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The Role of Fracture Liaison Services in Re-Fracture Prevention

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1. Introduction

1.1 The burden of osteoporotic fractures

Osteoporosis is a disorder of low bone mass and micro-architectural deterioration in bone, resulting in increased bone fragility and susceptibility to fractures even after minimal or inadequate trauma [Anonymous, Consensus conference, 1993]. On statistical grounds, more than 50% of postmenopausal women, and approximately 30% of men over the age of 60 years will suffer at least one minimal trauma fracture during their remaining lifetime [Kanis et al. 2000]. However, any osteoporotic fracture predisposes to further fractures, significant morbidity, and premature death. There is a 2-3 fold increase in the risk of repeat fractures after a first minimal trauma fracture. This is true for both men and women in all age categories [Langsetmo et al. 2009]. In the year 2000, there were about 8.9 million fractures worldwide [Johnell et al. 2006], of which 1.6 million were hip fractures. The number of hip fractures is expected to increase worldwide to 6.26 million by 2050 in the context of an ageing population, and longer life expectancy in the developing world [Sambrook P, Cooper C. 2006]. In Australia, the annual number of fractures is projected to increase by 250%, from 83,238 in 1996 to 207,657 fractures in 2051 as a result of the ageing population. Hip fractures are expected to quadruple over the same period of time [Sanders et al. 1999]. There is significant economic burden associated with minimal trauma fractures. In the USA the cost of minimal trauma fractures was estimated at US \$17 billion in 2005, with the annual cost predicted to increase by 50% in 2025 [Burge et al. 2007]. In Australia the cost of fragility fractures was AU\$ 7.4 billion in 2001 [Sambrook et al. 2002].

1.2 The treatment gap in osteoporosis

Despite the availability of advanced medical care and medications that reduce the risk of re-fracture by 30-90% [Giangregorio et al., 2006], the majority of patients with incident osteoporotic fractures are neither investigated nor treated for their underlying condition. This is referred to as the 'treatment gap in osteoporosis', which has been extensively documented in the international literature [Bliuc et al., 2005; Panneman et al., 2004; Shibli-Rahhal et al., 2011]. A systematic review [Giangregorio et al. 2006] revealed that following a minimal trauma fracture the median rate of bone mineral density (BMD) testing was as low as 10%, as was the initiation of treatment (Figs. 1, 2).

Fig. 1. The diagnostic gap: Low rate of investigations after a minimal trauma fracture. (Reproduced from Giangregorio et al., 2006, with permission.)

A thorough understanding of the factors contributing to the care gap in osteoporosis is pivotal to finding effective solutions. Generally speaking, significant deficits exist on three different levels: patient, doctor, and system level. On a patient and doctor level, a lack of awareness and understanding that a minimal trauma fracture should prompt a thorough evaluation for osteoporosis has been well documented [The Burden of Brittle Bones, 2007]. Patients may be reluctant to be evaluated due to perceived medication side effects, time constraints, costs, and language barriers. A desire to avoid polypharmacy may also contribute to the reluctance of elderly patients and their carers to initiate treatment. Doctors may have the misconception that the current treatments available for osteoporosis are ineffective or fraught with side effects, or they may not have the resources (e.g. for bone mineral density testing) or time to evaluate patients for osteoporosis, especially in an acute hospital setting. On a systems level, fragmentation of care further contributes to the “care gap”, in that no single care provider (primary care physician, orthopaedic surgeon, specialist physician, or primary care physician) takes responsibility for osteoporosis management. Furthermore, a lack of funding for osteoporosis may be a consequence of low priority of osteoporosis in the public mind. For instance, osteoporosis has to compete for funding with diseases such as breast cancer and leukaemia which have more ‘prestige’ and therefore lobbying power, probably because they are associated with death at a younger age. According to the National Institutes of Health in the US [<http://report.nih.gov/rcdc/categories/>], estimated funding for breast cancer research for the 2011 financial year was quadruple that for osteoporosis, despite a higher incidence of osteoporosis. That is, 12.5% of women in the US will develop breast cancer during their lifetime, whereas 50% of women will suffer from a minimal trauma fracture after the age of 60 years.

Fig. 2. The therapeutic gap: Low rate of osteoporosis treatment after a minimal trauma fracture. Key: BP = bisphosphonate, SERM = Selective Estrogen Receptor Modulator, HRT = Hormone Replacement Therapy. (Reproduced from Giangregorio et al., 2006, with permission.)

2. Fracture liaison services

2.1 Bridging the gap in osteoporosis care through fracture liaison services

The acute presentation of a patient with a minimal trauma fracture to a health care facility (usually an emergency department) is an easily identifiable clinical event. Care of these patients is then transferred to an orthopaedic service, either in an inpatient or an outpatient setting. This process represents a unique window of opportunity to identify, investigate and appropriately treat patients with osteoporosis [Gallacher, 2005]. Thus, over the last 10 years several groups across the world, including Australia, Canada, Europe and the USA have attempted to address the osteoporosis care gap via the development and clinical implementation of what is now generally known as “Fracture Liaison Services” (FLS). However, the published literature on FLS, while substantial and often of good quality, is characterized by enormous heterogeneity in the methods of patient identification, patient capture, and intensity of intervention. Thus, there is significant variation in the type of studies, patient characteristics, methodology and criteria of patient identification. The extent of engagement of the service in the investigation and treatment of the patient also varies significantly, together with outcomes in relation to bone mineral density (BMD) testing, treatment initiation, adherence, and re-fracture rates. This chapter will review the existing literature on FLS to provide a coherent overview of their methodology and outcomes.

2.2 Models of Care based upon intervention intensity

The spectrum of possible interventions prompted by a patient presenting to hospital with a minimal trauma fracture can be summarized as follows:

- i. Provision of specific “osteoporosis protocols” to staff at inpatient wards, orthopaedic fracture clinics and emergency departments;
- ii. Education of patients through letter (information sheet), or direct communication either ‘face-to-face’ or via telephone;
- iii. Alerting the Primary Care Physician (PCP) of the need to evaluate and treat their patient for osteoporosis via direct communication, letter, or email;
- iv. Assessment of clinical risk factors for osteoporosis;
- v. Offering BMD testing (osteodensitometry);
- vi. Investigation for secondary causes of osteoporosis;
- vii. Initiating treatment (both non-pharmacological and pharmacological);
- viii. Monitoring with regular follow-up, using a dedicated database to evaluate effectiveness of intervention.

Depending on the model of care implemented at any given site, the actual intervention can range from a simple, education-based model with high patient capture and turnover to more complex models involving most or all components listed above. More complex, intensive models typically incorporate patient education and risk assessment, with on-site bone densitometry testing, as well as treatment initiation. In these complex models of care it is often the fracture liaison co-coordinator who plays a pivotal role in orchestrating and co-ordinating care, after the minimal trauma fracture.

Given the heterogeneity in models of care and their reporting of outcomes, the following classification of FLS from ‘type A’ to ‘type D’ models of care, based upon the type and intensity of the intervention has been suggested (Table 1). ‘Type E’ model of care is a category unrelated to intervention intensity, representing inpatient intervention only:

Model of Care	Description
A	Identification, Assessment (risk factors, pathology testing, BMD), Treatment initiation
B	Identification, Assessment, Treatment recommendation only
C	Education of patient and Primary Care Physician
D	Education of patient only
E	Inpatient specialist consultation

Table 1. Categorical types of FLS according to Model of Care

This categorization of intervention types is graded from A through to D, with A representing the most intensive, all-encompassing intervention. Although each model of care is unique, there are significant variations in details of the intervention, and reporting of outcomes between each study. It is also important to note that health care environments and resources differ with countries, leading to the development of unique models of care.

2.3 ‘Type A’ models of care

Since 2000, there have been thirteen studies published describing a ‘type A’ model of care, heralding from Australia (four studies – Kuo et al., 2007; Vaile et al., 2007; Giles et al., 2010;

Lih et al., 2011), US (three studies – Edwards et al., 2005; Dell et al., 2008; Navarro et al., 2011), Canada (three studies – Bogoch et al., 2006; Majumdar et al., 2007 & 2011; Morrish et al., 2009) and Europe (two studies – Clunie et al., 2008; Boudou et al., 2011). A further two studies focused on the cost analysis of individual FLS (Sander et al., 2008; Cooper et al., 2011).

These clinical studies are unique in describing a co-ordinated model of care through which patients are identified, assessed and treated following a minimal trauma fracture as part of an all-encompassing service. Assessment includes evaluation of clinical risk factors for osteoporosis, a bone mineral density scan, radiographic or other imaging as required, and various pathology tests to exclude secondary causes of osteoporosis. This assessment is then followed by the initiation of appropriate non-pharmacological and pharmacological interventions. An example of a classical ‘type A’ model of care is the Concord Hospital FLS (Figure 3). Table 2 illustrates the summary of outcomes for ‘Type A’ model of care. For a more analytical evaluation of the cited studies see Appendix A.

Fig. 3. An example of the structure of a ‘Type A’ FLS. Key: MTF = Minimal Trauma Fracture; f/u = follow-up; LMO=Local Medical Officer or primary care physician

Country	Study	Study Type	BMD/Rx	BMD	Rx	Rx Adherence	Refractures	Cost Effectiveness
Australia	Vaile et al., 2007	Before & After	NA	All	51% v 11%	95% @ 12/12	NA	Y
	Lih et al. 2011	Prospective Controlled	NA	All	79% v 31%	NA	4.1 v 19.7% @ 4yr	Y
	Giles et al. 2010	Cross Sectional	NA	NA	NA	NA	NA	NA
	Kuo et al. 2007	Before & After	NA	83% v 10%	NA	10 months 80%	NA	NA
United States	Navarro et al. 2011	Cross Sectional	F: 92%, M: 75%, nil racial disparity	NA	NA	NA	NA	NA
	Dell et al. 2008	Prospective Observational	NA	58% in 2006, 16% in 2002 to	60% v 24%	NA	37.2% FRR in hip fractures	NA
	Edwards et al. 2005	Before & After	NA	100%	hip: 28% v 70% @ 6 months v 25% @ 12 months	NA	NA	NA
Canada	Majumdar et al., 2011	RCT	Appro Rx: 57% ('A') v 28% ('C')	81% v 52%	43% v 12%	NA	NA	NA
	Majumdar et al. 2007; Morrish et al. 2009	RCT	67% ('A') vs 45% ('B') vs 26% ('D')	80% vs 68% vs 29% (@ 6 months)	51% v 38% v 22% at 6 months	NA	No difference @ 12 months	Y
	Sander et al. 2008	Cost analysis of Bogoch						Y
	Bogoch et al. 2006	Cross Sectional	97% (including referral)	NA	NA	NA	NA	NA
EU	Clurrie et al. 2008	Cross Sectional	NA	91.2% (50-69yo)	NA	NA	NA	NA
	Boudouet et al. 2011	Cross Sectional	NA	NA	90.3% initiated	80% on Rx after one yr; after 27.4 months, 68% persistent w Rx	11.40%	NA

Table 2. ‘Type A’ Model of Care Fracture Liaison Services – Summary of Outcomes; Key: The first % figure in each cell represents the intervention group result and the second % figure represents the control group. ‘v’ =versus. F=female, M=male, BMD/Rx=BMD testing and/or treatment rates; RRR= relative risk reduction, BMD=BMD testing rates; Rx=treatment rates; See Appendix A for further details.

