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ORIGINAL ARTICLE

Fracture liaison services for the evaluation and management of patients with osteoporotic fracture: a cost-effectiveness evaluation based on data collected over 8 years of service provision

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Abstract
Summary The cost-effectiveness of Fracture Liaison Services (FLSs) for prevention of secondary fracture in osteoporosis patients in the United Kingdom (UK), and the cost associated with their widespread adoption, were evaluated. An estimated 18 fractures were prevented and £21,000 saved per 1,000 patients. Setup across the UK would cost an estimated £9.7 million.
Introduction Only 11% to 28% of patients with a fragility fracture receive osteoporosis treatment in the UK. FLSs provide an efficient means to identify patients and are endorsed by the Department of Health but have not been widely adopted. The objective of this study was to evaluate the cost-effectiveness of FLSs in the UK and the cost associated with their widespread adoption.
Methods A cost-effectiveness and budget-impact model was developed, utilising detailed audit data collected by the West Glasgow FLS.
Results For a hypothetical cohort of 1,000 fragility-fracture patients (740 requiring treatment), 686 received treatment in the FLS compared with 193 in usual care. Assessments and osteoporosis treatments cost an additional £83,598 and £206,544, respectively, in the FLS; 18 fractures (including 11 hip fractures) were prevented, giving an overall saving of £21,000. Setup costs for widespread adoption of FLSs across the UK were estimated at £9.7 million.
Conclusions FLSs are cost-effective for the prevention of further fractures in fragility-fracture patients. The cost of widespread adoption of FLS across the UK is small in comparison with other service provision and would be expected to result in important benefits in fractures avoided and reduced hospital bed occupancy.

Keywords Economics · Fracture · Fracture liaison service · Heath services · Osteoporosis · Secondary prevention

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Introduction

Patients with osteoporotic fracture are at high risk of further fractures and their associated morbidity [1]. Despite the existence of guidelines [2–5], there is no universally implemented policy in the United Kingdom (UK) to identify, assess, and treat individuals with osteoporosis or

those at high risk for fracture. Patients may be identified opportunistically, for example, during hospital care for a fragility fracture or by chance by their general practitioner (GP). However, most patients are not identified and treated. Audit data suggest that currently only 11% to 28% of patients with a fragility fracture receive treatment for osteoporosis (personal communication, McLellan, 12 April 2010) [6–8].

Fracture Liaison Services (FLSs) provide a simple, efficient means of identifying patients [1, 9] and are endorsed by the Department of Health for delivery of secondary fracture prevention [10]. However, only an estimated 63 FLSs currently serve the 185 Primary Care Organisations and 300 hospitals in England, Wales, and Northern Ireland (unpublished research commissioned by Novartis) [8, 11]. Barriers to the widespread adoption of FLSs may include uncertainty about their cost-effectiveness and the costs associated with setting up new FLS centres.

Economic evaluations of similar services in other health care systems have been reported [12–15]; however, only a simple exploratory analysis is available for the UK [16]. The objective of this study was to provide a comprehensive evaluation of the cost-effectiveness of an FLS in the UK and to estimate the costs associated with their widespread adoption.

The analysis was performed using an economic model underpinned by 8 years of detailed audit data collected by the West Glasgow FLS. Established in 1999 [1], this FLS provides substantial evidence and experience in establishing and running the service, which can be leveraged to efficiently establish other centres. In the economic model, these audit data were combined with evidence collated by the National Institute for Health and Clinical Excellence (NICE) and other published data to evaluate the cost-effectiveness of FLSs for the prevention of further fractures in patients who have experienced a fragility fracture. The analysis compares an FLS with the absence of an FLS, i.e. a mixture of no identification or assessment along with opportunistic hospital or GP assessment, henceforth referred to as usual care. The analysis was performed from the perspective of the National Health Service (NHS); costs represent 2009 values.

Methods

West Glasgow FLS

The Glasgow FLS assumes responsibility for fracture case-finding, assessment, diagnostic evaluations, and treatment recommendation for the secondary prevention of osteoporotic fractures. All men and women over the age of 50 years presenting with low-trauma fractures are offered bone mineral density (BMD) assessment, falls prevention, and treatment.

The Glasgow FLS has been described previously [1]. Briefly, patients aged 50 years or over presenting with a low-trauma fracture are identified by an osteoporosis nurse specialist (ONS). The ONS spends a short time with each patient, explaining osteoporosis, the importance of the FLS assessment, and what it involves. Patients are invited to attend the ONS fracture risk-assessment clinic. Where appropriate, a treatment recommendation is made by the ONS on the basis of assessment of future potential fracture risk. The recommendation is endorsed by the lead consultant and sent to the patient's GP for initiation of treatment in primary care.

Treatment is recommended in accordance with evidence-based practice and national osteoporosis treatment guidelines [2, 3, 5]. Patients with a non-vertebral fracture or a single vertebral fracture are offered BMD testing and are considered for bisphosphonate therapy if the T-score at the spine or hip is −1.6 or less (vertebral fracture), −2.0 or less (non-vertebral fracture, >60 years of age), or −2.5 or less (non-vertebral fracture, 50–59 years of age). Patients with two or more vertebral fractures are considered for bisphosphonate therapy without BMD testing. Patients with a contraindication to oral bisphosphonates or who are unable to comply with the instructions for administration (e.g., those with impaired cognitive function and no caregiver support) are not offered oral bisphosphonate treatment (or BMD testing). Patients at risk for refracture and for whom bisphosphonate therapy is unsuitable are recommended calcium and vitamin D supplementation. Patients already taking osteoporosis medication are offered a treatment and compliance review (without dual energy X-ray absorptiometry [DXA]).

Detailed data from the Glasgow FLS are maintained within the Glasgow Integrated System for the Management of Osteoporosis database, which holds data on all service activity and is used to generate the GP letters. Data collected over the first 18 months of the service have been reported previously [1]. For this economic evaluation, an updated analysis was performed of data collected by the West Glasgow FLS over an 8-year period from 1 November 1999 to 31 October 2007.

Economic model

An economic model was developed to estimate the costs associated with an FLS and the costs and improved outcomes that may be expected from higher treatment rates. An explanation of economic terms used in this paper is provided in the Online resource. Two identical cohorts of patients, all aged 50 years or older with a fragility fracture, entered the model. Fragility fracture was defined as a fracture sustained in a fall from a standing height or less and not occurring as a consequence of a road traffic accident. Skull and facial fractures were excluded. One cohort followed the FLS pathway; the other followed the usual-care pathway (Fig. 1).

