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ORIGINAL ARTICLE

Targeted intervention reduces refracture rates in patients with incident non-vertebral osteoporotic fractures: a 4-year prospective controlled study

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Abstract
Summary In the present prospective controlled observational study, we investigated the effect of a coordinated intervention program on 4-year refracture rates in patients with recent osteoporotic fractures. Compared to standard care, targeted identification, and management significantly reduced the risk of refracture by more than 80%.
Introduction The risk of refracture following an incident osteoporotic fracture is high. Despite the availability of treatments that reduce refracture and mortality rates, most patients with minimal trauma fracture (MTF) are not managed appropriately. The present prospective controlled observational study investigated the effect of a coordinated intervention program on 4-year refracture rates and time to refracture in patients with recent osteoporotic fractures.
Methods Patients presenting with a non-vertebral MTF were actively identified and offered referral to a dedicated intervention program. Patients attending the clinic underwent a standardized set of investigations, were treated as indicated and reviewed at 12-monthly intervals ('MTF group'). Patients who elected to follow-up with their primary care physician were assigned to the concurrent control group.
Results Groups were balanced for baseline anthropometric, socio-economic, and clinical risk factors. Over 4 years, 10 out of 246 patients (4.1%) in the MTF group and 31 of 157 patients (19.7%) in the control group suffered a new fracture, with a median time to refracture of 26 and 16 months, respectively ($p<0.01$). Compared to the intervention group, the risk of refracture was increased by 5.3-fold in the control group (95% CI: 2.8–12.2, $p<0.01$), and remained elevated (HR 5.63, 95%CI 2.73–11.6, $p<0.01$) after adjustment for other significant predictors of refracture such as age and body weight.
Conclusions In patients presenting with a minimal trauma non-vertebral fracture, active identification and management significantly reduces the risk of refracture (Australian New Zealand Clinical Trials Registry ACTRN 12606000108516).

Keywords Fracture · Fracture liaison service · Intervention · Osteoporosis · Quality improvement · Refracture

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Introduction

Osteoporosis currently affects an estimated 80 million people in the USA, Europe, Australia, and Japan alone [1]. Over the past decades, the prevalence of osteoporosis has steadily been rising. In Australia, 67,000 osteoporotic fractures were recorded in 2001. By 2007, this figure had increased to 87,100 fractures [2]. The US National Osteoporosis Foundation estimates that the prevalence of osteoporosis will rise from currently 52 million to over 61 million in 2020 [3], with a tripling in hip fracture incidence by 2040 [4].

One third of women and 20% of men will sustain a low trauma fracture in their lifetime [5]. In the USA, the annual cost related to osteoporotic fractures currently amounts to US $17 billion, with non-vertebral fractures accounting for 94% of the total burden [6]. In Australia, the annual cost

relating to osteoporosis was estimated at AU$ 7.4 billion in 2001 [2], and rapid increases in cost are predicted worldwide [6].

Apart from the financial burden to health systems, osteoporotic fractures are a major cause of adverse outcomes in individual patients, such as pain, disability, social isolation, depression, and premature death [7–10]. Incident osteoporotic fractures significantly increase the risk of further fragility fractures [11–15]. However, despite the availability of medications that reduce the risk of refracture by 25–70% [16], the majority of patients with incident osteoporotic fractures are neither investigated nor treated for their underlying condition [17–19]. The reasons for such management failures are complex and include inadequate awareness of the health hazards related to osteoporosis amongdoctors and patients, the lack of effective 'minimal trauma fracture services', and restricted access to services and treatment [20].

The current prospective controlled study investigated whether compared to standard primary care, active referral to, and long-term management by a dedicated post-fracture intervention program reduces 4-year refracture rates.

Study design and methods

The minimal trauma fracture (MTF) program was implemented in 2005 as a prospective controlled intervention study based at Concord Repatriation General Hospital (CRGH), a large tertiary referral center in Sydney, Australia. The study was approved by the Sydney South West Area Health Service Human Research Ethics Committee, and all patients gave informed consent prior to study inclusion. The study has been registered with the Australian New Zealand Clinical Trials Registry (ACTRN 12606000108516).