'Type A' model of care fracture liaison services – Summary of outcomes

The twelve studies evaluating a 'type A' model of care reviewed here varied greatly in regards to study design, ranging from randomised controlled trials to simple cross-sectional analyses. All except one study [Boudou et al., 2011] evaluated male and female patients, with information on racial background being reported in 3 out of 11 studies [Majumdar et al., 2007 & 2011; Navarro et al., 2011]. The number of patients ranged from 46 to 620,000, but most studies included between 200 to 400 subjects. Most studies included all fracture types. So far, only two FLS were analysed in regards to their cost-effectiveness but in both cases cost-effectiveness of the service was clearly established.

In terms of outcomes, all 'type A' FLS resulted in increased assessment, testing and treatment rates. In the four studies that included valid control groups, the average rate of BMD testing increased from 40.5% in the controls to 80.5% in the intervention groups [Majumdar et al., 2007 & 2011; Morrish et al., 2009 & Lih et al., 2011]. In the same studies, the average rate of anti-osteoporosis treatment initiation rose from 22% in the control groups to 58% in the intervention groups. Re-fracture rates were reported in only four studies. Lih and colleagues (2011) reported a significant improvement in re-fracture rate from 19.7% in the control group to 4.1% in the intervention group. Dell and colleagues (2008) reported a relative risk reduction of 37.2% for hip fractures, using historical data for comparison. Boudou and colleagues (2011) reported an 11.4% re-fracture rate after a mean follow-up period of 27.4 months, while the study by Morrish et al. (2009) was underpowered to demonstrate any significant changes in re-fracture rates after one year of follow-up.

A 'type A' intervention represents the most intensive and costly model of care, where patients are identified, assessed and treated for their osteoporosis after minimal trauma fracture. Central to the success of this model is the Fracture Liaison Co-ordinator (FLC), who orchestrates the identification, assessment and treatment of eligible patients. Thus, the barriers of patient education, primary care physician inertia and lack of a single care provider are addressed in one all-encompassing service. As expected, most 'type A' fracture liaison services differ by region due to the fact that they are embedded within different health care systems. This difference is primarily apparent if one compares the United States with Australia. While successful FLS have been developed in Australia, all of the services are based upon individual initiatives with no systemic support by the Area Health Service. As a result, patient numbers are relatively small. In contrast, the US system exemplified by the Kaiser Permanente group has the advantage of integrated, electronic health care delivery network, enabling the FLS to serve larger numbers of patients. In addition, there is a process of continual feedback to stimulate improvements in care over time. Non-electronic based intervention models have the disadvantage of being more labour-intensive. Overall, the critical component of these services is streamlining the transition from acute fracture care to osteoporosis care, targeted at reducing the risk of future fractures.

As a general observation, most 'type A' fracture liaison services identified patients from a number of sources, including emergency departments, outpatients clinics and inpatient wards. The setting in which assessment, treatment and follow-up occurs is generally on an outpatient basis, which requires patients to be ambulatory and not institutionalised. This is reflected by a comparatively "young" mean age of 68 years in 'type A' studies, as well as a

predilection for the recruitment of patients with non-hip fractures. Thus the care of patients with minimal trauma fractures can be conceptualised as having two arms – one arm for the frail elderly who constitute most patients with hip fractures, and the other arm for the younger, more ambulatory patients who tend to have non-hip fractures. Although it is important to treat the frail elderly patient for osteoporosis after a minimal trauma fracture, these patients are streamlined to the realm of the geriatricians who need to prioritise osteoporosis treatment in the context of multiple competing co-morbidities. On the other hand, the ‘type A’ fracture liaison service is ideally suited to younger patients with minimal trauma fractures because it is easier for them to attend outpatient clinics. In addition, identifying osteoporosis and treating osteoporosis early will reduce the risk of future fractures for those with a likely life expectancy beyond twenty years. Thus, the short term expenditure of a health care system on a ‘type A’ FLS, will have substantial health and economic benefits for the population as a whole, in any country or region of the world.

2.4 ‘Type B’ models of care

‘Type B’ models of intervention are slightly less intensive compared to ‘type A’ models of care in that treatment initiation is the responsibility of the primary care physician. That is, ‘type B’ interventions identify and assess patients with a minimal trauma fracture, then make treatment recommendations to the primary care physician. There have been eleven studies describing a ‘type B’ intervention, including New Zealand (one study – Sidwell et al., 2004) and Canada (one study – Morrish et al., 2009), the United States (two studies – Cuddihy et al., 2004 & Johnson et al., 2005), the United Kingdom (four studies – Charalambous et al., 2002; McLellan et al., 2003; Langridge et al., 2007 & McLellan et al., 2011) and the Netherlands (three studies – Chevalley et al., 2002; Astrand et al., 2006 & Huntjens et al., 2010). Table 3 illustrates the summary of outcomes for ‘Type B’ model of care. For a more analytical evaluation of the cited studies see Appendix B.

‘Type B’ model of care fracture liaison services – Summary of outcomes

We have identified eleven publications describing a ‘Type B’ intervention. One of these was a review of five different fracture liaison services in the Netherlands. Thus there are a total of 15 ‘Type B’ models of care described from New Zealand (n= 1), the United States (n =2), Canada (n = 1), and Europe (n= 11). Study types varied between randomised controlled / case control studies (n= 1 each), ‘before and after’ studies (n= 4) and cross-sectional analyses (n= 9). The average proportion of females was 72%, with one study recruiting only female patients, and another including 96% males. Racial background was reported in only one study, at 86% white Caucasian. The number of subjects varied from 96 to 11,096 with a median number of subjects per study of 934. The mean age across all studies was 68 years and the wrist was the most frequent site of fracture. This is in keeping with the fact that most patients were identified in an outpatient setting, and patients with dementia, or frail patients were excluded. All services apart from two [Sidwell et al., 2004 & Charalambous et al., 2002] utilized a fracture liaison co-ordinator.

In terms of outcomes, the overall rate of BMD testing and/or treatment reported in two studies was about 76% [Charalambous et al., 2002 & McLellan et al., 2003]. In four studies with control group outcomes, the average rate of bone mineral density testing in controls was 12.5%, and 57.5% in the intervention groups [McLellan et al., 2003; Cuddihy et al., 2004; Sidwell et al., 2004 & Johnson et al., 2005]. In three cross-sectional studies, the average rate of

Country	Study	Study Type	BMD/Rx	BMD	Rx	Rx A
New Zealand	Sidwell et al. 2004	Before & After	NA	78% vs 11%	34% vs 10% (@ 9 months)	
United States	Cuddihy et al. 2004	Before & After	NA	45% vs 16%	NA	36% m
	Johnson et al. 2005	Before & After	NA	63% vs 13%	Recommended (if OP on BMD): 19 v 7%	6-7n v 6n
Canada	Morrish et al. 2009	RCT	(see Majumdar et al. 2007, T			
EU (UK)	Langridge et al. 2007	Case control	NA	NA	37% (of 129)	
	Charalambous et al. 2002	Before & After	79% v 11%	NA	NA	
	McLellan et al. 2003	Cross Sectional	73.50%	44% (vs 10% historical control)	27% Rx wout BMD; 20% no Rx needed; no other outcomes	
	McLellan et al. 2011	Cross sectional	NA	49%	54% (11% on Rx previously)	12m
EU	Chevalley et al. 2002	Cross Sectional	NA	63%	63%	6mo of i
	Astrand et al. 2006	Cross Sectional	NA	93%	NA	
	Huntjens et al. 2010	Cross Sectional	NA	Y	NA	
	Huntjens et al. 2010	Cross Sectional	NA	Y	NA	
	Huntjens et al. 2010	Cross Sectional	NA	Y	NA	
	Huntjens et al. 2010	Cross Sectional	NA	Y	NA	
	Huntjens et al. 2010	Cross Sectional	NA	Y	NA	

Table 3. ‘Type B’ Model of Care Fracture Liaison Services – Summary of Outcomes.

Key: The first % figure in each cell represents the intervention group result and the second % figure group. ‘v’ =versus. BMD/Rx=BMD testing and/or treatment rates; BMD=BMD testing rates; Rx=treatment rates; See Appendix B for further details.

BMD testing was 68% [Chevalley et al., 2002; Astrand et al., 2006 & McLellan et al., 2011]. In three studies with control group outcomes for treatment rates, the average rate of initiation of anti-osteoporosis medications in controls was 9%, compared to 35% in the intervention groups [Sidwell et al., 2004; Johnson et al., 2005 & McLellan et al., 2011]. Cuddihy et al., 2004 and Johnson et al., 2005 reported adherence rates at six months, of 7.5% in the control group versus 24.5% in the intervention group. The Glasgow Fracture Liaison Service, reported re-fractures rates of 5.1% at 3.5 years follow-up, and 12% at 8 years follow-up [McLellan et al., 2011]. In the same study, the Glasgow service was been shown to be cost-effective.

Taken together, 'Type B' interventions appear to be nearly as effective as a 'Type A' interventions if implemented in the right setting. On the other hand, as shown by Majumdar and Morrish in a randomised controlled trial, there is an incremental benefit in BMD testing and treatment rates with 'Type A' versus 'Type B' models of care. Another interesting point is the high number of patients identified with this form of intervention – that is, a high turnover rate, which does not necessarily translate to anti-fracture benefits in the long term. This is illustrated by comparing the re-fracture rate of 4.1% (over 4 years) in the 'Type A' Concord Hospital service, with the re-fracture rate of 12% over 4 years in the 'Type B' Glasgow service. While both services differ in some aspects they are similar enough to allow a comparison of fracture outcomes. Therefore, the lower re-fracture rate in 'Type A' services may be related to greater attention given to patient follow-up and compliance within the service itself, rather than relying on external follow-up by the PCP. 'Type B' services seem to be most effective if there is a good rapport and communication between the primary care physician and the fracture liaison service.

2.5 'Type C' models of care

'Type C' models of care are characterised by a less intensive intervention, compared to 'A' and 'B' designs. Once patients are identified after their minimal trauma fracture they receive education regarding osteoporosis in general, risk factors for osteoporosis, lifestyle advice (including falls prevention) and the need for further assessment and treatment. The second component of this model of care involves engaging and alerting the primary care physician regarding the minimal trauma fracture, and the need for further assessment and treatment to reduce the risk of further fractures. Communication with patient or primary care physician is performed either 'face-to-face', via personalised letter, or a telephone call. No further assessment is performed with respect to bone mineral density testing or specific treatment for osteoporosis by the FLS.