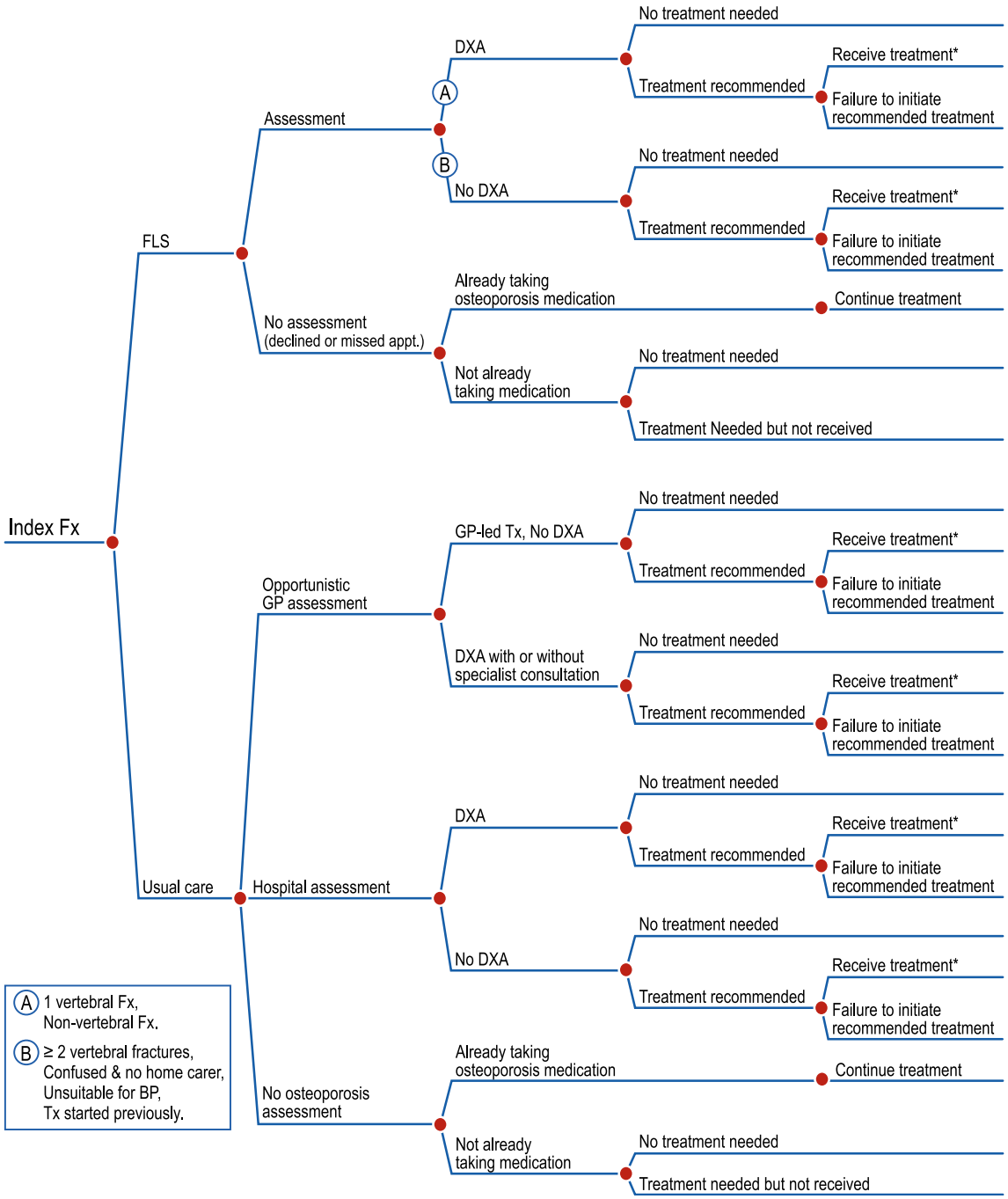

Fig. 1 Patient pathways for the FLS and usual care. *appt.* appointment, *BP* bisphosphonates, *DXA* dual energy X-ray absorptiometry, *FLS* Fracture Liaison Service, *Fx* fracture, *GP* general practitioner, *Tx* treatment. The *single asterisk* indicates that the arm includes patients who may already have been receiving treatment at the time of assessment

The FLS pathway was based on the "best practice" example provided by the Glasgow FLS, as described above. The situation in usual care is much more complex. The majority of patients are not identified. Some may consult their GP after discharge from hospital; or the GP may assess the patient without referral or may refer the patient to an open or direct access DXA service or to a specialist. Alternatively, patients may be assessed for osteoporosis while in hospital, with or without DXA or specialist involvement. Lastly, patients may not be assessed for osteoporosis either in hospital or by their GP. A proportion of these patients may already be taking osteoporosis medication; the remainder will not receive any further follow-up, and no treatment would be prescribed.

Treatment rates

For the FLS cohort, the proportion of patients with a fragility fracture requiring osteoporosis treatment that receive treatment and the type of treatment were based on the West Glasgow FLS audit data (see "Results" section).

In usual care, there is uncertainty about the proportion of patients with a fragility fracture who receive treatment for osteoporosis. Two national audits have given some indication of treatment rates following a fragility fracture. The National Audit of the Organisation of Services for Falls and Bone Health of Older People [8] estimated 28% of fragility-fracture patients initiated relevant medication by 12 weeks after fracture. The Information Centre for Health and Social Care [7] estimated 25% of females aged 75 years or older with a history of fragility fracture were prescribed a bone-sparing agent. Both of these estimates included FLS and non-FLS centres and therefore, are likely to overestimate the proportion of patients receiving treatment in usual care. An audit performed for NHS Quality Improvement Scotland [6] estimated that in 2000, 23% of patients were assessed and/or treated after fracture where no FLS was available (hip fracture=25%, wrist fracture=21%). This is also an overestimate of the number receiving treatment because it includes patients assessed and not needing treatment. Data for the five non-FLS centres from this audit were provided by McLellan (personal communication, 12 April 2010); the percentage of patients receiving treatment in non-FLS centres was estimated as 11%. The range of all estimates identified was 11% to 28%; the mid-point of this range (19.5%) was selected for the main analysis; the lower and upper ends of the range were explored in sensitivity analyses.

Estimates from the West Glasgow FLS indicated that 74% of fragility-fracture patients will require treatment (see Table 2 [table note a]); therefore, the proportion of patients with a fragility fracture requiring osteoporosis treatment who receive it in usual care is approximately 15% to 38% (0.11/0.74–0.28/0.74). The type of treatment was based on prescription data for the UK [17]. Bisphosphonates are the dominant treatment. Estimates of the number of patients receiving calcium and/or vitamin D only for osteoporosis were not available from prescription data; the same proportion as observed in the West Glasgow FLS was assumed.

Cost of FLS and usual-care assessments

Table 1 presents the costs of patient assessments. The average cost of FLS assessment per patient assessed was estimated by summing the cost of resources used to run the FLS over a 1-year period, divided by the number of patients assessed over the same period. Resources were based on those required to run the Glasgow FLS and are expected to be generalisable to similar FLSs across the UK.

In usual care, the proportion of patients with a fragility fracture who are assessed was estimated as 15.4% (see table note b of Table 1). The proportion of patients assessed by the alternative routes presented in Fig. 1 is unknown. The model assumed that GP assessment was the most common; this assumption was explored in sensitivity analysis. The proportion of assessed patients who receive a DXA scan was assumed to be equivalent to that observed in the West Glasgow FLS.

Modelling treatment costs, subsequent fractures, quality of life, and mortality

To estimate the impact of the increased use of osteoporosis treatment achieved by the FLS on treatment costs and outcomes, the economic model applied efficacy data from randomised controlled trials for the treatments received. For simplicity, the model focused on prevention of subsequent hip, wrist, and humerus fractures, which are expected to result in the greatest impact on costs and outcomes. New vertebral fractures were not modelled because they rarely present clinically (4% of all refractures [6]) and therefore have little direct impact on costs or outcomes. The model estimated the number of refractures, life-years, and quality-adjusted life-years (QALYs, a unit of measurement of both the quality and quantity of life lived).

A cohort health-state transition model (a Markov model) was selected as a simple and appropriate means of estimating costs and outcomes over patients' lifetimes (Fig. 2). The model's health states and parameters were based largely on the ScHARR Economic Model of Osteoporosis (SHEMO), developed to inform the NICE technology appraisals 160 and 161 [2, 3].

Markov models are used to model changes in patients' health states over time as a disease progresses. The health states in the model are represented by ellipses in Fig. 2. Time is partitioned into discrete periods, or cycles (in this case, 1 year). In each Markov cycle, patients' health states may change from their current health state to another health state, or they may remain in the same health state, according to a probability distribution. The changes of health state are called transitions (shown as arrows in Fig. 2), and the probabilities associated with various health-state changes are called transition probabilities.

