- and post-FU cohort (207 days ±168 days in pre-FU *versus* 200 ± 163 days in post-FLS, p=ns).

C. **Treatment rate**. Axelsson *et al*. [28] and Huntjens *et al*. [29] described different treatment rates in pre- and post-FU patient cohorts, respectively 13% and 22%. Post-FU cohorts had increased treatment rates up to 32% and 51%.

Huntjens *et al*. [30] only described an estimated treatment rate of approximately 50% in the FU group, as no data were available from no-FU hospitals.

D. **Mortality**. Over a 2-year follow-up, a Type A FU demonstrated a 35% reduction in patient mortality following fragility fracture compared with an equivalent non-FLS cohort. A large UK cohort study including hip fracture admission data from 11 hospitals (with a newly implemented orthogeriatric service and an FU program) reported 30-day and 1-year mortality reductions of 20% and 16%, respectively [31].

E. **Bone health assessment**. FU care, compared with either standard or pre-FU healthcare, is associated with a 2- to 18-fold increase in referrals for bone density assessment using dual energy X-ray absorptiometry (DXA). A Scottish study compared two hospitals and found that DXA scans were offered at a significantly higher rate in the center with a Type A FU (85% *vs* 6% for humeral fractures, 20% *vs* 9.7% for hip fractures) [32]. Another study, based in Edmonton, Canada, in which hip fracture patients were randomly assigned to either FU or standard care, also reported a significant increase in BMD testing in the FU group (p<0.01); the same department subsequently evaluated patients with wrist fractures, again showing increased BMD testing in the FU group (p<0.01) [33]. An Italian study reported that their Type A FLS model, for patients >65 years old, hospitalized for proximal femoral fracture, increased BMD testing more than threefold, from 14.5% to 47.6% (p<0.01) [34]. A similar finding was reported in an American study in which FU care during hip fracture rehabilitation increased BMD testing from 35% to 65% [35]. The Kaiser Permanente FU has published multiple reports addressing osteoporosis testing since its establishment in 2002, reporting a 247% increase in total annual DXA scans over the first 4 years [36], a 263% increase over the first 6 years of observations [37], and visual data showing a further increase in annual DXA scans 2 years later [38]. These intensive FU models are linked to higher referral rates compared to less intensive service models: an education-based Type C service reported that patients followed up via phone call at 3 months after a fragility fracture were more likely to have been recommended a DXA scan (p<0.01) than those belonging to a control group that received no further contact. Another study employing educational programs (Types C and D) reported no significant difference in BMD assessment between usual care and

groups with patients and/or physician intervention, suggesting that less intensive services may be less effective [39]. The same study compared an outpatient Type B service with a Type D service, and showed more BMD testing with the Type B intervention [40]. A two-center comparison study (Type B *vs* standard service), comparing follow up in postmenopausal women with hip fracture, found an increased rate of investigation of osteoporosis risk factors at the FU center [41]. However, only the following studies reported how many of these recommendations translated into actual referrals: in a Type A FU from Sydney, Australia, a total of 84% identified patients had a DXA scan [42]. Overall, in the context of FU programs, referral rates for DXA range from 67.4% to 73.4% in Scotland [43] and from 83.0% to 99.6% in the Netherlands [44], according to studies. Using an automated referral system has been reported to increase referral rate by 100% [45] (even though these systems showed a non-attendance rate of 45% because referral would either decline or not attend [46]).

F. **Osteoporosis treatment and adherence**. Currently, oral bisphosphonates are the most prescribed pharmacological agents to reduce future fracture risk; however, adherence to oral bisphosphonate therapy has been reported to be low, as only a third of patients decide to continue the therapy at 1-year follow-up [47]. Anti-osteoporosis drugs are available as daily, weekly or monthly oral tablets, as daily, three-monthly or six-monthly injections, or as annual infusions, so that the treatment can be optimally targeted to patients' needs in order to significantly reduce fracture rates [48]. Studies demonstrate that anti-osteoporosis treatments are more quickly established in FUs: Type A services reported an RR 1.50–4.25 for treatment initiation, with data gathered up to 2 years after the first check-up. In the Edmonton study, the FU service, compared with the standard one, showed increased prescription of bisphosphonates in the FU group at 6 months after hip fracture ($p<0.01$) and wrist fracture ($p=0.008$) [33]. The comparative study by the Fracture Prevention Clinic in Newcastle, Australia (Type A FLS *vs* standard service) also demonstrated increased treatment rates in the FU group after an average 2 years of follow-up ($p<0.01$) [26]. A study by Murray *et al*. [32] reported higher osteoporosis treatment rates at six-month follow-ups at the FU center (50% *vs* 27% for humeral fractures, 85% *vs* 20% for hip fractures). The inpatient FU model described by Ruggiero *et al*. (>65 years old, proximal femoral fracture, comparison with historical cohort) also demonstrated an increase in the rate of initiation of pharmacological treatment, from 17.16% to 48.51% ($p<0.01$) [34].