Table 4 summarises the outcomes from a total of twelve studies describing a 'type C' model of care: one from Australia, six from the United States, and five from Canada. For a more analytical evaluation of the cited studies see Appendix C.

'Type C' Model of care fracture liaison services – Summary of outcomes

There are twelve published studies describing 'type C' interventions, including four randomised controlled trials [Gardner et al., 2005; Feldstein et al., 2006; Solomon et al., 2007; Majumdar et al., 2008], four 'before and after' analyses [Inderjeeth et al., 2010; Harrington et al., 2005 (two studies); Hawker et al., 2003], two prospective controlled trials [Ashe et al., 2004; Majumdar et al., 2004], one cross sectional study [Skedros, 2004], and one cluster randomised trial [Cranney et al., 2008]. Patients were identified from wards, outpatient

departments and the emergency departments by a fracture liaison nurse in all but four studies, in which existing staff were utilized, such as orthopaedic surgeons [Cranney et al., 2008; Hawker et al., 2003; Skedros, 2004; Inderjeeth et al., 2010]. To determine outcomes, most patients were followed-up at six months after the intervention, apart from two studies which involved 10 and 18 month follow-up periods [Solomon et al., 2007 & Harrington et al., 2005 respectively]. The average rate of BMD testing and/or treatment for osteoporosis was reported in seven studies [Gardner et al., 2005; Feldstein et al., 2006; Harrington et al., 2005; Solomon et al., 2007; Majumdar et al., 2004 & 2008], with a rate in the control group of 11.7 % (range 5%-21%), compared to 39.2% (range 14%-71%) in the intervention group. This translated to a 27.5% improvement with the intervention. Derived from six studies [Inderjeeth et al., 2010; Majumdar et al., 2004 & 2008; Ashe et al., 2004; Hawker et al., 2003; Cranney et al., 2008], the average rate of BMD testing was 18% (range 3%-28%) in the control group and 59% (range 43%-92%) in the intervention group. This represents a risk difference of 41% with the intervention. Amongst the five studies reporting on anti-osteoporosis treatment [Inderjeeth et al., 2010; Feldstein et al., 2006; Majumdar et al., 2004 & 2008; Hawker et al., 2003], the average rate was 7.6% (range 5%-10%) in the control group, and 24.4% (range 11%-40%) in the intervention group. This translates to a 16.8% absolute improvement with intervention 'type C'.

The provision of information to patients and physicians was the key component of all 'type C' services. Despite this, there was still significant variability in the results with different studies. For instance the study by Solomon et al. (2007) only improved BMD testing and/or treatment by 4% (baseline of 10%). There may be a number of factors contributing to this poor result, such as the non-patient specific nature of the educational intervention for the primary care physicians in this study, whereby a list of patients was provided during a visit to the primary care physician by a pharmacist, who then provided general information about osteoporosis to the physician. Secondly, patient education took the form of an automated phone call to the patient, which is probably not as effective as personal "one-on-one" contact over the phone or face-to-face. Thirdly, there may have been resistance from physicians to the intervention, as pharmacists may not have as much impact on practice as a "respected opinion leader". This is in contrast to other studies which provided information to primary care physicians with the endorsement of a "respected opinion leader".

2.6 'Type D' models of care

'Type D' interventions represent a model of care in which patients receive specific osteoporosis education following a minimal trauma fracture. Patient education can take the form of a patient-specific letter, educational pamphlet, video, or personal communication to the patient via a telephone or 'face-to-face' interaction. Table 5 summarises the major outcomes reported in the three publications describing a 'Type D' model of care. For a more analytical evaluation of the cited studies see Appendix D.

'Type D' model of care fracture liaison services – Summary of outcomes

As illustrated in Table 5, patient education alone has little or no impact on rates of treatment initiation, despite an increase in the rate of BMD testing. Thus, it is unlikely that this form of intervention has any impact, unless combined with other components such as assessment and treatment for osteoporosis.

Country	Study	Study Type	BMD/Rx	BMD	Rx	Rx Adherence	Refractures	Cost Effectiveness
Australia	Inderjeeth et al. 2010	Before & After	NA	51% vs 3%	29% vs 6% (@ 10 to 13 month f/u)	NA	NA	NA
	Gardner et al. 2005	RCT	42% vs 19% (@ 6 months)	NA	NA	NA	NA	NA
United States	Feldstein et al. 2006	RCT	51.5% vs 43.1% v 5.9% (@ 6 months)	NA	6 month: 27.7% vs 20.2% v 5.0% (@ 6 months)	NA	NA	NA
	Harrington et al. 2005	Before & After	20% vs 5% (@ 6 months)	NA	NA	NA	NA	NA
	Harrington et al. 2005	Before & After	46% vs <10% (up to 18 months)	58% @ 18 months	NA	NA	NA	NA
	Skedros, 2004	Cross sectional	NA	NA	30% (@ 3 months)	NA	NA	NA
Canada	Solomon et al. 2007	RCT	14% vs 10% (@ 10 months)	NA	NA	NA	No difference	NA
	Majumdar et al. 2004	Prospective Controlled	71% v 21% (@ 6 months)	62% v 17% 6 months	40% vs 10% (@ 6 months)	NA	NA	NA
	Ashe et al. 2004	Prospective Controlled	NA	92% v 23%	NA	NA	NA	NA
	Hawker et al. 2003	Before & After	NA	Ordered 43% v 18%	11% vs 10%	NA	NA	NA
	Majumdar et al. 2008	RCT	38% vs 11%	52% vs 18%	22% vs 7%	NA	NA	NA
	Cranney et al. 2008	Cluster Randomized	NA	53% vs 28%	NA	NA	NA	NA

Table 4. ‘Type C’ Model of Care Fracture Liaison Services – Summary of Outcomes.
Key: The first % figure in each cell represents the intervention group result and the second % figure represents the control group. ‘v’ =versus. BMD/Rx=BMD testing and/or treatment rates; BMD=BMD testing rates; Rx=treatment rates; Y = Yes. See Appendix C for further details.

Country	Study	Study Type	BMD/Rx	BMD	Rx	Rx Adherence	Refractures	Cost Effectiveness
Australia	Bluc et al. 2006	RCT	38% vs 11%	38% vs 6%	6% vs 5%	NA	NA	NA
	Diamond T, Lindenberg M. 2002	Cross Sectional	NA	51%	29%	NA	NA	NA
Canada	Bessette et al., 2011	RCT	NA	15%('D') vs 12%(control)	14% vs 8%	NA	NA	NA

Table 5. ‘Type D’ Model of Care Fracture Liaison Services – Summary of Outcomes; Key: The first % figure in each cell represents the intervoention group result and the second % figure represents the control group. ‘v’ =versus. BMD/Rx=BMD testing and/or treatment rates; BMD=BMD testing rates; Rx=treatment rates; see Appendix D for further details.

2.7 ‘Type E’ models of care

‘Type E’ interventions are limited to inpatient specialist consultations. This intervention does not include any outpatient component and is the most heterogenous model as inpatient consultations vary significantly in the degree of intervention at each site. Table 6 illustrates the summary of outcomes for ‘Type E’ model of care. For a more analytical evaluation of the cited studies see Appendix E.

Country	Study	Study Type	BMD/Rx	BMD	Rx	I
Australia	Chong et al. 2008	Cross Sectional	NA	NA	NA	
	Jones et al. 2005	Before & After	NA	NA	24% vs 5%	
United States	Streeten et al. 2006	Cross Sectional	NA	66%	68% vs 3%	
	Jachna et al. 2003	Cross Sectional	NA	NA	No significant impact	
	Kamel et al. 2000	Cross Sectional	NA	3%	<10% (93% medical consultant)	
EU - UK	Wallace et al. 2011	Cross Sectional	NA	NA	90.5% vs 60.5%	

Table 6. ‘Type E’ Model of Care Fracture Liaison Services – Summary of Outcomes.
Key: The first % figure in each cell represents the intervention group result and the second % figure represents the control group. ‘v’ =versus.BMD/Rx=BMD testing and/ or treatment rates; BMD=BMD testing rates; Rx=treatment rates. See Appendix E for further details.

‘Type E’ model of care fracture liaison services - Summary of outcomes

Taken together, inpatient protocols together with ortho-geriatric and fracture liaison services improved treatment outcomes. However, inpatient physician consultation alone appeared to be ineffective. This is likely due to the fact that a specific osteoporosis consultation was not asked for in these studies. Summary statistics were not performed due to marked variability in the reporting of outcomes, making interpretation relative to other models of care less reliable. It is important to bear in mind that most of the studies published on fracture liaison services excluded frail, demented patients, often living in assisted accommodation. A separate assessment pathway is required, as their needs are very different from those who are still living at home. Perhaps a greater focus needs to be placed on falls prevention strategies in this sub-group.

3. Conclusions

In this chapter, an attempt has been made to collate, compare and discuss the methodology and outcomes of different types of fracture liaison services around the world. Comparisons between models, and even within the same intervention model are generally difficult due to a lack of standardised outcome measures. Nevertheless, Table 7 represents a summary of relevant outcome data (rates of BMD testing, rates of treatment initiation), categorised according to the model of care. Figure 4 illustrates the same outcome measures without correction against controls, which are often not valid (e.g. historical controls), or not reported. It is clear from this summary that the effectiveness of a fracture liaison service is related to the intensity of the intervention. Thus, ‘type A’ models of care are more effective than ‘type B’ models of care, and ‘type B’ models of care produce better outcomes than ‘type C’, or ‘D’ models of care. This relationship is also evident from a number of randomised controlled trials [Gardner et al., 2005; Bliuc et al., 2006; Feldstein et al., 2006; Majumdar et al., 2007 & 2008; Solomon et al., 2007; Morrish et al., 2009]. Clearly, the specific health care system in which a FLS is embedded is of pivotal importance. For example, a ‘type B’ model of care has been shown to be extremely effective in the UK due to the strong structural integration between primary care physicians and public hospitals. As would be expected, educational interventions alone (type C and D interventions) were less effective than types A and B interventions. An educational intervention system still had some limited benefits, and may be an option in resource poor areas.

Intervention Type	BMD (%)	Rx (%)
A	85 (58-100)	57 (45-90)
B	62 (44-93)	42 (27-63)
C	59 (43-92)	27 (11-40)
D	35 (15-51)	16 (6-29)

Table 7. Outcome measures according to intervention model of care, including the ranges of outcome rates (%) across studies.

A further factor which is likely to have a significant impact on the effectiveness of any intervention is the length of time between the fracture and the intervention. For example,

treatment rates at six months with the same ‘type C’ intervention was 22% if the intervention occurred immediately after the fracture [Majumdar et al., 2008], compared to 11% if the same intervention occurred one year after the fracture [Majumdar et al, 2011]. Perhaps the short period of pain associated with the fracture provides a ‘window of opportunity’ to instigate behavioural change in the patient.