Patients 45 years or older presenting to CRGH with a symptomatic non-vertebral fracture were prescreened to determine the nature and mechanism of the incident. Patients were eligible for referral to the MTF program if the fracture had resulted from minimal trauma, defined as a fall from standing height or a milder insult. All minimal trauma fractures except those of the face and skull were included. Fractures of the hip, pelvis, wrist, humerus, tibia, and fibula were classified as major factures, while all other fracture sites were considered minor. Patients were ineligible for referral to the MTF program if they were frail [21], lived in a hostel or nursing home, or presented an unacceptable medical or psychiatric risk. (Frail patients with a MTF are managed by an orthogeriatric service available at the same center.)

As undertreatment of osteoporosis is common in the community and associated with high refracture rates [17–19], the study was not randomized for ethical considerations. Thus, patients attending the MTF program formed the intervention group, while those who elected to follow-up with their primary care physician served as a concurrent control group.

Intervention group

Patients attending the MTF program underwent a standardized series of assessments and investigations. A detailed patient questionnaire was used to collect data on age, gender, body height and weight, fracture site, history of previous falls or fractures, calcium intake, physical activity, alcohol use, smoking, history of maternal osteoporosis or hip fracture, and secondary causes of osteoporosis (renal or hepatic disease, endogenous/ exogenous hypercortisolism, hyperthyroidism, hyperparathyroidism, lactose intolerance, rheumatoid arthritis, multiple myeloma). Falls risk was stratified by (1) the number of falls in the 12 months prior to the index fracture and (2) assessing falls risk factors. Dietary calcium intake was calculated on consumption frequency per week, while physical activity was estimated by frequency per week, duration (in minutes) and type of exercise. Alcohol intake was measured by estimating the average daily consumption of standard drinks. All responses documented in the questionnaires were verified by the investigators during the clinical visits.

Bone mineral density (BMD) at the hip and lumbar spine was measured by dual X-ray absorptiometry using a GE/ Lunar Prodigy (Lunar Corp. Madison, WI, USA; Software version 5.00.211). Scans were obtained by an experienced technician and results were reviewed by two investigators. Based on WHO diagnostic criteria, osteoporosis was defined either as a T-score ≤ -2.5, or as low bone mineral density (T-score ≤ -1.0 but ≥ -2.5) in the presence of a fragility fracture.

Thoracolumbar spine radiographs (lateral and AP views) were obtained in all patients. A vertebral fracture was defined as ≥20% loss in anterior or medial height. Radiographs were reported by an experienced radiologist and verified by the investigators. In case of discrepant interpretations, a consensus was reached through systematic re-review.

Blood and urine tests obtained at baseline in all patients attending the MTF program included electrolytes, renal and hepatic function, calcium, phosphate, TSH, parathyroid hormone, 25-hydroxyvitamin D, testosterone (men only), LH, FSH, serum electrophoresis, coeliac screen (IgA, TTG), and markers of bone turnover.

Patients diagnosed with osteoporosis were informed about their condition, the risks and benefits of treatment, and the need of long-term adherence and persistence with their medication. Patients were commenced on treatment as indicated, which in most cases included an anti-resorptive agent (i.e., bisphosphonates, raloxifene, strontium ranelate)

in combination with vitamin D (1,000–2,000 IU per day) and calcium (600–1,200 mg/day). All patients had access to government-subsidized medications approved in Australia for the secondary prevention of osteoporotic fractures. Patients were reviewed after 3 and 6 months following their initial visit, and annually thereafter. Annual follow-up visits included an assessment of medication compliance and adverse effects, a physical examination and follow-up questionnaire together with serial BMD scans and selected laboratory tests (e.g., 25-hydroxy vitamin D, PTH, and bone turnover markers).