In the FLS model, the primary difference between the experiences of the FLS and usual-care cohorts was the proportion of patients receiving treatment (in State 1). Patients in State 1 were assumed to stay on treatment for 5 years, in accordance with the SHEMO model [2, 3]. Within each Markov cycle, patients could experience a hip

fracture (move to State 3), wrist fracture (move to State 4), humerus fracture (move to State 5), remain in the treated state (State 1), or die of other causes (State 6). After 5 years of treatment, patients moved into a post-treatment state (not shown), where they experienced some continued protective effects of treatment for a further 5 years and then returned to the same risk for fracture as untreated patients.

Patients who are not treated (State 2) have the same possible transitions (with the exception of transition to the post-treatment state), but the probability of a fracture was higher than for treated patients.

Patients who experienced a fracture incurred the cost and quality-of-life impacts of the fracture and an increased risk for death associated with the fracture. The first year post-fracture was distinguished from subsequent years, as morbidity, mortality, and costs are greater in the first year. For simplicity, only the first refracture was modelled. Whilst this reflects the primary aim of an FLS (i.e. to prevent a secondary fracture), this may underestimate the total number of refractures and the full long-term benefit of the FLS and therefore, its cost-effectiveness.

The model population reflected the age and gender distribution of the West Glasgow FLS population (mean

Table 1 Cost of assessment of patients with a fragility fracture: FLS and usual care

Resource	Resource utilisation	Unit cost
FLS running costs (based on the West Glasgow FLS assessing 1,387 patients per year)		
Management	2 h per week to manage FLS workload × 41.3 weeks per year	Management time: £125 per hour (consultant, medical per contact hour [Section 13.4] PSSRU) [29]
Consultant-led clinic	1 consultant-led clinic visit for 3% of patients assessed by FLS (due to abnormalities in blood tests or severity of osteoporosis)	Rheumatology clinic visit: £210 (consultant-led: first attendance non-admitted face to face; rheumatology, 410); NHS Reference Costs 2008–2009 [30]
		Endocrinology clinic visit: £173 (consultant-led: first attendance non-admitted face to face: endocrinology); NHS Reference Costs 2008–2009 [30]
Osteoporosis nurse specialist	Osteoporosis nurse specialists (Band 6/7) 16 h per week × 41.3 weeks per year	£65 per hour of patient contact (Nurse advanced, includes lead specialist, clinical nurse specialist, senior specialist [Section 8.7] PSSRU) [29]
DXA scans	676 DXA scans per year	£73 (RA15Z: DXA scan; diagnostic imaging: outpatient); NHS Reference Costs 2008–2009: NHS Trusts and PCTs combined) [30]
Patient records, tracking, and letters	Clerical time for making appointments, maintaining patient records, folding letters, and putting them in an envelope	£24 per hour (Nurse, day ward (includes staff nurse, registered nurse, registered practitioner), per hour [Section 12.3] PSSRU) [29]
	All assessed patients generate one letter	
	1,387 letters per year at 1 min per letter=25 h per year	
Patient transport	2.5% of patients receiving a DXA require transport[a]	£16 (HTCS: hospital travel cost scheme); NHS Reference Costs 2008–2009: NHS Trusts and PCTs combined [30]
Average cost of FLS Assessment (per patient assessed)	Sum of the resources above divided by the number of patients assessed in a year (1,387)	£98
Cost of assessments in usual care		
Percentage of patients with a fragility fracture assessed[b]	11.8%	
Assessed during hospitalisation for index fracture[c]	0.59% total	
	0.36% with DXA[d] (20 min of nurse time, 1 DXA, 1 standard GP visit if treatment is recommended)	£114[e]
	0.23% without DXA[d] (20 min of nurse time, 1 standard GP visit if treatment is recommended)	£41[e]
Opportunistic GP assessment[f]	11.08% total	
	6.85% with open/direct access DXA[d] (1 extended GP visit, 1 DXA, 1 standard GP visit)	£160[e]
	4.23% without DXA[d] (1 extended GP visit)	£52[e]

Table 1 (continued)

Resource	Resource utilisation	Unit cost
Opportunistic GP assessment with specialist referral[g]	0.12% total	
	0.07% with DXA[d] (1 extended GP visit, 1 specialist visit, 1 DXA, 1 standard GP visit)	£352[e]
	0.05% without DXA[d] (1 extended GP visit, 1 specialist visit, 1 standard GP visit)	£278[e]
Average cost of usual care assessment (per patient assessed)	Calculated from data above	£119

DXA dual energy X-ray absorptiometry, *FLS* Fracture Liaison Service, *GP* general practitioner, *NHS* National Health Service, *PCT* Primary Care Trust, *PSSRU* Personal Social Services Research Unit, Unit Costs of Health and Social Care 2008

[a] Very frail patients (who would require transport) are unlikely to be brought in for DXA. These patients would likely be prescribed calcium and/or vitamin D without a DXA. The proportion of patients requiring transport to attend a DXA visit is estimated to be between 0 and 1:40 patients (Dr. McLellan, personal communication, 16 November 2009)

[b] An estimated 19.5% of patients with a fragility fracture receive treatment (see text). An estimated 11.5% are already receiving treatment at the time of fracture (West Glasgow FLS, see Results section); therefore, 8.0% (19.5–11.5%) have treatment initiated after the fragility fracture. An estimated 92% of patients that have a treatment recommended subsequently have treatment initiated (Glasgow follow-up studies, see Results section); therefore, an estimated 8.7% (8.0%/92%) have a treatment recommended. An estimated 74% of patients with a fragility fracture require osteoporosis treatment (Glasgow FLS, see Results section). Therefore, the total number of patients assessed in usual care=8.7%/74%=11.8%

[c] Assumes 5% of patients who had treatment recommended to them received recommendation during hospitalisation

[d] 62% of patients assessed for osteoporosis have a DXA (West Glasgow FLS)

[e] 20 min of nurse time at £44 per hour=£14.67 (Nurse, day ward [29]); DXA=£73 (RA15Z—DXA Scan; Diagnostic Imaging: Outpatient; NHS Reference Costs 2008–2009—NHS Trusts and PCTs combined); standard GP visit (consultation lasting 11.7 min)=£35 [29]; extended GP visit (consultation lasting 17.2 min)=£52 [29]; specialist visit=£191.50 (average of consultant-led: first attendance non-admitted face to face; Rheumatology=£210 and Endocrinology=£173; NHS Reference Costs 2008–2009 [30])

[f] Assumes 94% of patients who had treatment recommended were assessed by a GP with or without open or direct access DXA

[g] Assumes 1% of patients who had treatment recommended to them received recommendation after GP visit and specialist referral. McLellan et al. [6] reported little use of specialist visits

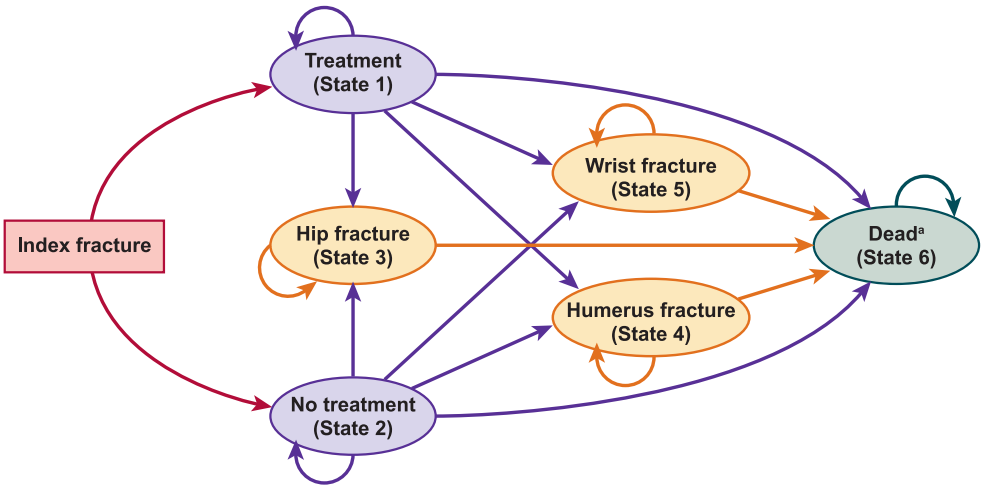

Fig. 2 Model structure diagram. *Superscript a* Patients may die as a result of their fracture or as a result of other causes. In the Markov model, patients exist in discrete health states (shown as *ellipses* in this figure), and time is partitioned into discrete 1-year periods (*cycles*). At the end of each cycle, a patient may move (transition) to another health state or they may remain in the same health state (shown as *arrows* in this figure). Two identical hypothetical cohorts of patients entered into two separate, identical models. In the FLS cohort, more patients began in the *Treatment* health state (*State 1*) than in the usual-care cohort. At the end of each cycle, patients could experience a refracture or die of other causes. Patients who are not treated (*State 2*) have the same possible transitions, but the probability of a fracture is higher than that for treated patients. Patients who experienced a fracture incurred the cost and quality-of-life impacts of the fracture and, for hip fracture only, an increased risk for death associated with the fracture

