

# Models of care for the secondary prevention of osteoporotic fractures: a systematic review and meta-analysis

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**Abstract** Most people presenting with incident osteoporotic fractures are neither assessed nor treated for osteoporosis to reduce their risk of further fractures, despite the availability of effective treatments. We evaluated the effectiveness of published models of care for the secondary prevention of osteoporotic fractures. We searched eight medical literature databases to identify reports published between 1996 and 2011, describing models of care for secondary fracture prevention. Information extracted from each publication included study design, patient characteristics, identification strategies, assessment and treatment initiation strategies, as well as outcome measures (rates of bone mineral density (BMD) testing, osteoporosis treatment initiation, adherence, re-fractures and cost-effectiveness). Meta-analyses of studies with valid control groups were conducted for two outcome measures: BMD testing and osteoporosis treatment initiation. Out of 574 references, 42 articles were identified as analysable. These studies were grouped into four general models of

care—type A: identification, assessment and treatment of patients as part of the service; type B: similar to A, without treatment initiation; type C: alerting patients plus primary care physicians; and type D: patient education only. Meta-regressions revealed a trend towards increased BMD testing ( $p=0.06$ ) and treatment initiation ( $p=0.03$ ) with increasing intensity of intervention. One type A service with a valid control group showed a significant decrease in re-fractures. Types A and B services were cost-effective, although definition of cost-effectiveness varied between studies. Fully coordinated, intensive models of care for secondary fracture prevention are more effective in improving patient outcomes than approaches involving alerts and/or education only.

**Keywords** Cost-effectiveness · Fracture liaison services · Models of care · Osteoporosis treatment · Re-fractures · Secondary fracture prevention

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## Introduction

Osteoporosis is a disorder of low bone mass and micro-architectural deterioration resulting in decreased mechanical strength and increased susceptibility to fractures even after minimal trauma [1]. These ‘minimal trauma fractures’ (also known as ‘osteoporotic’, ‘low trauma’ or ‘fragility’ fractures) are the hallmark of a chronic and disabling disease that affects both men and women worldwide. On statistical grounds, more than 50 % of postmenopausal women and 30 % of men over the age of 60 years will suffer at least one minimal trauma fracture during their remaining lifetime [2, 3]. Any osteoporotic fracture predisposes to further fractures, significant morbidity and premature death [4, 5]. Thus, following a first minimal trauma fracture both men and women have a two- to threefold increased risk of subsequent fracture [6–8].

For over two decades, we have known that the timely diagnosis and optimal treatment of osteoporosis prevents further fractures in these people. By now, several safe and effective medications are available [9–14] and virtually all osteoporosis guidelines recommend long-term treatment for people who have sustained a minimal trauma fracture [15–19]. However, the international literature provides ample proof that the majority of people presenting with a minimal trauma fracture are neither assessed for osteoporosis, nor appropriately managed to prevent further fractures [20–25]. Furthermore, this gap in care has not improved in recent years, as shown by Leslie et al. in 2012 [26].

## Aim

The Agency for Clinical Innovation (ACI) has been established by the New South Wales (NSW) Ministry of Health to help develop ‘high quality, safe and cost-effective ways to care for patients within the NSW public health system’ [27]. One of the goals of this initiative is to improve the care of people who have sustained minimal trauma fractures, thereby reducing the incidence of future fractures. Worldwide, numerous clinical care pathways and/or coordinated, systematic approaches to the secondary prevention of fractures in patients with osteoporosis have been trialled. The present literature review aims to critically appraise the available studies on such models of care in order to establish specific features associated with effective secondary fracture prevention programs.

## Methods

Medline, Premedline, Pubmed, Cochrane, Embase, Mosby, British Nursing Index (BNI) and Database of Abstracts of Reviews of Effectiveness (DARE) databases were searched

using the following key words singularly and in combination: ‘osteoporosis, fracture, strategy/ies, intervention/s, program/s, prevention, implementation, identification, minimal/low/fragility trauma fracture, quality improvement methodology and fracture liaison services’. Searches were limited to 1996–2011 inclusive, to articles written in English and concerning adults aged 45 years old and over. Studies relating to primary fracture prevention were excluded. Additional articles were identified by hand searching of the reference lists of articles selected for review. Two reviewers independently examined results of the searches for potentially relevant articles. Those articles that fulfilled the inclusion criteria were critically and independently appraised by at least two of us, extracting the following information: study design, patient characteristics (demographics, fracture type and setting), identification strategies (e.g. use of a coordinator), intervention strategies (e.g. health education, osteoporosis risk factor assessment, bone mineral density (BMD) testing and treatment), effect measures and effect size. Any discrepancies were resolved by consensus.

Studies with valid control groups were included in a meta-analysis of available outcome measures, namely rates of BMD testing and osteoporosis treatment initiation rates (defined as anti-resorptive or anabolic therapy, not including calcium or vitamin D supplementation), using risk difference (RD=difference in uptake rates between intervention and control). Meta-regression was used to assess the relationship between care type (as a continuous variable—3, 2, 1 and 0 for types A, B, C and D, respectively) and RD size. Stata v11 statistical package (StataCorp. 2009, *Stata Statistical Software: Release 11*. College Station, StataCorp LP, TX) was used to perform both meta-regression and meta-analyses.

Studies with no valid control groups or denominator data were described as part of the systematic review, as they provide important insights into the measures of effectiveness relating to each model of care.