In one study, even GP-initiated post-fracture treatment increased from 12.6% to 31.8% after 1 year of follow-up [28]. Another study that analyzed a cohort of older women with hip fractures, showed that GPs were more likely to prescribe FLS-recommended than standard care treatments ($p<0.01$) [41]. However, in the absence of treatment recommendations (i.e. Type C or D models), there was no difference in treatment initiation rates [39]. The analysis of treatment adherence revealed wide variation between studies: adherence at one-year follow-up has been reported to range from 44% to 80%. In Pennsylvania, USA, a study by the Geisinger Medical Center High-Risk patient Osteoporosis Clinic (HiROC), including patients followed up at 3 and 12 months, reported that adherence to treatment with oral bisphosphonates was 80.7% and 67.7% respectively [49]. In another study, adherence at 1 year improved since the start of a dedicated hip fracture FLS program ($p<0.01$) [34]. A Spanish study including patients followed up through phone calls at 3, 6, 12 and 24 months recorded treatment adherence rates of 72% at 1 year and 73% at 2 years, with significantly higher adherence among women and those who had previously been treated with a similar drug.

G. **Cost effectiveness**. Two randomized trials comparing FU care and usual care in hip fracture and wrist fracture patients reported that for every 100 patients managed, they were able to prevent 6 fractures (4 hips) and 3 fractures (1 hip), respectively, saving the health care system over US$ 250,000 to and gaining up to 4 quality-adjusted life years (QALY) [50,51]. An analysis from the Osteoporosis Exemplary Care Program in Toronto showed that assessing 500 patients per year would prevent 3 hip fractures, saving CA$ 48,950 per year [18], and calculated that the employment of an FU coordinator would still be a cost-effective measure even when managing as few as 350 patients per year [52]. In the USA, a Type A FLS-based model in Boston calculated that for every 10,000 patients managed, 153 fractures (109 hip) would be prevented, corresponding to an overall saving of US$ 66,879 with a gain of QALY of 37.4 years [53]. An FU in Glasgow, UK, developed a cost-effective budget-impact model, calculating that for 1,000 patients, the FLS prevented 18 fractures (11 hips), leading to an overall saving of £21,000 [54]. In a separate study based in Ontario, Canada, cost-effectiveness was compared between a less intensive Type C model and a Type A model. For the Ontario Fracture Clinic Screening program (Type C FLS), 4.3 QALYs were gained and an extra CA$ 83,000 was spent per 1,000 patients, equating to a cost of CA$ 19,132 per QALY gained. Their subsequent enhanced FLS, called the Bone Mineral Density Fast Track program (Type A FLS), was reported to be even more cost effective at CA$ 5,720 per QALY gained [55]. Hence, this almost 4-fold difference in cost-effectiveness suggests that a more intensive model may deliver better outcomes.

FUs: limits

To further improve FU models, several pitfalls must be addressed. Hospitals and healthcare centers alike often lack adequate structures able to provide this service. Funds are also an issue: some centers cannot meet the cost of a DXA testing machine. Furthermore, when downsizing, hospital managers may cut or reduce funds for FUs since their effectiveness is still being appraised. Meanwhile, patient adherence is an issue: many patients simply forget to take their medicines or find it unpleasant to have injections daily. Overall, the lack of perception of the benefits of FUs seems to be an important problem.

Concluding remarks

The FU is a ground-breaking option capable of responding to the health needs of the growing elderly population of

our country by providing effective and efficient management of osteoporosis-induced fractures. FUs can optimize the organizational framework of the different specialties involved in the management of the fractured patient. To date, there are no reference guidelines allowing the establishment of criteria for an optimal coordinated FU, even though this might resolve some of the issues surrounding FUs that we encountered in our research. FUs are proven to be associated with improved outcomes in terms of reducing future fractures, patient morbidity and mortality by establishing a multidisciplinary and global approach to the investigation and treatment of osteoporosis. Healthcare centers offering more intensive services (Type A or B) take full responsibility and achieve better results in terms of efficacy (i.e. a marked decrease in future fracture rates) than less intensive services. Evidence is available for Type A services, which identify, investigate and initiate treatment. We referenced some studies reporting results for Type B services [40,56], but there are no studies that directly compare Type A against Type B. According to our research, the Type A model provides the best efficacy overall; Type B models can easily be upgraded to Type A models to increase efficacy. The evidence strongly suggests that there is a need for wide spread implementation of FUs. In 2009, UK Department of Health developed and published a 5-year FLS model [57] based on a guidance document published the same year [58]. The model showed that these interventions could equate to a national saving of £8.5 million over 5 years. Meanwhile, many professional organizations have published reports or toolkits and set up campaigns in order to promote FLS implementation. Studies demonstrate that FUs are both cost-effective and cost-saving by lowering healthcare costs. However, the cost-effectiveness of each FUis related to its intrinsic features and its healthcare and social context. In conclusion, FUs are beneficial for patients and healthcare providers alike and should be widely implemented. FUs provide the best outcomes when using coordinated intensive services, which cover fragility fracture patient identification, investigation and treatment for osteoporosis, and long-term follow-up. We wish to stress that all fragility fracture patients must receive adequate osteoporosis management. Future research should address the barriers to appropriate management, pursue increased efficacy and implement treatment and diagnostic practices able to close the osteoporosis care gap.

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