age of 72 years; 78% female). The time horizon of the analysis was patients' remaining lifetimes (a maximum of 30 years). Future costs and outcomes were discounted at 3.5% per annum, as recommended by NICE [18].

Table 2 presents the data as applied in the model. The probability of refracture in State 1 (on treatment) was estimated by applying relative risks (RRs) for hip and non-vertebral fracture (since the number of wrist and humerus fractures in the source trials were limited) from the meta-analysis of randomised controlled trials performed for the NICE osteoporosis clinical guideline under development [19] to the baseline risk of refracture for an untreated population. Alternative RR estimates for the specific fracture types (where available), for non-vertebral fracture, and for vertebral fracture (the primary endpoint in most trials) were explored in sensitivity analyses. Treatments in the FLS cohort reflected the pattern of drugs recommended by the West Glasgow FLS; in the usual-care cohort, the pattern of drug use was estimated from prescription data [17] (Table 2).

In the majority of the randomised controlled trials, patients in the active and control groups received either calcium supplements or calcium and vitamin D supplements [19]. Efficacy data therefore represent a comparison with placebo plus calcium and vitamin D rather than no treatment. In order to estimate the efficacy of each intervention versus no treatment, an indirect comparison was performed using the RR for each intervention versus calcium and vitamin D and for calcium and vitamin D versus no treatment, using the method of Bucher et al. [20].

The risk of refracture for patients with a previous fragility fracture was estimated from a prospective study of 22,060 patients in Edinburgh [21]. These data represented outcomes for patients who were not assessed by an FLS in the UK between 1988 and 1999. Treatments prescribed during this period (1994–1998) have been reported [22]. The fraction of patients receiving each treatment (and no treatment) was combined with the RR estimates and the incidence of fracture to estimate the baseline incidence of fracture for patients receiving no treatment. These estimates were used to govern the probability of fracture in State 2 (no treatment). The probability of fracture in State 1 (treatment) was estimated by applying a weighted-average RR of fracture, calculated for the pattern of drug use in the FLS and usual-care arms (Table 2). At the end of 5 years of treatment, the RR was tapered linearly to a value of 1.0 over a period of 5 years [23].

Gastrointestinal adverse events were assumed to occur in 2.35% of patients receiving oral bisphosphonates [2]; the impact on costs and quality of life were included (see Table 2). Mortality associated with hip fracture was modelled using mortality rates directly attributable to hip fracture in the 12-month period following fracture [2, 3]. Wrist and humerus fracture were assumed to have no impact on the risk of death [2, 3]. All patients in the model were assumed to be at equal risk for death from other causes, governed by mortality rates for the UK general population [24].

Patients' health-related quality of life (HRQL) was modelled over time using utility weights for patients with osteoporosis but no fracture [25]. HRQL for patients experiencing a hip, wrist, or humerus fracture was adjusted using the utility-weight multipliers reported in a recent systematic review [26]. Costs assumed for osteoporosis treatments and fractures are presented in Table 2.

Sensitivity analyses

Sensitivity analyses were performed to investigate the stability of the results over a range of structural assumptions and input data values. In deterministic sensitivity analyses, the values of one or multiple variables were investigated while the remaining variables remained constant. In probabilistic sensitivity analyses, the uncertainty in the mean values of all key model parameters was explored simultaneously by random sampling from the statistical distributions (see Table 2).

Modelling impact of widespread adoption of FLSs across the UK on NHS costs and population health

A budget-impact analysis was performed in which the impact of widespread adoption of FLSs across the UK on NHS costs was estimated. Currently, approximately 63 FLS centres serve the 185 Primary Care Organisations (PCOs) in England, Wales, and Northern Ireland (unpublished research commissioned by Novartis) [8]. Provision of FLSs for all PCOs would require an additional 122 FLS centres to be established. The estimated cost associated with setting up a new FLS centre is presented in the Online resource. The number of additional DXA scanners required was estimated by calculating the number of additional scans that would need to be performed, divided by the number of scans that can be performed by a single scanner (4,600 per year; based on North Glasgow scanners, Glasgow FLS). The annual cost of FLS assessments and osteoporosis treatments was estimated by applying the assessment and treatment costs in the model (Table 2) to the estimated number of patients presenting with a fragility fracture in the UK ([24, 27], NICE costing template updated for population projections for 2010).

Results

West Glasgow FLS audit data

A total of 11,096 patients were identified by the West Glasgow FLS between 1 November 1999 and 31 October

Table 2 Model input parameters

Parameter	Value	Distribution for PSA	Source
Parameters estimated from the West Glasgow FLS Audit Data			
Mean age at index fracture, years	72	Fixed	West Glasgow FLS, for patients presenting with a fragility fracture
Percentage female at index fracture	78%	Fixed	West Glasgow FLS, for patients presenting with a fragility fracture
Percentage of patients with a fragility fracture who needed treatment for osteoporosis (*n*/*N*)	74% (6,706/9,060)	Beta distribution	West Glasgow FLS, patients recommended or already receiving treatment divided by the number of patients for whom the need for treatment was known[a]
Percentage of patients recommended treatment who received it: FLS cohort (range)	92% (88–96%)	Beta distribution	Glasgow FLS follow-up data[b]
Interventions received: FLS cohort (% of those receiving treatment)			
Alendronate	45%	Beta distribution[c]	West Glasgow FLS
Etidronate	2%	Beta distribution[c]	West Glasgow FLS
Risedronate	8%	Beta distribution[c]	West Glasgow FLS
Ibandronate	0%	Beta distribution[c]	West Glasgow FLS
Zoledronate	0%	Beta distribution[c]	West Glasgow FLS
Strontium ranelate	0%	Beta distribution[c]	West Glasgow FLS
Raloxifene	0%	Beta distribution[c]	West Glasgow FLS
vitamin D plus calcium only	45%	Beta distribution[c]	West Glasgow FLS
Parameters from published literature and other sources			
Percentage of patients needing treatment who received it: usual-care cohort (range)	26.5% (15–38%)	Beta distribution	See text and note [d]
Interventions received: usual-care cohort (% of those receiving treatment)			
Alendronate	38%	Beta distribution[e]	[17]
Etidronate	1%	Beta distribution[e]	[17]
Risedronate	9%	Beta distribution[e]	[17]
Ibandronate	3%	Beta distribution[e]	[17]
Zoledronate	1%	Beta distribution[e]	[17]
Strontium ranelate	2%	Beta distribution[e]	[17]
Raloxifene	1%	Beta distribution[e]	[17]
vitamin D plus calcium only	45%	Beta distribution[e]	Assumption (based on West Glasgow FLS[f], see Table 1)
Efficacy of treatments in preventing hip fracture, RR (95% CI)			
Alendronate vs. no treatment[g]	0.62 (0.40, 0.96)	Normal on log scale	[19] for hip fracture endpoint
Etidronate vs. no treatment[g]	1.02 (0.21, 4.94)	Normal on log scale	[19] for hip fracture endpoint
Risedronate vs. no treatment[g]	0.73 (0.58, 0.92)	Normal on log scale	[19] for hip fracture endpoint
Ibandronate vs. no treatment[g]	1.11 (0.83, 1.48)	Normal on log scale	[19] for hip fracture endpoint
Zoledronate vs. no treatment[g]	0.62 (0.47, 0.83)	Normal on log scale	[19] for hip fracture endpoint
Strontium ranelate vs. no treatment[g]	0.85 (0.61, 1.19)	Normal on log scale	[19] for hip fracture endpoint
Raloxifene vs. no treatment[g]	1.12 (0.64, 1.94)	Normal on log scale	[19] for hip fracture endpoint
vitamin D plus calcium vs. placebo or no intervention	0.79 (0.65, 0.97)	Normal on log scale	[19] for hip fracture endpoint
Efficacy of treatments in preventing wrist and humerus fracture, RR (95% CI)			
Alendronate vs. no treatment[g]	0.69 (0.58, 0.83)	Normal on log scale	[19] for non-vertebral fracture[h]
Etidronate vs. no treatment[g]	0.60 (0.24, 1.45)	Normal on log scale	[19] for non-vertebral fracture[h]
Risedronate vs. no treatment[g]	0.67 (0.57, 0.80)	Normal on log scale	[19] for non-vertebral fracture[h]
Ibandronate vs. no treatment[g]	0.92 (0.67, 1.25)	Normal on log scale	[19] for non-vertebral fracture[h]
Zoledronate vs. no treatment[g]	0.62 (0.52, 0.75)	Normal on log scale	[19] for non-vertebral fracture[h]
Strontium ranelate vs. no treatment[g]	0.71 (0.59, 0.87)	Normal on log scale	[19] for non-vertebral fracture[h]
Raloxifene vs. no treatment[g]	0.76 (0.62, 0.92)	Normal on log scale	[19] for non-vertebral fracture[h]
vitamin D plus calcium vs. placebo or no intervention	0.83 (0.73, 0.94)	Normal on log scale	[19] for non-vertebral fracture[h]