Control group

Demographic, anthropometric, and relevant clinical data was collected from all patients at baseline. At the time of identification, all patients were informed of the risks associated with a minimal trauma fracture. The patient's primary care physician was informed of the fracture via the regular discharge summary. Follow-up information was obtained via a questionnaire and telephone interview at study end; however, to minimize patient recall bias data was restricted to the variables listed in Table 1. All data was verified through the computerized hospital network database. As the majority of patients in the control group had no further investigations following their fracture, no data on bone mineral density, biochemistry, or imaging is available in this group.

Statistical analysis

The study was designed as a prospective observational trial with a concurrent control group. The present analysis includes patients presenting with a minimal trauma fracture between May 2005 and December 2007, with follow-up ending in October 2009.

Demographic characteristics and the baseline data of selected fracture risk factors were compared among the two groups (MTF and control) using $\chi 2$ test for categorical variables and Student's *t* test or Mann–Whitney *U* test for continuous variables. The primary outcome was to determine the effectiveness of the MTF program. This was defined as the confirmation of one or more further minimal trauma fractures. The secondary outcome was time to further fracture as calculated from the index fracture event to study completion. Clinical risk factors and comorbidities were analyzed using a Cox proportional hazards regression analysis. Hazard ratios and 95% confidence intervals were calculated using one-sided probability for the primary outcome. Forward and backward stepwise analyses were used to determine the most parsimonious model. Single variable validation analysis was performed to verify statistical calculations (SPSS statistical Version 17).

Table 1 Baseline characteristics of participants by group

N	MTF 246	Control 157	*P* value
Age, years (mean ± SD)	66.4±11	65.9±12.8	0.70[f]
Females Males	204 (83) 42 (17)	117 (75) 40 (25)	<0.05[e]
Gender F/M	5:1	3:1	
BMI, kg/m^2 (mean ± SD)	27.8±5.2	26.1±5.4	<0.05[e]
Height, cm (mean ± SD)	160.3±8.9	163.1±8.4	<0.01[f]
Weight, kg (mean ± SD)	71.7±15.5	69.3±14.5	0.12[f]
IRSAD (mean ± SD)	1036±59	1039±50	0.60[f]
Prevalent non-vertebral fracture[a]	13 (5.3)	13 (8.3)	0.23[e]
History of maternal hip fracture	8 (3.3)	3(1.9)	0.42[e]
Therapy with glucocorticoids (current or past)	10 (4.1)	9 (5.7)	0.44[e]
Currently smoking	26 (10.6)	11 (7)	0.23[e]
Current ethanol use[b]	22 (8.9)	9 (5.7)	0.24[e]
Falls in past 12 months before index fracture	74 (30)	34 (21.7)	0.09[e]
Site of index non-vertebral fracture			
Major[c]	171 (69.5)	100 (63.7)	0.26[e]
Proximal femur	30 (12)	1 (1.3)	
Wrist	86 (35)	67 (42.7)	0.12[e]
Minor[d]	75 (30.5)	56 (35.7)	0.28[e]

Values are denoted as *n* (%), unless otherwise indicated

IRSAD Index of Relative Socioeconomic Advantage and Disadvantage

[a] Any minimal trauma non-vertebral fracture that occurred after the age of 45 years;