A major deficit in the published literature on models of post-fracture care is the inconsistent reporting of results. This covers a spectrum of outcomes such as the identification rate of potentially eligible patients, the length of time between fracture and FLS evaluation, the extent of risk factor evaluation, the assessment for secondary causes for osteoporosis, the rate of BMD testing, the rate of treatment, adherence to anti-osteoporosis therapy, the definition of the term “appropriate care”, re-fracture rates, and formal cost-effectiveness evaluations. All of these measures would be important for quality assurance and to benchmark performance. Thus, guidelines on reporting outcomes may be of benefit in the future.

Fig. 4. Relationship between intervention intensity and outcomes. The dotted line represents the proportion of patients on treatment without any intervention.
Key: Rx = anti-osteoporosis treatment; BMD = bone mineral density testing.

Not only is their heterogeneity in outcomes, but also the very definition of a minimal trauma. Although the vast majority of studies define it as a fall from standing height or less, one study defined minimal trauma as the impact from a fall less than one metre in height [Bessette et al. 2011]. It is questionable if a fall from two or three steps, or inversion of the ankle should be defined as minimal trauma.

The vast majority of studies (91%) included both males and females, with the mean proportion of females in each study of 72%. Four studies (9%) included females only. Many studies confirm the well-known gender disparity in the evaluation and treatment of osteoporosis [Bogoch et al., 2006; Cuddihy et al., 2004; Dell et al 2008; Diamond and Lindenberg 2002; Kuo et al., 2007; Navarro et al., 2011].

The under-recognition of osteoporosis in men is illustrated by Cuddihy and colleagues, who noted amongst those who had a prior fracture, none of the men had a diagnosis of osteoporosis, whereas 79% of women did. Similarly, Bogoch and co-workers noticed that baseline osteoporosis treatment rates were lower in men (15.5%) than in women (39%). Kuo and colleagues also found the baseline osteoporosis management rates were lower in men (9%) compared with women (34%).

Furthermore, after institution of the Healthy Bones Program, the Kaiser Permanente group reported a significant gender disparity, with a higher treatment rate amongst women (92.1%) compared to men (75.2%) [Navarro et al. 2011]. In the same study, amongst those who sustained a further hip fracture, 73.5% of women and 30.7% of men were on osteoporosis treatment at the time of the fracture. With the institution of the Healthy Bones Program, Dell et al. (2008) reported an increase in the proportion of all BMD scans performed for men from 7.2% in 2002, to 14.5% in 2006. The proportion of all osteoporosis therapy dispensed for men went from 8% (2002) to 10% (2006), which is much lower than expected from the gender distribution in the studies (i.e., 25% were men).

The factors contributing to the gender disparity include men being less proactive with their health than women, due to lack of interest or awareness. Physicians may be more complacent with men due to a misperception that osteoporosis only affects women. Bliuc and colleagues (2006) found that men were less likely than women to respond to an information based intervention by going to their PCP for osteoporosis assessment. Amongst those who did see their PCP, men were less likely to have anti-resorptives recommended, indicating a physician-related barrier to treatment. Diamond and Lindenberg also reported lower treatment uptake rates amongst men who sustained a minimal trauma fracture and were found to have an osteoporotic range BMD T-score.

These studies indicate that the gender disparity needs to be addressed on different levels: patient, health care professional, and system level. Awareness of the gender disparity in recognition and treatment of osteoporosis may help clinicians target this group more effectively.

Ethnicity was only reported in five of forty two studies. Despite documented racial disparities in osteoporosis management in the United States [Wei et al., 2003; Epstein et al., 2010], it is reassuring to see an absence of racial disparity in the Kaiser Permanente system of care [Navarro et al. 2011].

Treatment rates may vary between health networks and countries due to different diagnostic and treatment thresholds. For example, in the South Glasgow service, patients with hip fractures were treated without a prior BMD scan, whereas in the West Glasgow service a BMD study was routinely performed in all patients and pharmacotherapy was initiated if the T-score was less than -2.0 SD. This threshold, however, differs from that of other centres (e.g. Majumdar et al., 2007: T-score of less than -1.5 SD). In the UK studies, only oral bisphosphonates were initiated, mostly due to cost considerations. Those patients who could not tolerate or receive oral bisphosphonates were treated with calcium and vitamin D only, a strategy which would certainly differ between countries.

Treatment rates are still suboptimal, even in 'type A' services. In order to improve capture rates, fracture liaison services will need to utilize integrated electronic health system databases. There is no doubt that there is a paucity of data on re-fracture rates, adherence, and cost-

effectiveness of intensive models of care, although initial results are promising. Attempts should be made at collaboration between centres, especially in fragmented health care networks within countries. Unfortunately, there is a paucity of data on FLS in the majority of the world's population. That is, the populations of the US, Canada, Australia, New Zealand and Europe only constitute 17% of the world's population. We need to ensure that treatment disparities between regions, genders, as well as race, are addressed. Therefore, although fracture liaison services have contributed significantly towards closing the care gap in osteoporosis management in patients after a minimal trauma fracture, there is room for significant improvements in post-fracture management of patients with osteoporosis.

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5. Appendices

5.1 Appendix A

5.1.1 'Type A' fracture liaison services in Australia

There have been four publications from Australia describing a 'Type A' intervention [Kuo et al., 2007; Vaile et al., 2007; Giles et al., 2010; Lih et al., 2011]. Individual hospital Fracture Liaison Services have grown over the last decade, out of individuals "championing" the cause of patients after a minimal trauma fracture. Each hospital has tailored their approach according to their resources and experience.

Australian residents fall under the umbrella of Medicare, a comprehensive health care system whereby free public hospital care is provided. Medicare Australia also funds the Pharmaceutical Benefits Scheme (PBS), whereby a comprehensive list of pharmaceuticals are subsidized. This system provides an ideal environment for fracture liaison services because medical practitioner consultation, osteodensitometry, and pathology testing are performed at no expense to the patient. A comprehensive list of specific anti-osteoporosis therapy is subsidized by the PBS, thus allowing patients to commence (and continue) treatment at minimal expense. Notably, calcium and vitamin D supplementation is not subsidized under this scheme.

Despite universal health care coverage in Australia, there is limited integration of health care information and collaboration between hospitals, probably due to historical precedent in funding structure of individual hospitals. Therefore various FLS have developed independently in individual hospitals, leading to smaller numbers of patients in each study (hundreds), in contrast to the Kaiser Permanente group in the US (thousands of patients) which is characterized by an integrated electronic medical record system spanning wide geographic areas.

The New South Wales (NSW) government is currently attempting to integrate and standardize post-fracture care in NSW, through the Agency for Clinical Innovation (ACI).

The ACI is focused on an agenda to develop FLS in all hospitals across NSW to address the care gap in osteoporosis. Ideally, this system would allow integration of all data in a central database to help benchmark performance.

Study types and patient characteristics

There have been two 'before and after' type studies [Kuo et al., 2007; Vaile et al., 2007], one cross-sectional study [Giles et al., 2010], and one prospective controlled study [Lih et al., 2011]. All studies were from Eastern New South Wales. Three studies had control groups: in the study by Lih and colleagues (2011), the control group was concurrent. That is, the control group was derived from eligible patients who presented to hospital with a minimal trauma fracture but for various reasons were not seen by the FLS. The other two studies reported historical control groups, which therefore provide less robust outcome data [Kuo et al., 2007; Vaile et al., 2007].

All studies recruited male and female patients, with the proportion of females varying from 71% to 79%. Race or ethnicity was not described in any of the four studies but given the demographics of Eastern New South Wales, it is likely that the majority of patients were of Caucasian ethnicity. The numbers of patients identified by each FLS ranged from 155 to 2049. All four studies included patients who sustained symptomatic fractures at any site although three studies excluded skull fractures [Kuo et al., 2007; Giles et al., 2010; Lih et al., 2011], and Kuo et al. (2007) excluded fractures of fingers and toes, whilst Lih and colleagues excluded vertebral fractures. In the three studies reporting on fracture sites, the proportion of patients with wrist fractures varied from 22-45%. The lower age limit was 50 years in two studies [Vaile et al., 2007; Giles et al., 2010], 45 years [Lih et al., 2011], and 20 years [Kuo et al., 2007]. The mean age of patients varied from 60 years to 75 years. The reason for the older demographic in the study by Giles and colleagues (2010) was the inclusion of patients residing in nursing homes, who were excluded from the other studies.

Patient identification methods and capture rates

The fracture liaison co-coordinator played a pivotal role in identifying eligible patients in all studies. This was performed in close collaboration with the staff of orthopaedic and emergency departments, including secretaries, nurses, allied health, and doctors. In the study by Giles and co-workers (2010), the successful utilization of an electronically derived patient list of relevant emergency department presentations, together with electronic prompts for referral on discharge letters, lead to the identification of all potentially eligible patients. Kuo and colleagues, recruited orthopaedic outpatients only. The other three studies recruited patients from varying combinations of orthopaedic ward, orthopaedic clinic, and the emergency department.

The 'capture rate', refers to the proportion of eligible patients who underwent some form of intervention. Remarkably, Giles and co-workers (2010) reported 100% capture, because everyone with a minimal trauma fracture was identified and given some form of intervention, such as letter to the patient and PCP indicating the importance of osteoporosis assessment, which is a model C intervention (see below). In the same study, about 38% of patients underwent a 'type A' intervention by attending the osteoporosis clinic. Lih and colleagues (2011) reported a capture rate of 41%, while in the remaining two studies no information of capture rates was provided. Although not specifically addressed in the

studies, streamlining the process of referral to the FLS from the orthopaedic surgeon or primary care physician is paramount if a service is to improve capture and assessment rates.

Interventions

There are minor variations in the reporting of the intervention applied. In all studies, the FLS was an outpatient clinic run by a fracture liaison co-ordinator. The intervention included the following components: (i) Patient education, (ii) Assessment and investigation; and (iii) treatment initiation. Education components included aspects of nutrition and diet, exercise, risk factor reduction and falls prevention. A full risk factor assessment occurred in two of the four studies [Kuo et al, 2007; Lih et al, 2011]. Patients were assessed by bone mineral density and pathology testing in all studies, while routine thoraco-lumbar spine X-rays were part of the evaluation in all but one study [Kuo et al., 2007]. Follow-up occurred annually in two studies [Vaile et al., 2007; Lih et al., 2011] but was not described in the remaining two reports.