Table 2 (continued)

Parameter	Value	Distribution for PSA	Source
Persistence on therapy, mean years	5	Fixed	[2, 3] (TA160; TA161)
Continuation of treatment effect after treatment discontinuation (RR tapers to 1.0 over a period of), years	5.0	Fixed	[2, 3] (TA160; TA161)
Percentage of patients receiving BPs that have GI AEs	2.35%	Fixed	[2] (TA160)
Quality-of-Life Data			
Utility-weight multipliers (95% CI)			
Hip fracture (year 1)	0.70 (0.64–0.77)	Beta	[26]
Hip fracture (year >1)	0.80 (0.68–0.96)	Beta	[26]
Hip fracture leading to nursing home	0.40	Fixed	[2]
Wrist fracture (year 1)	0.956 (0.86–1.00)	Beta	[26]
Humerus fracture (year 1)[i]	0.80 (0.68–0.96)	Beta	[26]
GI adverse event	0.91	Fixed	[3]
Costs			
Cost of treatments, drug cost per annum			
Alendronate	£15.12	–	Calculated based on [31]
Etidronate	£80.67	–	Calculated based on [31]
Risedronate	£249.24	–	Calculated based on [31]
Ibandronate (oral)	£220.80	–	Calculated based on [31]
Strontium ranelate	£333.71	–	Calculated based on [31]
Zoledronate (including drug administration)	£288.72	–	Calculated based on [31] plus 30 min of nurse time at £44 per hour
Raloxifene	£222.39	–	Calculated based on [31]
vitamin D plus calcium only	£44.17	–	Calculated based on [31]
Cost of blood tests (for patients starting BPs) ESR, FBC, U&E, LFTs, calcium, phosphate, TFT, vit D, immunoglobulins. Additional tests for male patients receiving bisphosphonates: testosterone, LH, and FSH	£1.34 per test (£15 in total)	Fixed	DAP841: biochemistry. NHS Reference Costs 2008–2009 [30]
Cost of monitoring (1 GP visit per year)	£35	Fixed	[29]
Cost of GI AEs[j]	£41.36	Fixed	Calculated based on [29, 31]
Cost of fractures leading to nursing home entry, first year after fracture			
Hip, aged 50–59	£37,175	Uniform ±10%	[2, 3][k, l]
Hip, aged 60–69[m]	£37,175	Uniform ±10%	[2, 3][k, l]
Hip, aged 70–79[n]	£38,727	Uniform ±10%	[2, 3][k, l]
Hip, aged ≥80[o]	£41,159	Uniform ±10%	[2, 3][k, l]
Cost of fractures leading to nursing home entry, second and subsequent years after fracture)			
Hip, aged 50–59	£27,985	Uniform ±10%	[2, 3][k, l]
Hip, aged 60–69[m]	£27,985	Uniform ±10%	[2, 3][k, l]
Hip, aged 70–79[n]	£28,790	Uniform ±10%	[2, 3][k, l]
Hip, aged ≥80[o]	£30,117	Uniform ±10%	[2, 3][k, l]
Cost of fractures not leading to nursing home entry			
Hip, aged 50–59	£6,125	Uniform ±10%	[2, 3][k, l]
Hip, aged 60–69[m]	£6,125	Uniform ±10%	[2, 3][k, l]
Hip, aged 70–79[n]	£7,705	Uniform ±10%	[2, 3][k, l]
Hip, aged ≥80[o]	£10,141	Uniform ±10%	[2, 3][k, l]
Wrist, age <80	£404	Uniform ±10%	[2, 3][k, l]
Wrist, age ≥80	£658	Uniform ±10%	[2, 3][k, l]
Humerus, age <80	£1,151	Uniform ±10%	[2, 3][k, l]
Humerus, age ≥80	£1,881	Uniform ±10%	[2, 3][k, l]
Mean length of hospital stay for fracture (percentage of fracture patients hospitalised)[o]	25 days		
Hip fracture	26.0 days (100%)	Fixed	[32]

Table 2 (continued)

Parameter	Value	Distribution for PSA	Source
Wrist fracture	5.4 days (25%)	Fixed	[32]
Humerus fracture	10.6 days (32%)	Fixed	[32]

AE adverse event, *BP* bisphosphonate, *CI* confidence interval, *FLS* Fracture Liaison Service, *GI* gastrointestinal, *GP* general practitioner, *NHS* National Health Service, *PSA* probability sensitivity analysis, *RR* relative risk, *TA* technology assessment, *ESR* erythrocyte sedimentation rate, *FBC* full blood count, *FSH* follicle stimulating hormone, *LFT* liver function test, *LH* luteinizing hormone, *TFT* thyroid function test, *U&E* urea and electrolytes, *vit D* vitamin D

[a] In the West Glasgow FLS, of the 11,096 presenting patients, 8,875 were assessed and a further 185 were already receiving treatment at initial identification. The total number of patients for whom the need for treatment was known was therefore 9,060 (8,875+185). A total of 6,706 patients either were recommended treatment or were already on treatment. The proportion of patients presenting with a fragility fracture that required treatment therefore was 74% (6,706/9,060)

[b] As described in the "Results" section (the "West Glasgow FLS audit data" subsection), in the Glasgow Direct Access DXA Service Audit, GPs instituted the recommended treatment in 96% of cases. In the Glasgow FLS patient survey, 86% to 88% of patients were taking the recommended treatment at 6 to 12 months. The selected value (92%) is the mid-point of this range

[c] Based on number of patients receiving each treatment and the total number of patients in the West Glasgow FLS