## Results

Out of 574 abstracts initially retrieved, only 42 articles remained for critical appraisal, after excluding letters to the editor, duplicated publications, conference abstracts and articles not directly related to secondary fracture prevention programs (e.g. describing the osteoporosis care gap, fracture predictors and assessment of health professional or patient knowledge). Some articles described more than one service, such as Huntjens et al. [28] which reviewed five intervention programs. There were a total of 44 primary intervention studies. The same service may have published more than one study. That is, the Glasgow fracture liaison service published three studies [29–31] while the Kaiser Permanente

group published two studies [32, 33]. The studies described by Lih et al. [34] and Bogoch et al. [35] published separate cost-effectiveness evaluations [36, 37].

We found a wide spectrum of interventions and their components, which are described as follows:

1. Provision of specific ‘osteoporosis protocols’ with written guidelines for the assessment and treatment of people with a minimal trauma fracture for staff working in inpatient wards, orthopaedic fracture clinics and emergency departments;
2. Health education of patients concerning osteoporosis as a disease and its management through a letter (information sheet) or direct communication either ‘face-to-face’ or via telephone;
3. Alerts to the primary care physician (PCP) of the need to evaluate and treat their patient for osteoporosis via direct communication, letter, or e-mail;
4. Assessment of clinical risk factors for osteoporosis;
5. BMD testing (bone densitometry);
6. Investigation for secondary causes of osteoporosis;
7. Treatment initiation (both non-pharmacological and pharmacological); and
8. Monitoring with regular follow-up.

Depending on the model of care implemented at any given site, the actual intervention ranged from a simple, education-based model with high patient capture and turnover to more complex models involving most or all components listed above. The latter 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 care following a minimal trauma fracture. Hence, given the heterogeneity of interventions, we classified models of care from types A to D, based upon the intensity of the intervention described.

#### Type A models of care ( $n=14$ studies)

Type A models of care (Table 1) represent a coordinated approach to secondary fracture prevention, where following a minimal trauma fracture, patients are identified, assessed and treated for osteoporosis as part of an all-encompassing service [32–35, 38–47]. A dedicated individual who coordinates this process, referred to as a fracture liaison co-coordinator is central to this model of care. The coordinator often utilised electronic patient lists and engaged with the orthopaedic department to optimise capture of suitable patients. Eleven out of 13 type A models of care reported the utilisation of a fracture liaison co-coordinator. Notably, the Kaiser Permanente group (representing one model of care) published two articles [32, 33].

Assessment includes evaluation of clinical risk factors for osteoporosis, a BMD scan, radiographic or other imaging as required, and pathology tests to exclude secondary causes of osteoporosis. This assessment is then followed by the initiation of appropriate non-pharmacological and pharmacological interventions. Figure 1 represents an overview of a prototypical type A model of care, conducted at Concord General Repatriation Hospital.

#### Type B models of care ( $n=18$ studies)

Type B models of care (Table 2) differ from type A models of care in that treatment initiation is the responsibility of the PCP [28–31, 48–57]. Thus, type B interventions identify and assess people with a minimal trauma fracture, then make treatment recommendations to the PCP without initiating the treatment itself. A fracture liaison co-coordinator is also pivotal to the success of this model of care. A good example of this type of program is the Glasgow service [29–31]. Huntjens et al. [28] described five type B models of care in the Netherlands, whilst three publications from the UK were from the Glasgow program [29–31]. Thus, a total of 16 type B model of care services have been described so far, of which 12 reported the utilisation of a fracture liaison co-coordinator.

#### Type C model of care ( $n=10$ studies)

Compared with types A and B designs, type C models of care (Table 3) are characterised by a less-intensive intervention [58–67]. In general, people identified as having suffered a minimal trauma fracture are educated about osteoporosis and receive lifestyle advice including falls prevention. Participants are also informed about the need for further assessment and treatment of their underlying skeletal condition. The second component of this model of care involves alerting the PCP of the person’s recent minimal trauma fracture, and the need for further assessment and treatment to reduce the risk of further fractures. Communication with the individual or PCP is performed either ‘face-to-face’, via personalised letter, e-mail, fax, video or a telephone call. No further assessment is performed with respect to BMD testing or specific treatment for osteoporosis by the fracture service. As can be expected from the less intensive nature of the intervention, only six of ten type C model of care studies required a fracture liaison co-coordinator.

#### Type D models of care ( $n=2$ studies)

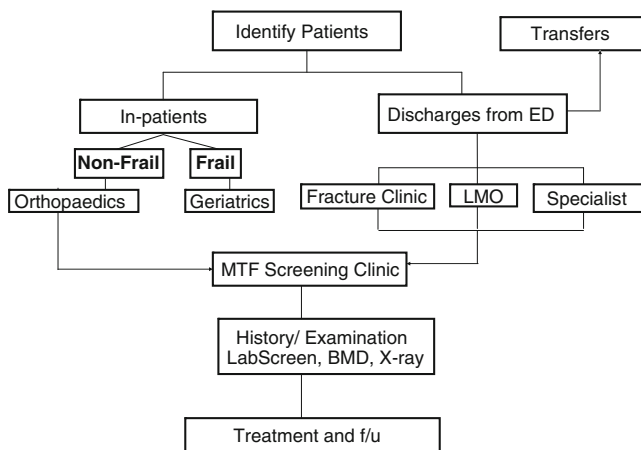
Type D interventions (Table 4) represent a model of care in which people presenting with a minimal trauma fracture receive specific osteoporosis education only [68, 69]. This can take the form of a patient-specific letter, educational