Outcomes

a. Risk factor analysis and pathology testing for secondary causes

Osteoporosis risk factor analysis was specifically described in two studies [Kuo et al., 2007; Lih et al., 2011]. For instance, Lih and co-workers reported 6.5% of patients had a prior non-vertebral fracture, whilst Kuo and co-workers reported that half of patients had sustained prior fractures. Pathology testing for secondary causes of osteoporosis was reported in three studies [Kuo et al, 2007; Vaile et al., 2007; Lih et al, 2011]. Vaile and colleagues reported a positive coeliac screen in 0.2% of patients. Kuo and co-workers (2007) found new diagnoses of hyperthyroidism in 2.1% of patients, primary hyperparathyroidism in 1.4%, and hypovitaminosis D in 41% (i.e. 25-OH-vitamin D level < 50 nmol/L).

b. BMD testing

The rate of BMD testing in those attending the service ranged from 83% to 100%, although Giles and co-workers (2010) have not included this data in their report. The reported rates for BMD assessment contrast with a 10% uptake rate of BMD testing in an information-based intervention ('type D') as per Kuo et al. 2007.

c. Pharmacological treatment

Lih and colleagues (2011) reported treatment rates of 79% in the intervention group compared to 31% in the control group. Vaile and colleagues (2007) revealed treatment rates were 51% in the intervention group compared to 11% in a historical control group. In this study, self-reported adherence at twelve months was 95%. In the study by Kuo and co-workers (2007), 80% of patients were adherent to treatment at a mean follow-up of 10 months with female gender and a diagnosis of osteoporosis being predictors of adherence.

d. Re-fracture rates

The only study describing re-fracture rates was by Lih and colleagues (2011). At four years of follow-up, a highly significant difference in re-fracture rates was reported: 4.1% in the group attending the fracture liaison service compared to 19.7% in the control group (Fig. 5). This difference corresponds to an 80% reduction in re-fracture rates in patients managed by a FLS.

e. Cost-effectiveness

An informal evaluation of cost-effectiveness of a ‘type A’ intervention was described by Vaile et al. (2007), estimating that if one hip fracture is prevented, savings of AUD23,000 could pay for the salary of a fracture liaison co-coordinator for six months, or for the osteoporosis evaluation of 54 patients with minimal trauma fractures.

A formal and more comprehensive cost-effectiveness analysis of the Concord Hospital Fracture Liaison service by Cooper et al. (2011) revealed that the service was highly cost effective with a cost of around AUD 20,000 – 30,000 per QALY gained, depending on the model examined. As the Concord Hospital FLS is a typical ‘type A’ model, it can be safely assumed that most, if not all, comprehensive FLS are cost-effective interventions.

f. Other outcome measures

A further outcome measure reported Giles and colleagues (2010) was an improvement in referral of eligible patients by orthopaedic surgeons, physicians and general practitioners, to the osteoporosis clinic. Referral rates improved from 9% prior to the fracture liaison service, to 34% after commencement of the fracture liaison service. Furthermore, the period of time from fracture occurrence to attendance at the osteoporosis clinic decreased from 68 days to 44 days.

Fig. 5. Cumulative re-fracture incidence by groups (reproduced from Lih et al., 2011 with permission)

5.1.2 ‘Type A’ fracture liaison services in the United States

In the United States, orthopaedic surgeons have been the “champions” at the forefront of co-ordinating osteoporosis care of patients after a minimal trauma fracture. In contrast to

Australia, some of the studies emanate from large, integrated health care networks, rather than individual hospitals. A good example is the Kaiser Permanente Group. This group is a health maintenance organization with 3.1 million members, spanning across eleven medical centres. The “Healthy Bones Program” consists of steps to identify patients at high risk of fractures, then assess and treat them for osteoporosis. The success of this program seems to be related to the utilization of a fully integrated electronic health record. The intervention consisted of a falls reduction program, assessment with DXA, evaluation for secondary causes, as well as a treatment plan. Monitoring occurred on a monthly basis, via reports for “care managers” (FLC) detailing those who needed treatment, and those who received treatment, thereby providing targets, and stimulating further improvements in care.

Study types and patient characteristics

Of the three studies from the United States, there was one ‘before and after’ analysis [Edwards et al., 2005], one prospective observational study [Dell et al., 2008], and one cross sectional study [Navarro et al., 2011]. All studies included males and females, with Edwards and co-workers (2011) reporting that 75% of subjects were female. Racial background was reported by Navarro et al. (2005) with White subjects representing 64% of the sample. The numbers of subjects varied significantly in each study. Edwards and co-workers (2005) included 203 subjects while in the remaining two studies from the Kaiser Permanente group, Navarro and co-workers included 13,412 subjects seen over a period of one year, and Dell and co-workers studied 620,000 subjects from 2002 to 2006. These large numbers were made possible by an electronically integrated health care system. In the latter two studies, inclusion criteria expanded beyond the patients with minimal trauma fractures to patients who had any risk factor for osteoporosis, including, for example, corticosteroid use or rheumatoid arthritis. All studies included patients with minimal trauma fractures at any site.

Patient identification methods and capture rates

All three studies utilized a fracture liaison co-coordinator. The Kaiser-Permanente model utilized health managers to identify care gaps through electronic lists, thereby identifying all patients in all settings (i.e. inpatients, outpatients, and emergency departments).

Interventions

All studies described a ‘type A’ FLS, which incorporated patient education, assessment and treatment initiation. All studies assessed and treated subjects on an outpatient basis.

Outcomes

a. Risk factor analysis and pathology testing for secondary causes

Information on the extent of patient assessment was generally limited, with only Edwards and colleagues (2005) reporting specific risk factor assessments. Specifically, 50% of patients had sustained prior fractures. Edwards and colleagues reported pathology testing for secondary causes of osteoporosis only in those with a BMD T-score less than -1.5 SD.

b. BMD testing

Navarro et al (2011) reported osteodensitometry testing and/or initiation of osteoporosis therapy in females of 92% as opposed to 75% in males, in a large cohort of 13,412 subjects. There was no disparity between racial groups. This is in contrast to the racial disparity in health care outcomes in the United States described by others [Wei et al. 2003, Epstein et al. 2010], indicating the significant societal benefits of an integrated electronic health care network.

The same group from Kaiser Permanente demonstrated that the implementation of their FLS resulted in an increase in bone mineral density testing from 21,557 tests in 2002 to 74,770 tests in 2006 [Dell et al., 2008]. This represented a 600% increase in BMD testing for males, and a 220% increase for females. The rate of increase in men was greater than for women, possibly due to the very low rates of testing in men at baseline in 2002 (fig 6).

c. Pharmacological treatment

In the same study [Dell et al., 2008] the number of patients on treatment with specific anti-osteoporosis medications increased from 33,208 in 2002 to 78,058 in 2006 (or from 24% to 60% of at-risk subjects) as shown in Figure 7. Similar to the data on BMD testing, the rate of increase for men was greater than that for women.

Fig. 6. Number of patients undergoing Dual X-ray Absorptiometry (DXA) for osteoporosis assessment [reproduced from Dell et al., 2008, with permission].

Edwards and co-workers (2005) reported improved treatment rates from 28% at baseline to 70% at six months post-discharge which then declined again to only 25% at twelve months post-discharge. This precipitous decline in adherence at twelve months reflects the need for specific osteoporosis follow-up to reinforce the ongoing need for therapy.

d. Refractures

Dell et al (2008) described the effect of the Healthy Bones Program on hip fracture rates. While there was no concurrent control group, the authors elected to estimate expected rates of hip fracture based on historical data from 1997 – 1999, and then compared these historical data to the actual rate of hip fractures observed in patients cared for by the FLS. Overall, there was a 37.2% relative risk reduction in hip fractures, using data from 2006 (figure 8).

Fig. 7. Number of patients on specific anti-osteoporosis treatment [reproduced from Dell et al.,2008, with permission].

Fig. 8. Age stratified rate of hip fracture seen versus rate of hip fracture expected [reproduced from Dell et al., 2008, with permission].

e. Cost-effectiveness

While there are no formal cost-effectiveness analyses for any of the US studies, one should remember that Kaiser Permanente is a closed health care network which pays for all expenses but also benefits from all savings. The fact that a private provider such as Kaiser Permanente has fully integrated a ‘type A’ FLS into their health care program strongly suggests that the model is not only cost-effective but actually cost-saving.

5.1.3 'Type A' fracture liaison services in Canada

Study types and patient characteristics

Three 'Type A' FLS have been described in a series of five publications – three randomized controlled trials (RCT) from the same FLS [Majumdar et al., 2007 & Morrish et al., 2009; Majumdar et al., 2011], and one cross-sectional study [Bogoch et al., 2006]. The first two randomized controlled trials compared three different FLS models: firstly a 'type A' versus 'type D' model of care [Majumdar et al., 2007] and secondly a 'type A' versus 'type B' model of care [Morrish et al., 2009] in patients with hip fractures. The third RCT by the same group involved patients with wrist fractures, comparing a 'type A' with 'type C' intervention [Majumdar et al., 2011]. The three services included both males and females, with the proportion of females varying from 65% to 77%. Patient numbers varied significantly in that the randomized controlled trials [Majumdar et al., 2007 & Morrish et al., 2009] had 110 patients in each arm, whilst the trial by Majumdar et al. (2011) had a total of 46 patients. The cross-sectional study evaluated 430 patients. The target population in the RCT's were 50 years of age and over. Between 82% and 95% of patients were white Caucasian. Bogoch and co-workers (2006) included female patients older than 40 years, and male patients over 50 years of age, with a minimal trauma fracture to the hip, wrist, humerus or vertebra.

Patient identification methods and capture rates

All three services utilized a Fracture Liaison Co-coordinator to identify eligible inpatients and outpatients. Bogoch et al. (2006) also engaged the orthopaedic staff in the identification process. There was no indication as to the completeness of identification of eligible patients.

Intervention methods

In all three studies, the FLC coordinated the identification, assessment (clinical risk factors, osteodensitometry, pathology) and treatment of patients with a fragility fracture. In the studies by Majumdar and Morrish it was specified that a letter was sent to the primary care physician once treatment was initiated.

Outcomes

a. Risk factor analysis and pathology testing for secondary causes

Osteoporosis risk factors were evaluated in all studies. A past history of minimal trauma fractures was documented in 37% (Majumdar et al. 2007 & Morrish) and 26% (Bogoch). Majumdar and colleagues (2011) was the only trial which stated pathology testing for secondary causes of osteoporosis were performed, although the proportion of positive results was not reported.

b. BMD testing and treatment rates

In the study by Majumdar et al. (2007), 80% of patients in the intervention group underwent BMD testing at six months post-fracture, compared to only 29% in the control group. About 51% of patients in the intervention group were commenced on bisphosphonates at six months, compared to 22% in the control group. A further result reported was "Appropriate Care", which was defined as the proportion of patients commenced on bisphosphonates when the BMD T-score was < -1.5 SD. Appropriate care was achieved in 67% of patients in the intervention group, versus 26% in the control group. The underlying cause of the low rate of appropriate care was not reported.

As an extension of the above trial, patients assigned to the control group (‘standard care’) were allocated to a new intervention after six months. This new intervention consisted of a BMD scan organised by the FLC (‘Type B’ intervention) with results being sent to the primary care physician [Morrish et al. 2009]. As a result, the rates of BMD testing, treatment with a bisphosphonate, and “appropriate care” improved compared to usual care (‘Type D intervention’), but not to the extent of case management (‘Type A’ intervention) (fig. 9).

Fig. 9. Comparison of case manager, facilitated BMD testing, and usual care in patients with a hip fracture [reproduced from Morrish et al., with permission].