[b] >3 Standard drinks per day

[c] Hip, pelvis, wrist, humerus, tibia and fibula

[d] Other fractures sites except face/skull

[e] Chi-square test

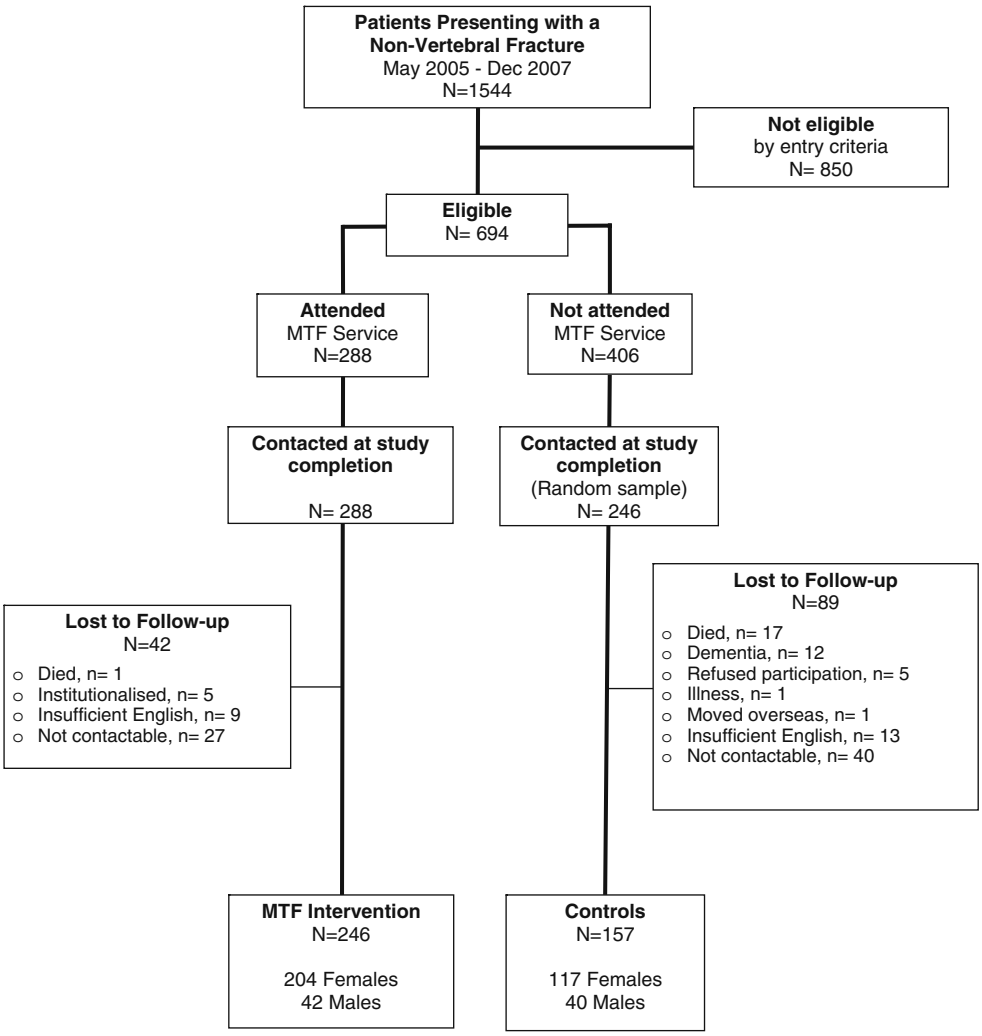
[f] Student's *t* test

Socioeconomic data for the intervention and control groups were obtained from the Australian Bureau of Statistics (ABS) 2006 census. The residential address of each subject during the study period was matched with the ABS Index for Relative Socioeconomic Advantage/Disadvantage. This score is based on profiling by area and ranks occupation and income profiles. A low score correlates with a more disadvantaged area.

Results

A total of 1,544 patients presented to the orthopedic fracture clinic between May 2005 and December 2007. Of these, 850 patients (55%) were not eligible for referral to the MTF program by entry criteria. Of the remaining 694 patients, 288 individuals attended the service of which 42 patients were lost to follow-up (Fig. 1). A total of 406 eligible patients elected not to attend the MTF program,

Fig. 1 Disposition of participants



mostly for personal or family reasons. Of these, 246 patients were randomly selected for final data collection at study end, by which time 89 individuals had been lost to follow-up (Fig. 1). The final analysis therefore included 403 patients. Neither the randomly selected controls nor the patients lost to follow-up differed in characteristics from the main study population (data not shown).