**Table 1** Characteristics of participants, BMD testing and treatment initiation in intervention type A studies

Country	Study name	Study type	Settings	Identification methods	Fracture site	Age	% female	Number	BMD (control)	BMD (intervention)	Treatment (control)	Treatment (intervention)
Australia	Vaile et al. [47]	Before and after	OP, IP and ED	FLC	All (nil breakdown)	>55	–	1,140	31 157	983 983	17 157	334 983
	Lih et al. [34]	Cohort	OP, IP and ED	FLC	All (35 % wrist)	66 (mean)	80	403	–	246 246	51 157	198 246
	Giles et al. [41]	Cross sectional	OP, IP and ED	FLC and EMR	All (30 % hip)	75 (mean)	75	2,049	–	–	–	–
	Kuo et al. [43]	Before and after	OP	FLC	All (1 only reported)	64 (mean)	71	278	40 155	95 115	32 155	35 123
	Jones et al. [42]	Before and after	IP	IP protocol	Hip (NOF)	81 (mean)	72	254	–	–	8 161	22 93
USA	Navarro et al. [33]	Cross sectional	OP, IP and ED	FLC	All	>60	–	–	–	–	–	–
	Dell et al. [32]	Before and after	OP, IP and ED	FLC	–	>50	–	620,000	21,557	74,770	33,208	78,058
	Streeten et al. [46]	Cohort <sup>a</sup>	IP	IP protocol	Hip (C, 100 %); hip (L, 53 %)	70 (mean)	46 %	84	0 31	27 53	1 31	28 53
	Edwards et al. [40]	Before and after	IP	FLC	All	73 (mean)	82	203	–	165 165	14 38	93 151
Canada	Majumdar et al. [45]	RCT	OP	FLC	Wrist	60 (median)	68	46	13 25	17 21	3 25	9 21
	Majumdar et al. [44]	RCT	OP and IP	FLC	Hip	75.9 (median)	65	220	32 110	88 110	24 110	56 110
	Bogoch et al. [35]	Cross sectional	OP and IP	FLC and ortho-surgeons	All	73 (mean)	79	349	–	–	–	–
Europe	Clunie et al. [39]	Cross sectional	OP and IP	FLC	All	50–69	–	1112	–	1,024 1,112	–	–
	Boudou et al. [38]	Cross sectional	OP, IP and ED	FLC and EMR	All (hip/wrist/humerus)	72.9 (mean)	100	155	–	–	–	140 155

<sup>a</sup> Retrospective cohort for the hip fracture component only; 25 non-hip fractures were added 'post-hoc' to the intervention group

RCT randomised controlled trial, OP outpatient, IP in-patient, ED emergency department, FLC fracture liaison coordinator, EMR electronic medical record, C control, I intervention, N number of participants, NOF neck of femur



**Fig. 1** Structure of a typical fracture liaison service. *MTF* minimal trauma fracture, *f/u* follow-up, *LMO* local medical officer, *BMD* bone mineral density

pamphlet, video or personal communication to the person via a telephone or ‘face-to-face’ interaction. There is no physician education in this model.

Study design, target population and settings

#### Study types

Ten studies were randomised controlled trials, including one cluster randomised controlled trial, and five were cohort studies. As expected in quality improvement methodology, the ‘before and after’ design was a common design ( $n=11$ ), and there was one cross-sectional analytical study (Tables 1, 2, 3 and 4). The 17 cross-sectional surveys with no concurrent or historical controls to allow effectiveness assessment for BMD testing and treatment initiation were not included in the meta-analyses. Furthermore, three ‘controlled’ studies which did not provide denominator data for either both or one of the outcomes [32, 52, 54] were not included in the relevant meta-analyses.

#### Target population/setting

The studies emanated from the USA ( $n=11$ ), Canada ( $n=10$ ), Australia ( $n=8$ ), Europe ( $n=10$ ), the UK ( $n=4$ ) and New Zealand ( $n=1$ ).

Facilities involved in the intervention were most commonly university teaching hospitals, community-based health services such as NHS Trusts in Scotland [30] and large health maintenance organisations [32]. Settings in which patients were identified included in-patient departments only—usually orthopaedic wards ( $n=6$ ), outpatient departments only—orthopaedic clinics ( $n=8$ ), emergency departments ( $n=1$ ), a combination of the latter ( $n=24$ ) or radiology practices ( $n=3$ ). Settings were not reported in two studies.

Six studies enrolled women only, whilst the remaining studies had both men and women. Of the studies with both men and women, only 25 reported on the percentage of females, which ranged from 4 to 86 %, with a mean of 70.8 %.

Most interventions included participants with a wide range of fracture sites such as hip, wrist, humerus, ankle, foot and hand ( $n=31$ ), while some studies enrolled only either hip fractures ( $n=5$ ) or wrist fractures ( $n=6$ ) or both hip and wrist fractures ( $n=1$ ). One study did not report the fracture sites.

Ethnicity was reported in only eight studies [33, 44–46, 54, 55, 62, 65, 70, 71]. The proportion of white Caucasian subjects varied between 64 and 95 % (data not shown in tables due to space limitations).

#### Assessment of intervention effectiveness

Effectiveness assessment was restricted to studies with control groups and denominator data ( $n=25$ ), using clinically relevant endpoints consistently reported in most studies, namely BMD testing and treatment initiation rates (as defined above). Meta-analyses of these outcome measures were performed, stratified by model of care (types A vs. B vs. C vs. D). A meta-analyses of adherence and re-fracture rates were not performed due to an inadequate number of studies reporting these outcomes. Cost-effectiveness findings are also summarised below.