[d] Approximately 11–28% (mid-point: 19.5%) of patients with a fragility fracture received treatment for osteoporosis (see text). Assuming 74% of patients with a fragility fracture need treatment (Glasgow FLS data), the probability that patients needing treatment receive it is 0.195/0.74=0.263

[e] Based on the number of normalised counting units for each treatment and the total in the IMS dataset [17]

[f] The estimate of 45% includes calcium and vitamin D only and hormone replacement therapy (usually with calcium and vitamin D). Hormone replacement therapy was not included as an intervention in the model because it is rarely used now; patients receiving hormone replacement therapy in the West Glasgow FLS were included in the calcium plus vitamin D only group in the model

[g] In many of the source trials, both treatment groups received calcium and/or vitamin D supplementation. RRs have been adjusted for the RR for calcium and/or vitamin D vs. no treatment in order to estimate the RR for each intervention vs. no treatment

[h] The non-vertebral fracture endpoint was used because data specific to wrist and humerus fracture are sparse (see text)

[i] Peasgood et al. [26] were unable to report a utility multiplier for humerus fracture as insufficient data were identified. The estimate for hip fracture year >1 was assumed

[j] A course of omeprazole (£6.36) plus a GP visit (£35.00)

[k] Inflated to 2008–2009 values using NHS Pay and Prices Index [29]

[l] Includes total length of stay in acute orthopaedic care plus any subsequent rehabilitation, acute hospital, or continuing NHS care stays directly afterwards (until patient left this setting) [29]

[m] 8% of patients were assumed to be discharged to a nursing home [11], with a first year cost of £31,299 and a subsequent annual cost of £23,562 [2, 3]

[n] 8% of patients were assumed to be discharged to a nursing home [11], with a first year cost of £32,606 and a subsequent annual cost of £24,240 [2, 3]

[o] 8% of patients were assumed to be discharged to a nursing home [11], with a first year cost of £34,654 and a subsequent annual cost of £25,357 [2, 3]

2007—an average of 1,387 per year. Table 3 presents descriptive characteristics of the population. The mean age at fracture presentation was 72 years (range, 50–104 years); 78% (8,668/11,096) were female. The most common presenting fractures were radius/ulna (29.0%), hip (23.9%), and humerus (13.5%). Of those patients with prior fracture data, 71.1% had no prior fracture, 20.1% had one prior fracture, and 8.8% had two or more prior fractures.

Of the 11,096 patients, 8,875 (80%) were assessed, 5,405 (49%) received a DXA scan, 1,848 (17%) received a medication and compliance review without DXA, and 1,541 (14%) were recommended calcium and vitamin D supplements without DXA. Appropriate treatment had been previously initiated in 1,273 (11%) patients, and treatment was recommended by the FLS for a further 5,433 (49%) patients, making a total of 6,706 (60%) patients recommended for treatment. Approximately 20% of patients (2,221) were not assessed because they did not attend after originally agreeing to an assessment, failed to respond to the letter of invitation, refused to attend, were too unwell, or were awaiting assessment at the time of database analysis. Of these patients, 185 were already receiving treatment at initial identification.

Bisphosphonates were the most common treatment (existing or recommended), representing 54% of all treatments. Strontium ranelate, raloxifene, and hormone replacement therapy were recommended to 0.4%, 0.8%, and 2.7% of patients, respectively. Adequate intakes of calcium and vitamin D were recommended to all patients; 42% were recommended calcium and vitamin D only. In follow-up surveys conducted by the FLS, the recommended treatment was initiated in primary care in 96% of patients and was being taken by 86% to 88% of patients

after 12 months.[1] The analysis applied a range of 88% to 96%; the mid-point (92%) was applied in the base case analysis.

The occurrence of refracture in the West Glasgow FLS population was recorded. A Kaplan–Meier analysis for the time to first refracture is presented in the Online resource. This was not used in the analysis because there were no comparative data for the same patient population in usual care. However, the model predictions for the occurrence of fractures in the FLS cohort were compared with these data as a model-validity check.

Economic analysis

Table 4 presents the results of the base-case analysis (in which all model parameters were set to mean values). In the hypothetical cohorts of 1,000 patients, 686 patients received treatment in the FLS cohort compared with 193 in the usual-care cohort. There were 18 fewer fractures in the FLS cohort than the usual-care cohort (11 hip, 5 wrist, and 3 humerus), resulting in three life-years gained, 22 QALYs gained, 266 hospital bed days saved, and a cost-saving of £312,000 from fractures avoided. The cost of assessments was £98,000 and £14,000 for the FLS and usual care, respectively; the cost of drugs was £292,000 and £85,000, respectively. Overall, the FLS saved an estimated £21,000 over the lifetimes of 1,000 patients.

As a model-validation check, the model prediction for the number of fractures in the FLS cohort was compared with that observed in the West Glasgow FLS (presented in the Online resource). In the model, the cumulative incidence of fracture (hip, wrist, or humerus) among patients initiating treatment was 8% at 4 years. In the Glasgow FLS, the equivalent data, including all refracture types, was 12% (95% CIs 11%–13%) at 4 years. This is a little higher than the model predicts, which may reflect the fact that the model includes only hip, wrist, and humerus fractures and that the population of Glasgow may be at higher risk of refracture than the UK population as a whole due to a greater burden of comorbid conditions.

In the probabilistic sensitivity analysis (Table 4), the mean number of patients receiving treatment was significantly higher in the FLS cohort (493 more per 1,000 patients; 95% CIs 394–587). The mean number of fractures was significantly lower in the FLS cohort (18 fewer per 1,000 patients; 10–24), and the cost of fractures was significantly lower (£312,000 less per 1,000 patients; £120,283–£464,958). Overall costs were lower for the FLS cohort by £21,452, but the difference was not significant (CIs −£156,101 to +£154,494).

The lower and upper ends of the range of estimates for the percentage of patients receiving treatment in usual care were explored (Table 4). The FLS was still cost-saving in both analyses; cost-savings ranged from £19,000 to £24,000.

Further sensitivity analysis results are presented in Online resource. Results were most sensitive to the efficacy data applied. Using the most favourable efficacy data, 36 fractures were avoided and £199,312 saved per 1,000 patients. Using the least favourable efficacy data, 15 fractures were avoided and the FLS was £84,076 more expensive per 1,000 patients; the incremental cost per QALY was £5,740. Analyses were performed to investigate the impacts of reduced persistence and compliance in clinical practice and of assuming loss of treatment effect over 1 year after treatment discontinuation. In the least favourable of these analyses, the incremental cost per QALY was £3,102. Using the two most efficacious interventions from this analysis for the prevention of hip fractures (alendronate and zoledronate in 80% and 20% of patients receiving active treatment, respectively), 28 fractures (including 18 hip fractures) were avoided and £85,263 was saved per 1,000 patients.

In the budget-impact analysis, the cost of establishing an additional 122 FLS centres was estimated as £1.6 million. An estimated 151 additional DXA scanners would be required at a purchase cost of £53,000 per scanner (personal communication from GE Healthcare Ltd, dated 17 March 2010). Total setup costs, including purchase of these DXA scanners, were estimated as £9.7 million. The additional annual costs of FLS assessments and osteoporosis treatment were £140 million and £71 million, respectively, based on 1.6 million men and women presenting with a fragility fracture in the UK in 2011. An estimated 31,000 fractures (representing a saving of £522 million) would be prevented over the lifetimes of the cohort of patients assessed each year.

Discussion

An FLS provides a simple, efficient means to identify patients eligible for secondary prevention of osteoporotic fracture following a fragility fracture. In usual care, the proportion of patients with a fragility fracture requiring osteoporosis treatment who receive it was estimated as approximately 15% to 38%. Data from the West Glasgow FLS suggest that this may be increased to 88% to 96% in an FLS setting. The average cost per assessment was lower

[1] In an audit of the Glasgow Direct Access DXA Service, GPs instituted the recommended treatment in 96% of cases and another treatment in most remaining cases. In a survey of patients recommended treatment by the Glasgow FLS 6 to 12 months after initiation of therapy, of the 66% of those who responded, 86% to 88% indicated they were taking the recommended treatment.

for the nurse-led FLS than for the variety of assessment and referral routes in usual care (£98 and £119, respectively).