Patient characteristics at baseline are summarized in Table 1 and were similar in both groups except for a lower mean body height, a higher BMI, and a higher proportion of females in the MTF group. Groups did not differ in socioeconomic status, clinical risk factors for low bone density or fractures, or the frequency of prevalent non-vertebral osteoporotic fractures that had occurred after the age of 45 years. There was no difference in the frequency of index fractures classified as major vs. minor fractures. However, the distribution of specific index fractures differed between groups. In the MTF group, radius, humerus (n=38, 15.8%) and proximal femur fractures were most common, while in the control group most initial fractures occurred at the radius, metatarsals (n=29, 18.6%), and the humerus (n=25, 16%; Table 1).

The incidence of refracture differed significantly between groups. There were 10 (4.1%) new fractures in 10 patients managed by the MTF program, and 31 (19.7%) new fractures in 31 patients in the control group (P<0.01, Table 2). Given a median follow-up time of 38 months in the MTF group and 36 months in the control group, there were 1.3 refractures per 100 person-years in the intervention group, and 7.2 refractures per 100 person-years in the control group. Thus, the risk of suffering a further fracture within the study period was 5.3-fold higher (95% CI 2.61–10.87, p<0.001) in the control group receiving standard care compared to the MTF group. The median time to first re-fracture was 26 months (interquartile range: 18.5–33.5) in the MTF group, and 16 months (interquartile range: 8–23) in the control group (P<0.01).

The cumulative incidence of first refracture in the MTF and control group was 0.5% vs. 7.5% at 12 months, and 1.5% vs. 17% at 24 months, respectively (Fig. 2). As expected from multivariable analysis (see below), the effect of the intervention on the cumulative incidence of refracture remained significant when refracture rates were calculated separately for patients below and above 70 years of age

Table 2 Incidence of and time to first new fracture within 4 years by group

	MTF	Control	
Further fracture *N* (%)	10/246 (4.1)	31/157 (19.7)	OR=5.3 (95%CI: 2.6–10.9) p <0.01[a]
Mean time of review (months ± SD)	37.7±9.2	35.2±14	0.028[b]
Mean time to refracture (months ± SD)	25.8±8.3	16.3±6.6	<0.01[c]
Site of refracture by group			
Hip	1 (0.4)	8 (5.1)[d]	
Wrist	0	10 (6.4)	
Humerus	3 (1.2)	4 (2.5)[d]	
Ankle	2 (0.8)	5 (3.2)	
Ribs	2 (0.8)	3 (1.9)	
Vertebrae	1 (0.4)	NR	
Pelvis	1 (0.4)	0	
Hand	0	1 (0.6)	

Data are presented as *n* and (% of total group)

NR not recorded

[a] Chi-square test

[b] Student *t* test

[c] Mann–Whitney test

[d] A further five hip fractures and one humerus fracture had occurred in six patients who had died during follow-up. These fractures were not included in the analysis

(Fig. 3). The effect of the intervention on refracture was also independent of gender and the type of fracture at baseline (major vs. minor; data not shown).

With the exception of pelvic fractures, major and minor fractures at all sites occurred more frequently in the control than in the MTF group. This was particularly evident in the more frequent fracture sites such as the hip and wrist (Table 2).

Of the 157 patients in the control group, 86 (54.8%) received no treatment following their minimal trauma fracture. Of these, nine (10.5%) suffered a further osteoporotic fracture within the study period. In contrast, 80.5% of patients attending the MTF program were commenced on a specific anti-resorptive agent (usually an oral bisphosphonate) plus calcium and vitamin D supplementation ("triple therapy"; see Methods and Table 3). More than 95% of patients in the MTF group remained on their initial treatment through the study period. Of the 198 MTF patients on triple therapy, 10 (5.1%) sustained a further fracture during follow-up. In the control group, 51 patients (32.5%) were commenced on triple therapy by their primary care physician. Of these, 14 (27.4%) sustained a refracture during the study period (Table 3). Due to the study design, no information is available on adherence to medication in the control group.