##### 1. BMD testing (Figs. 2, 3 and 4; Table 5)

Meta-analyses of the RD in BMD testing rates between intervention and control groups were conducted separately for each model of care: types A ( $n=5$ ), B ( $n=7$ ) and C ( $n=9$ ). Meta-regression analysis of RD showed a trend towards better outcomes with more intensive interventions (coefficient=0.13; 95 % CI, 0.00 to 0.25;  $p=0.06$ ).

##### 2. Treatment initiation (Figs. 5, 6, and 7, Table 5)

Meta-analyses of the RD in treatment initiation rates were also conducted separately for each model of care: types A ( $n=8$ ), B ( $n=5$ ), C ( $n=7$ ) and D ( $n=1$ ). Meta-regression analysis of RD showed a significant trend towards better outcomes with more intensive interventions (coefficient=0.07; 95 % CI, 0.01 to 0.14;  $p=0.03$ ).

##### 3. Adherence (Table 6)

Self-reported adherence was described in five type A studies [38, 40, 43, 46, 47] and two type B studies [31, 51]. Due to an inadequate number of studies reporting this measure, and significant variation in the duration of follow-up, a meta-analysis could not be performed. Amongst type A studies, adherence varied between 34 and 95 % at 12 months. In one type B study, there was 86 % adherence

**Table 2** Characteristics of participants, BMD testing and treatment initiation in intervention type B studies

Country	Study name	Study type	Settings	Identification methods	Fracture site	Age	% female	Number	BMD (control)	BMD (intervention)	Treatment (control)	Treatment (intervention)
Australia	Blüe et al. [49]	RCT	OP	FLC	All	52.7 (mean)	50	154	5/75	30/79	5/75	4/79
New Zealand	Sidwell et al. [56]	Before and after	IP	Existing staff and IP protocol	All (mostly hip 133/193 control; 101/178 I)	81 (mean)	75	371	20/178	158/193	16/178	40/193
USA	Cuddihy et al. [52]	Before and after	OP and IP	FLC and EMR	Wrist	68 (mean)	86	402	17/343	42/59	— <sup>a</sup>	— <sup>a</sup>
	Johnson et al. [54]	Before and after	OP	FLC and EMR	All	59 (mean)	4	262	16/126	85/103	— <sup>a</sup>	— <sup>a</sup>
	Harrington et al. [53] (cycle 2)	Cohort	—	FLC and ortho-billing data	All	—	—	92	0/55	27/37	3/55	22/37
Canada	Morrish et al. [55]	RCT	OP and IP	FLC	Hip	75.9 (median)	65	220	32/110	75/110	24/110	42/110
Europe (UK)	Langridge et al. [29]	Cross sectional	OP, IP and ED	FLC	All (hip, 28 %)	77.8 (median)	—	2,489	—	—	—	48/129
	Charalambous et al. [50]	Before and after	OP and IP	Existing staff and protocol	Hip and wrist	>50	100	166	—	—	—	—
	McLellan et al. [30]	Cross sectional	OP, IP and ED	FLC	All (hip, 23 %)	>50	77	3,653	—	2,077/3,083	—	1,061/3,653
	McLellan et al. [31]	Cross sectional	OP, IP and ED	FLC	All	72 (mean)	78	8,875	—	5,486/8,875	—	3,902/8,875
Europe	Wallace et al. [57]	Cross sectional analytical 1	IP	—	Hip	Median 84	100	88	0/46	1/42	28/46	38/42
	Chevalley et al. [51]	Cross sectional	OP and IP	—	All (hip 45 %)	73 (mean)	81	385	—	243/385	—	128/385
	Astrand et al. [48]	Cross sectional	OP and IP	FLC and EMR	All	>50	79	256	—	239/256	—	—
	Hunijens et al. [28]	Cross sectional	OP and ED	FLC and EMR	All	>50	—	2,224	—	1,955/2,224	—	—
	Hunijens et al. [28]	Cross sectional	OP and ED	FLC and EMR	All	>50	—	847	—	703/847	—	—
	Hunijens et al. [28]	Cross sectional	Radiology	FLC	All	>50	—	1,409	—	1,133/1,409	—	—
	Hunijens et al. [28]	Cross sectional	Radiology	FLC	All	>50	—	1,699	—	1,298/1,699	—	—
	Hunijens et al. [28]	Cross sectional	IP and ED	FLC	All	>50	—	1,020	—	875/1,020	—	—

RCT randomised controlled trial, OP outpatient, IP in-patient, ED emergency department, FLC fracture liaison coordinator, EMR electronic medical record, C control, I intervention, N number of participants