A further study by Majumdar et al. (2011) which included patients with wrist fractures only, revealed a BMD testing rate of 81% (‘type A’) versus 52% (‘Type C’). The rate of bisphosphonate treatment was better with intensive intervention, at 43% (‘type A’) versus 12% (‘type C’).

In the study by Bogoch et al (2006), the proportion of all patients who were previously diagnosed and treated for osteoporosis was 34%, which is higher than expected from the published literature. This study also reported a rate of “appropriate attention” for osteoporosis of 96%, which encompassed referral, diagnosis or treatment of osteoporosis. This unique outcome measure is a good example of the heterogeneity of outcome reporting in various studies, making direct comparison between studies problematic. Reiterating the gender disparity, women (39%) were more likely than men (15%), to have had diagnosis and treatment for osteoporosis prior to their fracture.

c. Re-fractures

Morrish et al. (2009) reported 10 new fractures after a limited follow-up of twelve months. While the authors state that there was no difference in re-fracture rates between groups, they did not specify how many fractures occurred in each arm of the study. Thus, it is likely that the study was underpowered to allow any conclusions on reductions in fracture risk.

d. Cost-effectiveness

Sander and colleagues (2008) performed a cost-effectiveness analysis of the 'type A' model of care described by Bogoch et al. (2006). The FLS was predicted to reduce the annual hip fracture rate from 34 with usual care, to 31, resulting in a cost saving of C\$ 49,950. This cost-saving held true assuming at least 350 patients were seen by the FLS over a year. The two limitations of this analysis was firstly, the lack of a control group, resulting in the need to make assumptions in the usual care group based on historical data. Secondly, the cost-saving may not be translated to smaller institutions which have a lower volume of patients seen in the FLS. There was no formal cost-effectiveness evaluation for the RCT by Majumdar et al. (2007) and Morrish et al. (2009), although it was reported that the 'type A' model of care evaluation cost \$56 versus \$24 for a 'type B' model of care.

5.1.4 'Type A' fracture liaison services in Europe

Study types and patient characteristics

Two cross-sectional studies have described the implementation of a 'Type A' fracture liaison service, one from the United Kingdom [Clunie et al., 2008] and one from France [Boudou et al., 2011]. Clunie and co-workers recruited 2491 male or female patients older than 50 years with a minimal trauma fracture at any site. More than 50% of patients had a hip or wrist fracture. The study by Boudou et al. (2011), evaluated 155 female patients over 50 years of age with wrist, humerus or femur fractures. Racial background was not reported in either study.

Patient identification methods and capture rates

In the study by Clunie et al. (2008), patients were identified in either outpatient or inpatient settings by a FLC. It is unclear as to the proportion of potentially eligible patients who were identified. The study from France also employed a FLC, who utilized an electronic medical record system to identify patients. More than 90% of patients were identified, with only 20% of patients captured for evaluation by the FLS.

Intervention methods

In both studies, patients underwent a complete risk factor assessment, including pathology tests for secondary causes of osteoporosis as well as BMD testing. According to Clunie et al (2008), patients were referred to the Bone clinic when appropriate. Patients more than 75 years of age were assessed for falls risk and referred to the primary care physician. The schema for this service is shown in Figure 10, as another example of a 'Type A' intervention.

Outcomes

a. Risk factor analysis and pathology testing for secondary causes

Patients in both studies underwent risk factor assessment and investigations for secondary causes of osteoporosis. Notably, Clunie et al. (2008) quoted their previous publication relating to the same service, whereby 6% of patients routinely screened for secondary causes of osteoporosis regardless of osteodensitometry results, had a new diagnosis such as hyperthyroidism or primary hyperparathyroidism [Clunie et al., 2005].

b. BMD testing

Clunie and colleagues (2008) reported a high rate (91.2%) of osteodensitometry in those 50-69 years of age, whereas the rate of osteodensitometry was not reported by Boudou and co-workers (2011).

Fig. 10. Structure of ‘Type A’ fracture liaison service [reproduced from Clunie et al. 2008, with permission].

c. Pharmacological treatment

In the trial by Boudou et al. (2011), approximately 90% of patients initiated treatment prescribed by the FLS, and 80% of these remained on treatment at one year follow-up. After a further follow-up of 27.4 +/- 11.7 months, 68% of patients were persistent with treatment. This trial represents one of the very few studies that report adherence data within the setting of a FLS. Reasons for discontinuation of therapy were adverse events, lack of primary care physician encouragement, and polypharmacy. Clunie and colleagues (2008) did not report treatment rates.

d. Re-fractures

After a mean follow-up period of 27.4 +/-11.7 months, 11.4% had sustained a further fracture [Boudou et al. 2011]. The rate of further fractures was not described by Clunie et al. (2008).

e. Cost-effectiveness

Nil data.

5.2 Appendix B

5.2.1 'Type B' fracture liaison services in Europe

5.2.1.1 United Kingdom

In the United Kingdom, there has been a concerted, collective effort towards re-fracture prevention by attempting to establish fracture liaison services in all hospitals based on the Glasgow FLS model [Mitchell 2011]. The strong advocacy towards re-fracture prevention has been supported and catalysed by patient and professional organisations (e.g. the UK National Osteoporosis Society), the government (through integration into a policy framework and providing financial incentives to health providers who adhere to the guidelines), and pharmaceutical companies (through provision of funding). The publication of the second edition of the 'Blue Book' in 2007 provided comprehensive guidelines to promote high quality care of minimal trauma fracture patients in the UK. Specifically, the 'Blue Book' provides guidelines and standards of care for the peri-operative management of patients with a minimal trauma fracture (particularly hip fractures), as well as guidelines on secondary fracture prevention through fracture liaison services. The third major component of the 'Blue Book' details the importance of contributing to and utilising the National Hip Fracture Database (NHFD) allowing the benchmarking of hip fracture care across the UK, thereby catalysing improvements in clinical care. Critical to the implementation of these guidelines was the multi-disciplinary authorship and the strong endorsement it received from most relevant professional organisations. As a testimony to the success of the program, all 200 hospitals in England, Wales and Northern Ireland have subscribed to the database. In addition, the most recent report from the NHFD in 2010 describes 75% of 36,000 hip fracture patients receiving assessment or treatment for osteoporosis prior to being discharged from hospital.

Study types and patient characteristics

There are four publications describing FLS in the UK, originating from two services. The first two were cross-sectional studies describing the Glasgow FLS, which is the model upon which most FLS in the UK are built [McClellan et al., 2003, 2011]. A case control study of the same service evaluated characteristics of those with re-fractures [Langridge et al., 2007]. The second service based in Royal Manchester Infirmary was described in a 'before and after' analysis [Charalambous et al., 2002]. The Glasgow FLS included 4,671 patients, older than 50 years, who sustained a minimal trauma fracture over an 18 month period. Both male and female patients were included. Approximately 30% of patients sustained wrist fractures, and about 23% had sustained hip fractures. Exclusion criteria included patients with skull or facial fractures, patients with dementia, or those unable to tolerate oral bisphosphonate therapy. The study by Charalambous was limited to only female patients with a minimal trauma fracture to the wrist and hip. The number of patients was also smaller, with 100 pre-intervention and 66 in the intervention phase.

Patient identification methods and capture rates

The Glasgow service utilized a fracture liaison co-coordinator to capture patients from orthopaedic wards, orthopaedic outpatient clinics, as well as the emergency department.

The co-coordinator visited wards regularly, with patient lists maintained by close contact with orthopaedic staff, and utilizing the hospital information technology systems. Thus, almost 100% of patients were identified; although only 78% attended the service (22% had declined the intervention). Charalambous and colleagues (2002) identified orthopaedic inpatients and outpatients, using a monthly list of patients with new fractures. Instead of a co-coordinator, a protocol was instituted to refer patients for osteoporosis evaluation or direct referral for BMD. No comment was made regarding the proportion of potentially eligible patients identified.

Intervention methods

The Glasgow service provided patient education, together with outpatient assessment, followed by treatment recommendations to the PCP. On the other hand, Charalambous and colleagues did initiate inpatient assessment of those with hip fractures (older than 60 years), with direct referral for BMD, followed by recommendations for further assessment and treatment.

Outcomes

a. Risk factor analysis and pathology screening for secondary causes

Risk factor assessment was performed in both studies while pathology screening for secondary causes of bone loss was described only in the Glasgow service. The results of pathology screening was not reported.

b. BMD testing and treatment

The first set of outcome data for the Glasgow service revealed that 44% of patients underwent BMD testing, compared to 10% in historical controls, and 29% of patients were recommended pharmacotherapy [McLellan et al. 2003]. The most recent outcome data from the Glasgow FLS evaluated the rate of patient capture, assessment, treatment, and cost-effectiveness over 8 years of service provision [McLellan et al. 2011]. A total of 11,096 patients were identified, of whom 8,875 (80%) were assessed. The number of patients who underwent BMD scans was 5,405 (49%). Oral bisphosphonate treatment was recommended in 54%, whilst 1,273 (11%) were on treatment previously. As a testimony to the effectiveness of a close liaison between the FLS and the PCP, the study found that 96% of patients had the recommended treatment initiated in primary care. Treatment persistence was reported as 86% at 12 months.

At Manchester Royal Infirmary the implementation of a protocol was shown to be effective in improving “appropriate osteoporosis management” in female patients [Charalambous et al. 2002]. In this study, “appropriate management” simply entailed initiating a referral to a doctor for evaluation of osteoporosis, or initiation of calcium and vitamin D as per protocol.¹

Pre-intervention, 22% (11/50) of in-patients with hip fractures and 0% of patients with distal radial fractures received “appropriate management”. Post-intervention, the corresponding numbers were 76% and 81%, respectively.

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¹ This highlights the differences in the definition of ‘appropriate care’, which appears to be a term of considerable heterogeneity. Thus, a number of studies define ‘appropriate care’ as a clinical assessment with or without a BMD scan, with or without initiation of treatment. Other definitions refer to receiving osteoporosis treatment in keeping with the local guidelines, based on T-scores.

c. Re-fractures

The South Glasgow service published data from January 2001 to August 2004 with up to 3.5 years follow-up of patients older than 65 years [Langridge et al. 2007]. Of the 2,489 patients seen by the service, 129 had re-fractured (5.2%). About 37% of these patients were taking calcium, vitamin D *and* a bisphosphonate. Unfortunately there was no control group to which these results could have been compared. On the other hand, McLellan et al. (2011) reported a 12% rate of re-fracture over 4 years for the West Glasgow service.

d. Cost-effectiveness

The cost-effectiveness analysis of the Glasgow service was based upon an 8% re-fracture rate at 4 years, although the actual re-fracture rate was reported to be 12% [McLellan et al., 2011]. The cost per Quality Adjusted Life Year (QALY) gained was 5,740 pounds. According to the least favourable efficacy data, fifteen fractures are avoided, at the expense of 84,076 pounds per 1000 patients. According to the most favourable efficacy data, thirty six fractures are avoided and 199,132 pounds saved per 1000 patients. Using a hypothetical cohort of 1000 patients, it was estimated there would be 18 fewer fractures with the fracture liaison service. These results illustrate the effectiveness of a 'type B' intervention in the UK setting.