The results of this analysis suggest that FLSs are cost-effective compared with usual care for the prevention of further fractures in patients who have experienced a fragility fracture. In the base-case analysis, 18 fractures were prevented, with an overall cost-saving of £21,000 over the lifetimes of the cohort of 1,000 patients (i.e. the FLS was the dominant strategy, being more effective at a lower cost).

The key sources of uncertainty in the model were the proportion of patients receiving treatment in usual care and the efficacy of the treatments in clinical practice. These and other parameters were explored in sensitivity analyses. An FLS was not cost-saving in all cases; but where it was not cost-saving it was highly cost-effective. The mean incre-

Table 3 Descriptive characteristics of the population assessed by the West Glasgow FLS (1 November 1999–31 October 2007)

Characteristic	Females		Males		Total	
Number of fracture presentations	8,668		2,428		11,096	
Mean age, years (std dev)	73.3	(12.0)	68.8	(11.7)	72.3	NA
Age range, years	50–104		50–102		50–104	
Presenting fracture type						
Radius/ulna, *n* (%)	2,718	(31.4%)	503	(20.7%)	3,221	(29.0%)
Hip, *n* (%)	2,068	(23.9%)	582	(24.0%)	2,650	(23.9%)
Humerus, *n* (%)	1,111	(12.8%)	388	(16.0%)	1,499	(13.5%)
Ankle, *n* (%)	779	(9.0%)	263	(10.8%)	1,042	(9.4%)
Hand/foot, *n* (%)	825	(9.5%)	241	(9.9%)	1,066	(9.6%)
Pelvis, pubic ramus, *n* (%)	252	(2.9%)	59	(2.4%)	311	(2.8%)
Clavicle, *n* (%)	129	(1.5%)	112	(4.6%)	241	(2.2%)
Tibia/fibula, *n* (%)	232	(2.7%)	83	(3.4%)	315	(2.8%)
Vertebra, clinical, *n* (%)	232	(2.7%)	115	(4.7%)	347	(3.1%)
Femoral shaft, *n* (%)	223	(2.6%)	52	(2.1%)	275	(2.5%)
Other, *n* (%)	99	(1.1%)	29	(1.2%)	128	(1.2%)
Fracture presentations with prior fracture data[a], *n* (%)	3,915	(45.2%)	1,080	(44.5%)	4,995	(45.0%)
No previous fracture, *n* (%)[b]	2,711	(69.2%)	840	(77.8%)	3,551	(71.1%)
1 previous fracture, *n* (%)[b]	836	(21.4%)	170	(15.7%)	1,006	(20.1%)
2 or more previous fractures, *n* (%)[b]	368	(9.4%)	70	(6.5%)	438	(8.8%)
Fracture presentations with risk factor data, *n* (%)	4,254	(49.1%)	1,150	(47.4%)	5,404	(48.7%)
Smoker[c], *n* (%)[d]	1,075	(25.3%)	421	(36.6%)	1,496	(27.7%)
Alcohol excess[e], *n* (%)[d]	178	(4.2%)	339	(29.5%)	517	(4.7%)
Low BMI (<21 kg/m^2), *n* (%)[d]	379	(8.9%)	111	(9.7%)	490	(4.4%)
Maternal history of hip fracture, *n* (%)[d]	325	(7.6%)	68	(5.9%)	393	(3.5%)
Family history of osteoporosis, *n* (%)[d]	600	(14.1%)	95	(8.3%)	695	(6.3%)
Assessment by FLS						
Assessment with DXA, *n* (%)	4,320	(49.8%)	1,166	(48.0%)	5,486	(49.4%)
DXA completed, *n* (%)	4,254	(49.1%)	1,151	(47.4%)	5,405	(48.7%)
Osteoporosis, *n* (%)	2,092	(24.1%)	411	(16.9%)	2,503	(22.6%)
Osteopenia, n (%)	1,707	(19.7%)	581	(23.9%)	2,288	(20.6%)
No osteoporosis or osteopenia, *n* (%)	455	(5.2%)	159	(6.5%)	614	(5.5%)
Medication and compliance review without DXA; referral to falls service, *n* (%)	1,612	(18.6%)	236	(9.7%)	1,848	(16.7%)
Recommended Ca/vit D without DXA; referral to falls service, *n* (%)	1,196	(13.8%)	345	(14.2%)	1,541	(13.9%)
Total assessed by FLS, *n* (%)	7,128	(82.2%)	1,747	(72.0%)	8,875	(80.0%)
Total not assessed by FLS[f], *n* (%)	1,540	(17.8%)	681	(28.0%)	2,221	(20.0%)
Treatment recommendation						
Treatment needed[g], *n* (%)	5,537	(63.9%)	1,169	(48.1%)	6,706	(60.4%)
Appropriate treatment started previously, *n* (%)	1,126	(13.0%)	147	(6.1%)	1,273	(11.5%)
Treatment recommended by FLS, *n* (%)	4,411	(50.9%)	1,022	(42.1%)	5,433	(49.0%)
No clinical need for treatment, *n* (%)	1,745	(20.1%)	608	(25.0%)	2,353	(21.2%)

Table 3 (continued)

Characteristic	Females		Males		Total	
Clinical need for treatment unknown[h], *n* (%)	1,385	(16.0%)	651	(26.8%)	2,036	(18.3%)
Type of treatment (existing or recommended)						
Bisphosphonate[i] (usually with Ca/vit D), *n* (%)[j]	3,056	(55.2%)	577	(49.4%)	3,633	(54.2%)
Strontium ranelate (with Ca/vit D), *n* (%)[j]	22	(0.4%)	6	(0.5%)	28	(0.4%)
Raloxifene (with Ca/vit D), *n* (%)[j]	57	(1.0%)	0	(0%)	57	(0.8%)
HRT (usually with Ca/vit D), *n* (%)[j]	184	(3.3%)	0	(0%)	184	(2.7%)
Ca/vit D only, *n* (%)[j]	2,218	(40.1%)	586	(50.1%)	2,804	(41.8%)

BMI body mass index, *Ca/vit D* calcium and vitamin D supplementation, *DXA* dual energy X-ray absorptiometry, *FLS* Fracture Liaison Service, *HRT* hormone replacement therapy, *NA* not available, *std dev* standard deviation

[a] History of prior fracture at first FLS assessment. Collected for patients receiving a DXA scan only

[b] Percentage of those with prior fracture data (recorded only for patients receiving a DVA scan)

[c] Defined as ten or more cigarettes per day currently or within the last 6 months

[d] Percentage of those with risk factor data

[e] Defined as more than 3 units per day or 21 units per week

[f] Includes patients who were awaiting assessment, who did not attend assessment after originally agreeing to attend, who did not attend assessment after failing to respond to letter of invitation, or who refused or who were too unwell to attend assessment

[g] Includes patients who did not attend assessment but for whom osteoporosis treatment was noted at case identification

[h] Includes patients who were awaiting clinic and/or DXA and who did not attend or refused assessment. Excludes patients who did not attend assessment but for whom osteoporosis treatment was noted at case identification

[i] Of patients recommended a bisphosphonate, 82% were recommended alendronate, 3% etidronate, 0.3% ibandronate, and 15% risedronate

[j] Percentage of patients with existing or recommended treatment

mental cost-effectiveness ratio remained below £6,000 per QALY in all analyses, well below the threshold of £20,000 per QALY implemented by NICE in the UK [18].

The results of this analysis suggest that in the first 8 years of the West Glasgow FLS (processing over 11,000 fractures in a population of approximately 250,000 patients), at least 122 hip fractures and at least 81 wrist and humeral fractures were avoided.