None of the patients in the MTF group placed on calcium and vitamin D supplementation alone sustained a refracture, whereas 40% of patients in the control group on the same supplementation suffered a further fracture within the study period (Table 3). Further analyses by group and type of treatment revealed that in the MTF group, patients placed on calcium and vitamin D supplements only were significantly younger (p<0.04) than those on triple therapy, whereas control patients did not differ in any of their anthropometric measures or risk factors (data not shown).

In univariate analyses, group (MTF program vs. standard care), age, weight, and BMI all were significant predictors

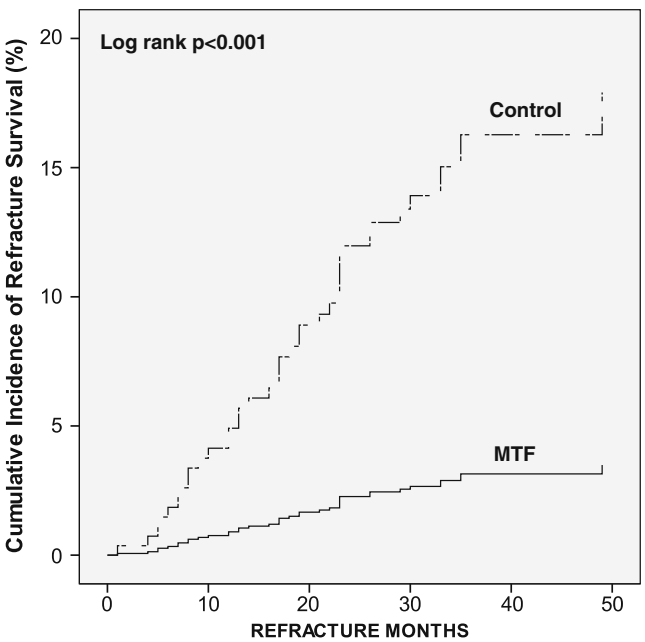


Fig. 2 Cumulative refracture incidence by group (all patients)