5.2.1.2 'Type B' fracture liaison services outside the UK

Study types and patient characteristics

There are three cross-sectional studies describing 'type B' models of care in Switzerland [Chevalley et al., 2002], Sweden [Astrand et al., 2006], and the Netherlands [Huntjens et al., 2010]. The study from the Netherlands compared five large FLS within the same health care system. All of these European FLS enrolled both male and female patients 50 years of age or older, who presented with a minimal trauma fractures at any site. The proportion of female patients seen in each service ranged from 70% to 88%, with a mean of 78%. The proportion of patients who sustained wrist fractures varied from 3.6% to 58%, with a mean of 27%. The proportion of patients who sustained hip fractures varied from 1.0% to 45%, with a mean of 13%. The number of patients in each study varied from 238 to 2224. The follow-up period ranged from 12 months to 58 months, with a mean of 43 months. The number of patients seen per centre per month varied from 11 to 47, with a mean of 25. In all studies, dementia and pathological fractures were excluded. In the Swedish study, patients who were out of area and non-English speaking were excluded.

Patient identification methods and capture rates

All seven fracture liaison services (apart from Chevalley and colleagues) utilized a co-coordinator to identify patients from the wards, orthopaedic outpatients, the emergency department or radiology. Two sites from the Netherlands utilized radiology reports alone to identify eligible patients. Three services (two from Netherlands and the Swedish study) incorporated electronic medical record and the co-coordinator to identify patients. The proportion of eligible patients identified, who attended the service was not described.

Intervention methods

In all studies patients underwent osteoporosis assessment and treatment recommendations as outpatients, with components as would be expected from the 'type B' intervention. The details

of intervention methods are not described by Huntjens et al. (2010), although Chevalley and colleagues (2002) described a multidisciplinary educational intervention. The extent to which the services educated patients is unclear in the studies from the Netherlands.

Outcomes

a. Risk factor analysis and pathology screening for secondary causes

The assessment of risk factors was described in all seven studies. Six of the seven services reported pathology screening for secondary of osteoporosis (apart from Astrand and co-workers); however the threshold varied between fracture liaison services. For instance, in the Netherlands, two FLS reported performing screening tests for secondary causes of osteoporosis in patients younger than 70 years, with a T-score equal to or less than -3.0 SD, whilst another would do so in any patients with a BMD T-score less than -2.0 SD. A fourth FLS in the Netherlands, investigated only men for secondary causes of osteoporosis.

b. BMD testing

All fracture liaison services performed bone mineral density testing. However, only Chevalley et al. and Astrand et al. reported the actual proportion of patients undergoing BMD testing (63% and 93% respectively).

c. Pharmacological treatment

Treatment outcomes were only reported by Chevalley and colleagues - about 33% of patients were recommended anti-osteoporosis medication, of which 66% were initiated on therapy. Adherence declined to 67%, at six months follow-up.

d. Re-fractures

Nil data

e. Cost-effectiveness

Nil data

5.2.2 'Type B' fracture liaison services in the United States

Study types and patient characteristics

In the two 'before and after' studies from the United States, the study by Johnson et al. (2005) focused on male patients (96% of the study population), while the second report included mainly female patients [Cuddihy et al., 2004]. The study by Johnson et al. analysed outcomes in 126 pre-intervention and 136 post-intervention subjects (mean age: 60 years; 64% white Caucasian). Of note, this study looked at all fracture types, including high trauma fractures. As a result, only 32% of fractures were due to 'minimal trauma'. Cuddihy et al. recruited 96 subjects aged 44yrs or older with a minimal trauma fracture to the wrist (mean age: 68 years).

Patient identification methods and capture rates

Both services utilized fracture liaison co-coordinators, who accessed an electronic database to identify patients, from either orthopaedic clinics or wards. Cuddihy et al. reported 100% identification of potentially eligible patients, made possible by the electronic database.

About 61% of those identified attended the fracture liaison service. Johnson and colleagues did not report the rate of identification of potentially eligible patients.

Intervention methods

As is standard in a 'type B' model of care, patients in both groups were assessed for osteoporosis by performing a BMD scan, followed by a referral to the primary care physician with treatment recommendations.

Outcomes

a. Risk factor analysis and pathology testing for secondary causes

Evaluation of risk factors for osteoporosis was specifically reported by Cuddihy et al. (2004), with 37% (19/51) of women and 50% (4/8) for men sustaining prior fractures. Johnson et al. (2005) reported evaluation of osteoporosis risk factors in only the intervention group who underwent BMD testing. Cuddihy et al. (2004) did not detect any secondary causes for osteoporosis after assessing 32 out of 59 patients, whilst Johnson et al (2005) did not report screening for secondary causes.

b. BMD testing

Osteoporosis assessment increased from 16% at baseline, to 45% at six months, although males had a lower rate of BMD testing compared to females [Cuddihy et al. 2004]. In the study by Johnson et al., the rate of BMD testing changed from 13% (16/126) in the pre-intervention group to 63% (85/136) in the intervention group.

c. Pharmacological treatment

Adherence to osteoporosis specific treatment increased from 9% to 36% at six months [Cuddihy et al., 2004]. In the study by Johnson et al., the proportion of patients recommended specific osteoporosis medications increased from 7% to 19%, which is a surprisingly low number, although the majority of patients had traumatic fractures. At six months following the intervention, only 6% of patients in the pre-intervention group were receiving specific osteoporosis treatment, compared to 13% for the intervention group.

5.2.3 'Type B' fracture liaison services in New Zealand

Study types and patient characteristics

A single 'before and after' study from New Zealand reported on 329 subjects in a pre-intervention group, and 193 subjects in the intervention group, of whom 78% were women. About 69% of patients had sustained a hip fracture [Sidwell et al. 2004].

Patient identification methods and capture rates

Patient identification did not require a fracture liaison nurse, because an *inpatient* protocol was implemented in an ortho-geriatrics ward. Therefore, existing staff were educated to implement the protocol. It is unclear if all potentially eligible patients were captured.

Intervention methods

Staff identified patients with a minimal trauma fracture, assessed them with BMD scan and pathology tests, and sent a report to the primary care physician with treatment recommendations.

Outcomes

a. Risk factor analysis and pathology testing for secondary causes

The evaluation of risk factors for osteoporosis was not reported, although pathology testing for secondary causes of osteoporosis was performed in 63% of patients.

b. BMD testing

BMD testing increased from 11% (pre-intervention group) to 78% in the intervention group.

c. Pharmacological treatment

At nine months post-fracture, those on calcium or vitamin D increased from 13% to 52%. Bisphosphonates or HRT prescription increased from 10% to 31%.

d. Re-fractures

Nil data.

e. Cost-effectiveness

Nil data.

5.3 Appendix C

5.3.1 'Type C' fracture liaison services in the United States

Study types and patient characteristics

We identified six reports describing a 'type C' intervention in the United States. Three were randomised controlled trials (RCT's) [Gardner et al., 2005; Feldstein et al., 2006 & Solomon et al., 2007], one was a cross-sectional design [Skedros et al., 2004], and two were 'before and after' studies, described in the same article [Harrington et al., 2005]. One study included only female patients [Harrington et al., 2005], whilst the other five studies included both male and female patients. The proportion of females reported in two studies was 78% and 86% [Skedros et al., 2004; Gardner et al., 2005]. Two studies included only patients with hip fractures [Gardner et al., 2005; Harrington et al., 2005], whilst the other studies included patients with minimal trauma fractures at any site. The total number of patients in each study varied from 69 to 1973, with the median number of participants in each study being 283. Most studies recruited patients greater than 50 years of age. Three studies specified exclusion criteria, such as dementia, nursing home residence and previous osteoporosis investigation or treatment [Skedros et al., 2004; Gardner et al., 2005; Feldstein et al., 2006].

Patient identification methods and capture rates

A fracture liaison co-coordinator was critical to the implementation of each service, apart from one [Skedros et al., 2004], in which orthopaedic surgeons were asked to educate and recommend further assessment for osteoporosis. In three studies electronic medical records were employed to help with identification of patients [Harrington et al., 2005; Feldstein et al., 2006; Solomon et al., 2007]. The settings in which the intervention took place varied from exclusively outpatient or inpatient, to mixed settings.

Intervention methods

The methods of intervention did not differ significantly between four of the six studies. Uniquely, one RCT compared three groups, using varying degrees of educational interventions [Feldstein et al. 2006]. This study was a well-powered, randomised controlled trial of female patients only. The three groups were 'usual care' (n=101), electronic reminder to PCP (n=101), and electronic reminder to PCP with educational letter mailed to the patient (n=109). Thus, there was an effective comparison between different 'type C' intervention and no intervention at all. Another randomised controlled study used an educational intervention consisting of a one-on-one interview with a PCP by a *pharmacist*, together with a letter and automated phone call to patients regarding the assessment of their bone health [Solomon et al., 2007].

Outcomes

a. Risk factor analysis and Blood tests for secondary causes

Evaluation of risk factors was reported in only one trial [Harrington et al., 2005]. As expected from an educational intervention, pathology testing was not performed, and a clinical risk factor assessment was not a part of this model.

b. BMD testing and Pharmacological treatment

Five studies reported on the outcome of BMD testing and/or treatment with specific anti-osteoporosis therapies with follow-up periods varying from six months (3 studies) to 18 months. The intervention effect ranged from 14% to 46%, with the control or baseline results ranging from 5% to 19%. The average improvement compared to baseline was 23% across all studies. Of interest, the study by Solomon et al. (2007) failed to detect a clinically significant improvement in BMD testing or treatment (14% in intervention group vs. 10% in control group). This is in stark contrast in to all other studies with similar interventions.

Feldstein and co-workers (2006) reported improved BMD testing rates at six months in the intervention group (20%), compared to 5% in the control group. Treatment rates were 20% and 30% in studies by Feldstein and Skedros respectively.

c. Re-fractures

Solomon et al. reported no difference in re-fracture rates at 10 months follow-up, but the study was not powered for this outcome. No other studies reported on re-fractures.

d. Cost-effectiveness

Nil data.

5.3.2 'Type C' fracture liaison services in Canada

Study types and patient characteristics

We identified five reports on 'Type C' models of care from Canada. The study types include one randomized controlled trial [Majumdar et al., 2008], two prospective controlled trials [Ashe et al., 2004; Majumdar et al., 2004], one 'before and after' analysis [Hawker et al., 2003], and one cluster randomized trial [Cranney et al., 2008]. All studies included both male and female patients, with the proportion of females ranging between 74%-78%. Racial

background was described as mostly White in one study [Hawker et al., 2003], and 79% White in the study by Majumdar and co-workers (2004). The numbers of patients in each study varied from 51 to 278, with the mean number of participants per study of 195. Most studies recruited patients above 49 years of age, with a mean age of 67 years. All of the trials apart from one [Hawker et al., 2003] included patients with minimal trauma fractures to the wrist only, although one study included moderate trauma wrist fractures as well [Ashe et al., 2004].