Limitations of our analysis are as follows. The analysis relied on a modelling approach to estimate the difference in the number of refractures between the FLS and usual-care cohorts. Comparative data collected under controlled conditions (i.e., within a randomised observational study) would be preferable but are not available at this time. Refracture data collected by the West Glasgow FLS may not be used directly because no data collected under comparable conditions are available for usual care in a comparable population. This analysis focused on refractures of the hip, wrist, and humerus, which constitute approximately two thirds of all refractures [16]. Higher treatment rates also would be expected to reduce the incidence of refractures of the pelvis, lower limb, hands, feet, and vertebrae [16], as well as sub-clinical vertebral fractures which are associated with a higher risk of subsequent fracture and mortality [6]. The cost offsets and benefits associated with prevention of these additional fracture types are not modelled in this study, while the costs of assessing patients with all types of initial fractures were included. In addition, this analysis focused on prevention of the first refracture; subsequent refractures were not modelled. These simplifications may result in underestimation of the total number of refractures and the full long-term cost-savings and benefits of the FLS.

Our results are broadly consistent with the findings of the Department of Health analysis for the UK [16] and the findings reported for similar services in Canada [12–14] and the USA [15]. In the Department of Health analysis [16], an estimated £290,708 was saved over a 5-year period in NHS acute and community services and local authority social care costs, against an additional £234,181 in revenue costs (falling both in year 1 and covering drug therapy for 5 years spent by the NHS on this patient cohort). This was for an annual patient cohort of 797 hip, humerus, spine, and forearm fractures, anticipated from a population of 320,000. At a national level, this equated to saving approximately £8.5 million over 5 years.

In a Canadian model, a hospital-based care manager assessing patients aged 50 years or older with hip fractures was dominant over usual care [12, 13]. For every 100 patient-cases managed, six fractures (four hip fractures) were prevented, four QALYs were gained, and Can $260,000 (year 2006 values) were saved. An osteoporosis coordinator [14] appointed to manage outpatients and inpatients with fragility fractures in Toronto, Canada, was

Table 4 Base-case and key sensitivity analysis results[a]: estimated costs and outcomes for a cohort of 1,000 patients with a fragility fracture

	FLS	Usual care	Increment (FLS minus usual care)
Number of patients requiring treatment (95% CI[b])	740 (731–749)	740 (731–749)	0
Number of patients with treatment initiated (95% CI[b])	686 (655–718)	193 (114–276)	493 (394–587)
Number of refractures (95% CI[b])			
Hip	102 (93–113)	113 (105–119)	−11 (−16 to −4)
Wrist	87 (81–91)	91 (86–96)	−5 (−7 to −2)
Humerus	47 (44–50)	50 (47–52)	−3 (−4 to −1)
Total	236 (220–250)	254 (237–266)	−18 (−24 to −10)
Number of hospital bed days due to fracture	3,170	2,904	266
Number of deaths due to hip fracture (95% CI[b])	11 (10–12)	12 (11–12)	−1 (−1–0)
Life-years[c] (95% CI[b])	4,683 (4,679–4,685)	4,680 (4,678–4,682)	3 (1–5)
QALYs[c] (95% CI[b])	7,257 (6,574–7,488)	7,235 (6,560–7,467)	22 (7–37)
Cost of assessment	£97,677	£14,078	£83,598
Cost of osteoporosis treatments[d] (95% CI[b])	£291,745 (276,785–303,874)	£85,202 (49,689–120,462)	£206,544 (162,470–246,998)
Cost of refractures (95% CI[b])	£2,015,295 (1,878,031–2,423,122)	£2,326,889 (2,211,617–2,655,066)	−£311,593 (−464,958 to −120,283)
Total cost (95% CI[b])	£2,404,717 (2,254,692–2,793,312)	£2,426,169 (2,332,425–2,757,554)	−£21,452 (−156,101–154,494)
	Base-case (19.5% treated in usual care)	**11% treated in usual care**	**28% treated in usual care**
Fractures avoided	18 (10–24)	21 (10–24)	15 (10–24)
QALYs gained	22 (7–37)	26 (7–36)	19 (7–36)
Cost saved	£21,452 (−156,101–154,494)	£19,336 (−160,533–149,784)	£23,537 (−145,101–171,888)

CI confidence interval, *FLS* Fracture Liaison Service, *QALY* quality-adjusted life-year

[a] Additional sensitivity analyses are presented in the Online resource (Table A-2)

[b] 95% CIs were estimated by probabilistic sensitivity analysis. This analysis modelled the uncertainty related to input variables by using probability distributions of their point estimates, consistent with the data types (details of the parameter distributions are presented in Table 3). For each simulation run, a value from the distribution of each variable was chosen at random, generating one set of outputs. This was repeated so that a large number of iterations (1,000) generated a distribution of outcomes and costs. The 95% CIs presented in the table represent the 95% CI of the distributions generated

[c] Total life-years and QALYs for the 740 patients with osteoporosis requiring treatment. Life-years and QALYs for patients with a fragility fracture who, when assessed, do not have osteoporosis are excluded from the analysis because they are equivalent in the FLS and usual-care cohorts

[d] Total cost for an average of 5 years of treatment, including drugs, administration, monitoring, and GI adverse events (for oral bisphosphonates)

predicted to reduce the incidence of future hip fractures from 34 to 31 in the first year, with net hospital savings of Can$48,950 (year 2004 values). Greater savings were anticipated after the first year, when additional costs such as rehabilitation and dependency costs were considered. In the USA [15], the "Healthy Bones Program" in Kaiser Southern California (a United States health-maintenance organisation) led to an average reduction in the hip fracture rate of 37.2% and reduced fracture costs by US $30.8 million in 2006.

The setup and annual running costs associated with widespread adoption of FLSs across the UK (excluding the cost of additional treatments) were estimated as £9.7 and £140 million, respectively. This is similar in magnitude to other service provision [28].

Widespread availability of FLSs would be expected to result in important benefits. An estimated 18 fractures would be avoided and three life-years saved, per 1,000 patients assessed, over patients' lifetimes. Delegating initial care and treatment recommendations to nurse specialists with expertise in osteoporosis and fracture secondary prevention would be expected to result in more widespread and consistent implementation of evidence-based guidance on the use of treatments for secondary prevention of osteoporotic fractures (e.g., NICE guidance and Scottish Medicines Consortium advice). Widespread availability of FLSs would be expected to free up hospital beds and NHS resources. FLSs also are able to coordinate additional beneficial services, including exercise classes, physiotherapy sessions, distribution of written educational material, and educational classes.

Failure to treat following fragility fracture may constitute a medico-legal hazard, particularly since the publication of NICE Technology Assessment 161 [3]. The FLS achieves unrivalled rates of assessment and treatment for secondary fracture prevention.

Summary and conclusion

FLSs are cost-effective compared with current service provision for the prevention of further fractures in patients who have experienced a fragility fracture. The cost of widespread adoption of FLS across the UK is small in comparison with other service provision and could result in important benefits of fractures avoided and reduced hospital bed occupancy.

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Conflicts of interest AR McLellan has received honoraria (Speaker's Fees) from Novartis & has participated in advisory boards supported by Novartis. D Roberts and F Adekunle are employees of Novartis Pharmaceuticals UK Ltd and hold shares in the company. Novartis Pharmaceuticals UK Ltd provided funding to RTI Health Solutions to perform the research reported in the manuscript. Novartis Pharmaceuticals UK Ltd is the manufacturer of zoledronic acid 5 mg (also known as zoledronate), one of the osteoporosis treatments mentioned in the manuscript. Novartis Pharmaceuticals UK Ltd provided statistical support for the analysis of anonymised patient level data from the West Glasgow FLS that was provided by Dr AR McLellan.

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