<sup>a</sup> Unable to ascertain denominator data

**Table 3** Characteristics of participants, BMD testing and treatment initiation in intervention type C studies

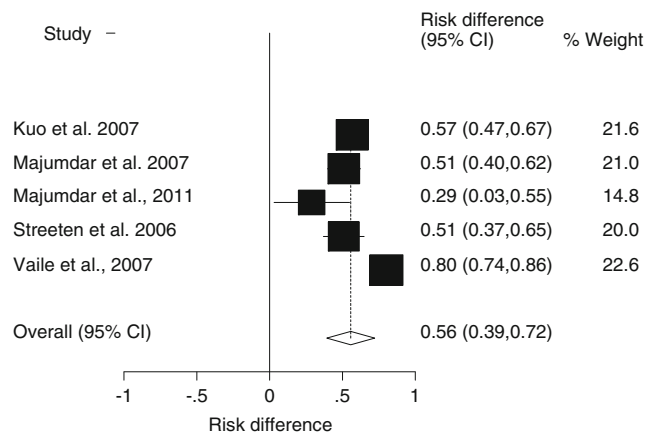
Country	Study name	Study type	Settings	Identification methods	Fracture site	Age	% female	Number	BMD (control)	BMD (intervention)	Treatment (control)	Treatment (intervention)
Australia	Indejeeth et al. [63]	Before and after	ED	Existing staff (ED clinicians, GP)	All (nil breakdown)	>65	–	245	6 200	18 45	12 200	14 45
USA	Gardner et al. [61]	RCT	IP	FLC	Hip	82 (mean)	78	72	6 36	12 36	6 36	10 36
	Feldstein et al. [60]	RCT	OP and IP	FLC and EMR	All (C—hip, 8.9 % and wrist, 14.9 % and I—hip, 14.7 % and wrist, 15.6 %)	72 (mean); >50	100	210	2 101	36 109	5 101	22 109
Canada	Skedros [66]	Cross sectional	?	Orthopaedic surgeon	All	69.5 (mean)	86	69	–	–	–	2 169
	Solomon et al. [67]	RCT	OP	FLC and EMR	All (nil breakdown)	–	–	229	4 95	11 134	1 95	6 134
	Majumdar et al. [65]	Cohort	OP and ED	FLC and EMR	Wrist	66 (median)	78	102	8 47	34 55	5 47	22 55
	Ashe et al. [58]	Cohort	OP	FLC	Wrist	71.5 (mean)	80	34	5 22	11 12	–	–
	Hawker et al. [62]	Before and after	OP	Orthopaedic surgeon	All (I—wrist, 64/139 and hip, 19/139 and C—wrist, 64/139 and hip, 25/139)	66 (mean)	74	278	23 139	49 139	–	–
	Majumdar et al. [64]	RCT	OP and ED	FLC	Wrist	60 (median)	77	272	24 135	71 137	10 135	30 137
Cranney et al. [59]	Cluster RCT	OP and ED	Existing staff	Wrist	69 (mean)	100	270	36 145	64 125	15 145	35 125	

RCT randomised controlled trial, OP outpatient, IP in-patient, ED emergency department, FLC fracture liaison coordinator, EMR electronic medical record, C control, I intervention, N number of participants

**Table 4** Characteristics of participants, BMD testing and treatment initiation in intervention type D studies

Country	Study name	Study type	Settings	Identification methods	Fracture site	Age	% female	Number	BMD (control)	BMD (intervention)	Treatment (control)	Treatment (intervention)
Australia	Diamond and Lindenberg [69]	Cross sectional	Radiology	Radiology records	All	76 (mean)	64	161	–	82 161	–	46 161
Canada	Bessette et al. [68]	RCT	OP	EMR (database)	All	62 (mean)	100	1,174	–	–	31 386	90 788

RCT randomised controlled trial, OP outpatient, IP in-patient, ED emergency department, FLC fracture liaison coordinator, EMR electronic medical record, C control, I intervention, N number of participants



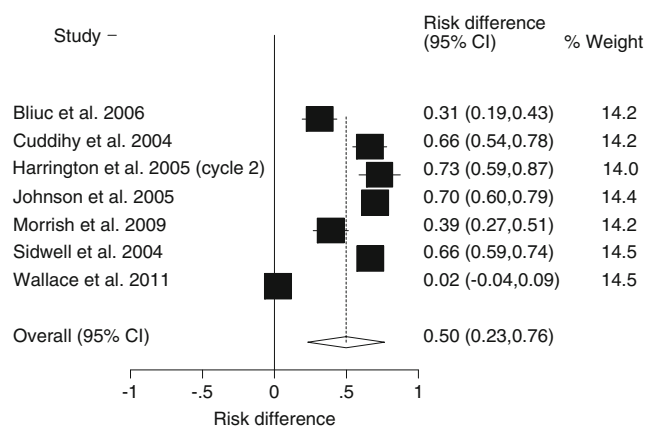
(A positive risk difference result favours intervention group)

**Fig. 2** Meta-analysis of BMD testing rates, using risk difference in intervention type A studies

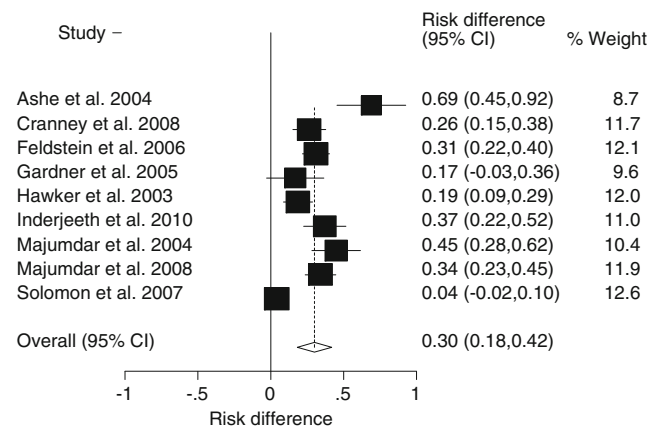
at 12 months [31]. None of the studies utilised pharmacy claims data to describe adherence.