Patient identification methods and capture rates

Three studies utilized fracture liaison co-coordinators [Ashe et al., 2004; Majumdar et al., 2004, Majumdar et al., 2008], whilst one study utilized existing staff [Cranney et al., 2008], and another enlisted the help of the orthopaedic surgeons to identify eligible patients [Hawker et al., 2003]. Patients were identified in the emergency department and orthopaedic clinics.

Intervention methods

Intervention methods for 'type C' services have been described in section 2.5 and all of the Canadian services adhered to this model, with little to no variation between studies.

Outcomes

a. Risk factor analysis

Analysis of osteoporosis risk factors was reported in two studies [Hawker et al., 2003; Majumdar et al., 2008]. Hawker and co-workers reported the rate of prevalent fractures amongst subjects of 20%, whilst Majumdar and co-workers reported a rate of 48%.

b. BMD testing

The rate of BMD testing and/or treatment was reported by Majumdar et al., 2004 & 2008. In the 2004 study, at six months, the intervention group did better than the control group (71% versus 21%). In the 2008 study, 38% of the intervention group versus 11% of the control group underwent BMD testing and / or treatment. The average improvement in the outcome was 38.5%.

The rate of BMD testing was reported in all studies, at three to six months follow-up. The rate of BMD testing in the intervention group ranged from 43% to 92%, and in the control group ranged from 18%-28%. The average improvement in BMD testing was 40%.

c. Pharmacological treatment

Three studies reported the rates of anti-osteoporosis treatment after three to six months follow-up [Hawker et al., 2003; Majumdar et al., 2004 and 2008]. The rate of treatment in the intervention groups ranged from 11% to 40%, compared to 7%-10% in the control groups. The average improvement in treatment rates was 15%. The significant variability in results between studies may be due to factors which are difficult to report such as the details of the explanation of osteoporosis, and rapport between co-coordinator and patients.

d. Re-fractures

Nil data.

e. Cost-effectiveness

Nil data.

5.3.3 'Type C' fracture liaison services in Australia**Study types and patient characteristics**

Inderjeeth and colleagues (2010) from Perth, Western Australia, published a 'before and after' study, using a historical control group. There were 200 patients in the pre-intervention group and 194 in the intervention group. The educational intervention targeted patients discharged directly from the emergency department, older than 65 years with a minimal trauma fracture at any site.

Patient identification methods and capture rates

Patient identification occurred by utilizing existing hospital staff (e.g. emergency department clinicians), and primary care physicians were made aware of the need for osteoporosis assessment in these patients. Approximately 34% of eligible patients underwent the intervention.

Outcomes**a. Risk factor analysis and pathology testing for secondary causes**

Nil data

b. BMD testing

At 12 months follow-up, the rate of BMD testing was 45% in the intervention group vs. 3% in the pre-intervention group.

c. Pharmacological treatment

Calcium and vitamin D supplementation increased from 12% to 37%. Initiation of osteoporosis specific treatment increased from 6% to 30%.

d. Re-fractures

Nil data.

e. Cost-effectiveness

Nil data.

f. Other outcome measures:

Referral to the bone clinic increased from 4% pre-intervention to 26% with the intervention.

5.4 Appendix D**5.4.1 Description of 'Type D' model of care fracture liaison Services****Study types and patient characteristics**

We have identified three publications describing 'type D' interventions, two from Australia [Bliuc et al., 2006; Diamond and Lindenberg et al., 2002] and one from Canada [Bessette et

al., 2011]. Two were randomized controlled trials [Bliuc et al. and Bessette et al.] while the third was a cross-sectional analysis [Diamond and Lindenberg, 2002]. In the two Australian studies, 65% of patients were females with an average of 160 subjects in each study. On the other hand, the Canadian study recruited 1314 patients who were all female. Bliuc and colleagues recruited patients over 20 years of age, with one-third sustaining a moderate trauma fracture. Diamond and Lindenberg included patients 45 years or older with minimal trauma fractures. Bessette and co-workers included patients above 49 years of age who sustained a 'minimal trauma' fracture at any site. As an indicator of heterogeneity between studies even of the same 'type', 'minimal trauma' was defined as a fall from a height of one metre or less by Bessette and colleagues. This contrasts with most other studies, define 'minimal trauma' as a fall from standing height or less.

Patient identification methods and capture rates

Diamond and Lindenberg identified patients from a private radiology practice, who had sustained a minimal trauma fracture. No co-ordinator was required for this study. About 64% of eligible patients were contacted. On the other hand, Bliuc and colleagues identified patients from the orthopaedic clinic via a fracture liaison co-ordinator. About 46% of eligible patients received the intervention. Bessette and colleagues identified patients from hospital orthopaedic clinics, as well as from the Quebec Ministry of Health database.

Intervention methods

In the study by Diamond and Lindenberg, patients were asked to fill out a survey about osteoporosis, encouraging them to have their bone health assessed. Bliuc and colleagues randomised patients to receiving either a letter educating patients about osteoporosis risk factors, or a similar letter together with an offer for a free BMD scan. Bessette and colleagues divided their cohort into three groups: i) control group ii) letter to patient group iii) letter to patient together with 15min video.

Outcomes

a. Risk factor analysis and pathology testing for secondary causes

Bliuc and colleagues as well as Bessette and co-workers, reported osteoporosis risk factors extensively in both groups, with well matched baseline characteristics. About 46% (Bliuc et al.) and 24% (Bessette et al.) of patients had a prior fracture. There was no information on risk factors by Diamond and Lindenberg, and neither study reported on testing for secondary causes of osteoporosis. .

b. BMD testing

In the study by Bliuc and colleagues, at six-months follow-up, the rate of BMD testing was 38% in those offered the BMD scan compared to 7% in patients who received a letter only. Female sex was a predictor for having a BMD performed. Diamond and Lindenberg reported a rate of BMD testing of 51% at twelve months. Bessette and co-workers revealed a very small effect of the intervention, with only 15% undergoing BMD testing compared to 12% in the control group.

c. Pharmacological treatment

Diamond and Lindenberg reported that 29% of patients were commenced on specific anti-osteoporosis treatment following the intervention, none of whom were men. This indicates

the significant gender disparity often evident in osteoporosis management. Bliuc and colleagues reported treatment rates of 6% (free BMD scan group) and 5% (letter only group), at six months, reflecting the limited effectiveness of a 'type D' intervention. Bessette and colleagues reported a treatment rate of 11% (intervention) versus 8% without the intervention, which is not a clinically significant difference.

d. Re-fractures

Nil data

e. Cost-effectiveness

Nil data

5.5 Appendix E

5.5.1 Description of 'Type E' model of care fracture liaison services

Study types and patient characteristics

We have identified six studies describing 'type E' interventions in the United States [n=3 - Kamel et al., 2000; Jachna et al., 2003; Streeten et al., 2006], Australia [n=2 - Jones et al., 2005; Chong et al., 2008] and the United Kingdom [n=1 - Wallace et al., 2011]. There were five cross-sectional studies and one 'before and after' analysis [Jones et al., 2005]. In the majority of cases patients included were inpatients who had minimal trauma fractures to the hip, with females representing approximately 67% of the subjects. The number of patients in each study varied from 82 to 834, with a median number of patients of 170. At 80 years, the mean age of subjects was significantly greater than in the other intervention models.

Patient identification methods and capture rates

Only one of the studies utilized a fracture liaison co-coordinator [Wallace et al., 2011], whilst two studies had an inpatient protocol for existing staff to use [Jones et al., 2005; Streeten et al., 2006]. One study asked the orthopaedic team to identify eligible patients [Chong et al., 2008].

Intervention methods

Intervention methods varied from an inpatient fracture protocol, to the involvement of an ortho geriatrics team. In one study, the protocol was introduced to all rotating interns, providing guidelines for commencement of anti-resorptive therapy and ortho geriatric consultation [Jones et al., 2005].

Outcomes

a. Risk factor analysis and pathology testing for secondary causes

Two studies reported risk factor analysis [Streeten et al., 2006; Wallace et al., 2011] as well as pathology testing as part of the intervention [Streeten et al., 2006; Jones et al., 2005]. Reflecting an older and sicker cohort than in the other intervention types, Jones and colleagues found that 77% of patients had hypovitaminosis D (i.e., 25-OH-vitamin D level below 50 nmol/L) and 34% of patients had secondary causes for osteoporosis identified.

b. BMD testing

Implementation of a strategy using an inpatient protocol appeared to be more effective in initiating BMD testing compared to a general medical consultation. Such protocols resulted in BMD testing rates of 66% versus 3% in the absence of a protocol [Streeten et al., 2006].

c. Pharmacological treatment according to intervention type

The rate of inpatient bisphosphonate prescription increased from 5% pre-intervention to 24% with and after the intervention (*inpatient protocol*) [Jones et al., 2005]. Wallace and colleagues (2011), showed improved treatment rates of 90.5% for hip fracture patients in a hospital with an ortho-geriatric service as well as a FLS, compared to 60.5% in a hospital with an ortho-geriatrics service only.

Inpatient physician consultation for patients admitted with a minimal trauma fracture to the hip is ineffective in improving osteoporosis care. That is, at discharge only 7% of patients were on bisphosphonates in one study [Jachna et al. 2003], and 5% in another study [Kamel et al. 2000]. It is important to note that these were retrospective chart reviews, and that the consulting physicians were not asked to specifically manage the patients' bone health.

Specific inpatient Endocrinology consultation for osteoporosis has been shown to be partly effective [Streeten et al, 2006] when compared to no consultation, in a study with 84 subjects. The intervention improved calcium and vitamin D commencement (75% vs 3%), and Bisphosphonate commencement (68% vs. 0%). Of those followed-up, 79% vs. 17% were taking calcium or vitamin D, and 65% vs. 0% taking a bisphosphonate (of those contacted). However, the mean follow-up was much longer for the non-intervention group (39 months) compared to the intervention group (18 months).

d. Re-fractures

Nil data.

e. Cost-effectiveness

Nil data.

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"Both among scientists and clinical practitioners, some find it easier to rely upon trivial explanations, while others never stop looking for answers". With these surprising words, Augusto Murri, an Italian master in clinical medicine, reminds us that medical practice should be a continuous journey towards knowledge and the quality of care. The book brings together contributions by over 50 authors from many countries, all around the world, from Europe to Africa, from Asia to Australia, from North to South America. Different cultures are presented together, from those with advanced technologies to those of intangible spirituality, but they are all connected by five professional attributes, that in the 1978 the Institute of Medicine (IOM)¹ stated as essentials of practicing good Primary Care: accessibility, comprehensiveness, coordination, continuity and accountability. The content of the book is organized according to these 5 attributes, to give the reader an international overview of hot topics and new insights in Primary Care, all around the world.

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