#### 4. Re-fracture rates (Table 7)

Re-fracture rates were reported in only six studies—four were type A models of care [32, 34, 38, 44], whilst two were type B models of care [29, 31]. Amongst the type A studies, Lih et al. [34] reported a significant improvement in re-fracture rates after 4 years, from 19.7 % in the control group to 4.1 % in the intervention group. Dell et al. [32] reported an overall relative risk reduction of 37.2 % for hip fractures over 3 years, using historical data for comparison. Dell et al. utilised both primary and secondary prevention strategies, with no data available for secondary prevention strategies alone. Boudou et al. [38] had no control group to allow comments on effectiveness at reducing re-fractures, whilst the study by Majumdar et al. [44] was underpowered to demonstrate any significant changes. Amongst the type B models of care, Langridge et al. [29] and McLellan et al. [31] did not



(A positive risk difference result favours intervention group)

**Fig. 3** Meta-analysis of BMD testing rates, using risk difference in intervention type B studies

(A positive risk difference result favours intervention group)

**Fig. 4** Meta-analysis of BMD testing rates, using risk difference in intervention type C studies

have a control group to allow assessment of fracture reduction. However, 10 years since the development of the Glasgow FLS in 1999, hip fracture rates in Glasgow have reduced by 7.3 % vs. a 17 % increase in England, where only 37 % of localities operated a fracture liaison service by late 2010 [72, 73].

#### 5. Cost-effectiveness

Only five studies provided cost-effectiveness data (four from type A and one from type B models of care). Amongst the type A studies, an informal evaluation of cost-effectiveness utilising predicted (rather than observed) re-fracture rates was described by Vaile et al. [47], estimating that if one hip fracture was prevented, savings of AUD 23,000 would pay for the salary of a fracture liaison coordinator for six months, or for the osteoporosis evaluation of 54 patients with minimal trauma fractures. Similarly, Sander et al. [37] performed a cost-effectiveness analysis using predicted re-fracture rates from data described by Bogoch et al. [35]. The FLS was predicted to reduce the annual hip fracture rate from 34 with usual care, to 31, resulting in a cost saving of CAD 49,950. This cost-saving held true assuming at least 350 patients were seen by the FLS over a year. The predicted re-fracture rates were based upon the study patient characteristics such as site of fracture, age, gender, BMD and treatment rates.

A more formal and comprehensive cost-effectiveness analysis [36], utilised re-fracture rates observed amongst intervention and control groups in the study by Lih et al. [34]. The service was highly cost-effective with a cost of around AUD 20,000–30,000 per Quality Adjusted Life Year (QALY) gained, depending on the assumptions made. Dell et al. [32] estimated that the Healthy Bones Program saved more than US \$30.8 million for Kaiser Permanente Southern California in 2006, based upon the hip fracture rates observed with the intervention, compared with hip fracture rates predicted from historical data. The cost-effectiveness



**Table 5** Meta-analysis summary: uptake rates and risk difference for BMD testing and treatment initiation by intervention type

Intervention type	BMD testing				Treatment initiation			
	No. of studies	Percent tested in intervention group (%)	Percent tested in control group (%)	Risk difference (95 % CI) <i>p</i>	No. of studies	Percent treated in intervention group (%)	Percent treated in control group (%)	Risk difference (95 % CI) <i>p</i>
Model of care 'A'	5	79.4	23.8	0.56 (0.39–0.72) <0.001	8	46.4	17.9	0.29 (0.19–0.40) <0.001
Model of care 'B'	7	59.5	9.2	0.50 (0.23–0.76) <0.001	5	40.6	19.9	0.21 (0.05–0.37) 0.01
Model of care 'C'	9	43.4	13.5	0.30 (0.18–0.42) <0.001	7	23.4	7.5	0.16 (0.07–0.25) 0.001
Model of care 'D'					1	8.0	11.4	0.03 (0.00–0.07) 0.06

Uptake rates are weighted as per weights given with each meta-analysis (refer to Figs. 2, 3, 4, 5, 6 and 7)

analysis of the Glasgow service [31], representing a type B model of care, was based upon a predicted 8 % re-fracture rate at 4 years. This analysis showed that the cost per QALY gained was GBP 5,740. Even using the least favourable efficacy data, 15 fractures were avoided at the expense of GBP 84,076/1,000 individuals with fractures.

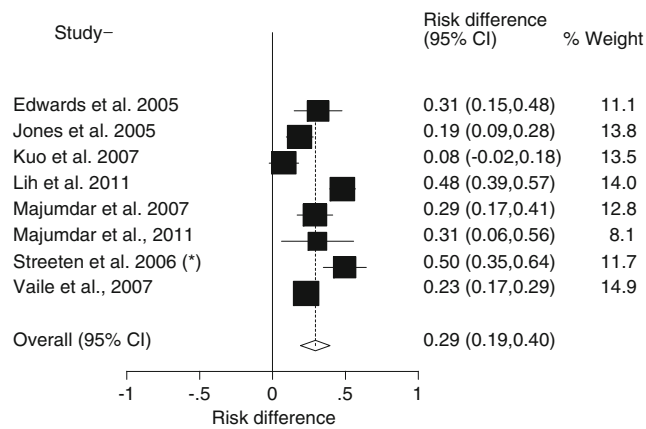
Other factors influencing intervention effectiveness

Factors influencing intervention effectiveness apart from intervention intensity included:

1. Length of time between the fracture and the intervention—Treatment rates at 6 months with the same type C intervention was 22 % if the intervention occurred immediately after the fracture [64], compared with 11 % if the same intervention occurred 1 year after the fracture [45].
2. Gender—The under recognition of osteoporosis in men is illustrated by Cuddihy et al. [52] 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 et al. [35] observed that baseline osteoporosis treatment rates were lower in men (15.5 %) than in women (39 %). Kuo et al. [43] also found that pre-intervention treatment rates were lower in men (9 %) compared with women (34 %). Bliuc et al. [49] found that men were less likely than women to respond to an information-based intervention by going to their PCP for osteoporosis assessment. Even amongst those who did see their PCP, men were less likely to have specific therapy recommended, indicating an additional physician-related barrier to treatment. Diamond and Lindenberg [69] also reported lower treatment uptake rates amongst men who sustained a minimal trauma fracture even in the presence of low BMD. Furthermore, after institution of the Healthy Bones Program, the Kaiser Permanente group reported a higher treatment rate amongst women (92.1 %) compared with men (75.2 %) [33]. 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. Furthermore, with the institution of the Healthy Bones Program, there was a smaller increase in BMD testing and treatment rates in men compared with women [32].

## Discussion

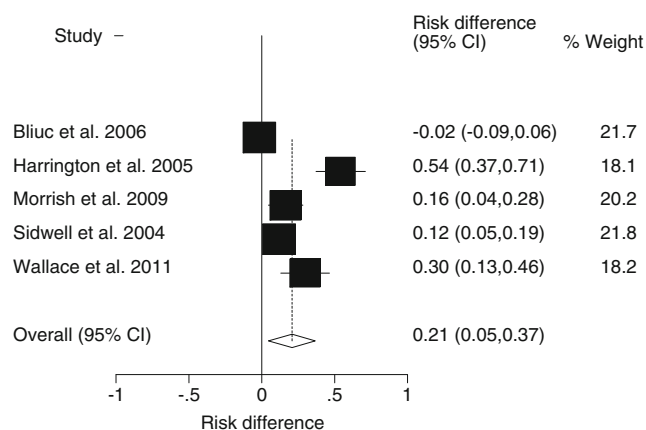
In this systematic review and meta-analysis, an attempt has been made to collate, compare and discuss the methodology and outcomes of different types of secondary fracture prevention programs around the world. We found that comparisons between models, even within the same or similar type of intervention were difficult due to a lack of standardised



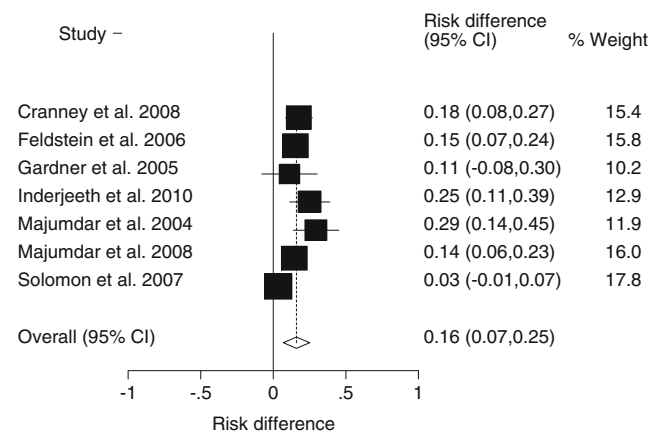
(A positive risk difference result favours intervention group)

**Fig. 5** Meta-analysis of treatment initiation rates, using risk difference in intervention type A studies

outcome measures. Nevertheless, the meta-analyses of sufficiently controlled studies demonstrated a trend towards greater effectiveness of a fracture liaison service with increasing intensity of the intervention. This trend was significant for treatment initiation, which we consider the more important immediate outcome of any intervention aimed at reducing re-fractures. Specifically, these findings suggest that a type A model of care is likely to be more effective than type B interventions, which in turn produces better clinical outcomes than type C or D programs. Certainly, participant or patient education alone appears to have little or no impact on rates of treatment initiation. These findings are consistent with a systematic review conducted by Sale et al. [74], strengthening the argument for the effectiveness of more intensive, coordinated interventions. Finally, there is good evidence that more intensive interventions such as types A and B models are cost-effective in terms of health economic analysis.



(A positive risk difference result favours intervention group)

**Fig. 6** Meta-analysis of treatment initiation rates, using risk difference in intervention type B studies

(A positive risk difference result favours intervention group)

**Fig. 7** Meta-analysis of treatment initiation rates, using risk difference in intervention type C studies

This literature review has a number of strengths and weaknesses. The strengths centre around the extensive nature of the search conducted, thereby providing a complete and up-to-date overview of systematic models of care for the secondary prevention of osteoporotic fractures. Furthermore, we were able to categorise intervention types by extent and intensity and found that these categories correlate with major clinical outcomes (re-fracture rates) as well as process measures (BMD testing rates; treatment initiation rates) and cost-effectiveness.

The major limitation for the analysis is the significant heterogeneity between studies in regards to clinical outcomes, patient numbers, study design (concurrent controls, controls as part of RCTs and historical controls), risk of bias, gender proportions and fracture sites. In an exploratory analysis, the low quality of studies explained some of the heterogeneity. However, a substantial proportion of the heterogeneity remained after excluding studies with high risk of bias or limiting studies to RCT. Also, adherence to therapy could not be analysed due to varying duration of follow-up and a lack of standardisation in reporting.

There are a number of important lessons learnt from the present study: firstly, the specific health care system in which a care pathway is embedded is of pivotal importance. For example, a type B model of care was effective in the UK due to the strong structural integration between PCP and public hospitals. Likely to add to the effectiveness of this system, is the introduction (as of 1st April 2012) of financial incentives for PCPs in the UK to commence and continue anti-osteoporosis treatment [75]. Notably, although patient and PCP educational interventions alone (type C interventions) were less effective than type A or B interventions, they still had some limited benefits, and therefore may be an option in resource-poor areas.

Secondly, the factors that impact on the effectiveness of an intervention, apart from intensity of the intervention, are the

**Table 6** Studies reporting adherence

Study name	Study type	Model of care	Adherence (intervention)			
			Numerator	Denominator	% adherence	Follow-up (months)
Vaile et al. [47]	Before and after	A	197	207	95	12
Kuo et al. [43]	Before and after	A	35	44	79	10
Edwards et al. [40]	Before and after	A	32	93	34	12
Streeten et al. [46]	Cross sectional	A	22	28	79	18
Boudou et al. [38]	Cross sectional	A	112	140	80	12
McLellan et al. [31]	Cross sectional	B	3,221	3,746	86	12
Chevalley et al. [51]	Cross sectional	B	30	45	67	6

length of time between the fracture and the intervention [45, 64]. It seems that the immediate period after the fracture provides a ‘window of opportunity’ to instigate behavioural change.

Thirdly, several studies confirmed the gender disparity in the recognition, investigation and treatment of osteoporosis [32, 33, 35, 43, 49, 52, 69]. A combination of patient and physician-related factors are likely explanations: men may be less proactive about their health than women and less aware of the risk of osteoporosis. Physicians may be more complacent about osteoporosis in men due to the misperception that osteoporosis only affects women. 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 would help clinicians target this group more effectively.

Fourthly, there was under-reporting of ethnicity with only eight studies reporting on this characteristic. Reporting ethnicity is important to assess for racial disparities in osteoporosis management, which have been previously documented in the USA [76] but not in the Kaiser Permanente system of care [33].

A major deficit in the published literature on models of post-fracture care is the inconsistent reporting of results. This covers a spectrum of measures such as the identification rate of potentially eligible participants, the length of time between fracture and evaluation by a dedicated service or program, the rate of assessment for clinical risk factors and secondary causes for osteoporosis, the rate of BMD testing, the rate of treatment, adherence to 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 are required.

The assessment, treatment and follow-up of patients, especially in type A models of care occurred on an outpatient basis, which requires patients to be ambulatory. As a result, participants were relatively ‘young’ and had often sustained non-hip fractures. Thus, the care of people with minimal trauma fractures can be conceptualised as having two arms—one arm for the frail elderly, who constitute most patients with hip and pelvic fractures, and the other arm for the younger, more ambulatory people who tend to have non-hip fragility fractures. Although it is important to treat the frail elderly person for osteoporosis after a minimal trauma fracture, these people are usually under the care of geriatricians. On the other hand, type A fracture liaison services are ideally suited to somewhat younger people 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 6 months. This short time-line is based on data of rapid efficacy of treatment (within 6 months) and the early clustering of subsequent fractures after an initial fracture event [77]. Thus, the short term expenditure of a health care system on type A models of care, complemented by ortho-geriatric services, will have substantial health and economic benefits for the population as a whole, in any country or region of the world.

**Table 7** Studies reporting re-fracture rates

Study name	Refractures (control)	Refractures (intervention)
Lih et al. [34]	31 157 at 35.2 months	10 246 at 37.7 months
Dell et al. [32]	2,510 (expected hip fractures)	1,575
Majumdar et al. [44] and Morrish et al. [55]	No numbers	No numbers
Boudou et al. [38]	–	14 155
Langridge et al. [29]	–	129 2,489 (3 years)
McLellan et al. [31]	–	468 3,902 (12 % at 4 years)

Treatment rates are still suboptimal, even in people attending type A services. In order to improve capture rates, fracture liaison services will need to utilise integrated electronic health system databases. There is no doubt that there is a paucity of data on treatment adherence, re-fracture rates 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 post-fracture models of care in the majority of the world's population in developing nations, in which availability of treatment let alone diagnostic tools is likely to be cost limiting.

Adherence to osteoporosis treatment is an important surrogate outcome to measure the effectiveness of models of care for re-fracture prevention. Numerous studies utilising pharmaceutical claims data have demonstrated that compliance measured by a Medication Possession Ratio (the proportion of days a patient is in possession of a medication over an observation period) of greater than or equal to 0.8 is associated with fracture risk reduction [78–81]. None of the models of care in our literature review described adherence utilising pharmaceutical claims data. The most comprehensive evaluation of adherence was conducted by Boudou et al. [38] who described a self-reported adherence of 80 % at 12 months follow-up. Future research should focus on describing adherence to osteoporosis medication using pharmaceutical claims data amongst secondary fracture prevention services.

In summary, whilst fracture liaison services have contributed significantly towards closing the care gap in osteoporosis management in patients after a minimal trauma fracture, there remains room for improvement. Further well-designed prospective studies are required to strengthen the evidence for the precise cost-effectiveness and fracture reduction with systematic approaches to the secondary prevention of osteoporotic fractures. Patient education alone had little or no impact on treatment initiation. Currently, the ideal approach to secondary fracture prevention is a type A model of care in an integrated electronic health care network, overseen by a coordinator and utilising a dedicated database measuring performance.

**Conflicts of interest** None.

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