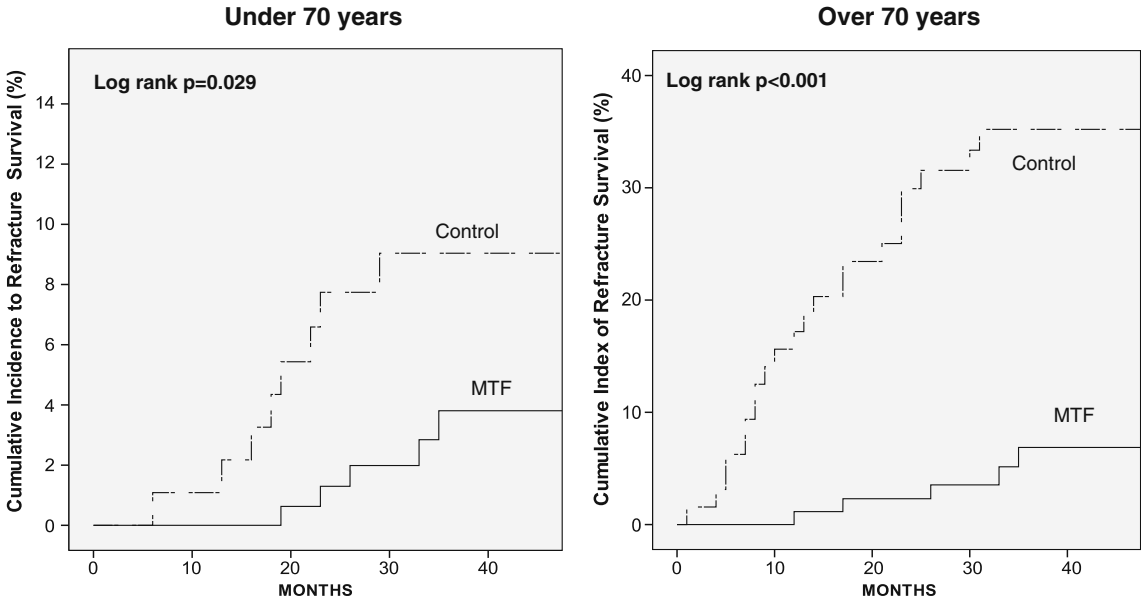


Fig. 3 Cumulative refracture incidence by age and group

of refracture (Table 4). In multivariable regression analyses of significant univariate predictors, group (HR 5.63, 95%CI 2.73–11.6), age (HR 1.04 per 10 year increase, 95%CI 1.01–1.07), and weight (HR 0.96 per 10 kg increase, 95% CI 0.93–0.98) remained statistically significant predictors of refracture for the entire study population ($P<0.01$ each).

Discussion

Following an initial fragility fracture, the risk of subsequent fracture increases by 1.6 to 4.3-fold at any given age [20]. Refractures are associated with a prolonged length of stay (on average 22 days), adding significantly to the cost of osteoporosis [22]. Studies worldwide indicate that the majority of patients with osteoporotic fractures do not receive appropriate treatment [23–25], despite the availability of effective therapies [16]. Hence, refractures are frequent but potentially preventable complications that impose a significant and avoidable burden on patient quality of life and health economics [26, 27]. The current prospective controlled study clearly demonstrates that active identification and management of patients with incident minimal trauma non-vertebral fractures through a coordinated intervention program reduces 4-year absolute refracture risk from 19.7% to 4.1%, along with a significant increase in time to refracture.

Numerous clinical care pathways to reduce osteoporotic refracture rates have been trialed in the past. The most parsimonious approaches involve patient and/or primary care physician education through electronic messaging, telephone calls, or mail. While some of these information-based interventions have increased treatment rates [28–31], other studies have found that such programs increase investigation and follow-up, but not treatment for osteoporosis [32, 33].

Table 3 Treatment modalities and refracture by group

	Treatment	On treatment *N* (% of total)	Refractured (*N*)	Refractured (%)
MTF	Calcium and vitamin D only	48 (19.5)	0	0
	Bisphosphonate+calcium+vitamin D	194 (78.9)	10	5.1
	Other[a]+calcium+vitamin D	4 (1.6)	0	0
	Total	246	10	4.1
Control	Calcium and vitamin D only	20 (12.7)	8	40.0
	Bisphosphonate+calcium+vitamin D	49 (31.2)	14	28.6
	Other*+calcium+vitamin D	2 (1.3)	0	0
	No specific therapy	86 (54.8)	9	10.5
	Total	157	31	19.7

[a] Strontium ranelate, raloxifene, recombinant human parathyroid hormone

Table 4 Clinical predictors of refracture (univariate analysis)

	HR[a] (95% CI)	*P* value
Group (control vs. intervention)	5.33 (2.61–10.87)	<0.001
Gender (female)	1.53 (0.64–3.64)	0.33
Age (per 10 years)	1.56 (1.19–2.04)	<0.01
Weight (per 10 kg)	0.60 (0.47–0.77)	<0.01
Height	0.97 (0.94–1.01)	0.15
BMI (per unit increase)	0.87 (0.81–0.94)	<0.01
IRSAD	1 (0.993–1.003)	0.5
History of falls	1.72 (0.92–3.2)	0.09
Ethanol consumption	1.68 (0.66–4.3)	0.28
Smoking	1.44 (0.56–3.7)	0.45
Prednisone use	0.1 (0.24–4.1)	0.11
Prevalent fracture	0.76 (0.18–3.16)	0.71
Fracture type (major vs. minor)[a]	1.38 (0.69–2.70)	0.37

IRSAD Index for Relative Socioeconomic Advantage and Disadvantage

[a] Cox proportional hazards model

[b] As defined in Table 1

Solomon et al. [34] demonstrated that an information-based intervention targeting primary care physicians and their at-risk patients increased the frequency of osteodensitometry and prescriptions for osteoporosis medication. However, the proportion of at-risk patients receiving osteoporosis management still remained very low. Hence, purely information-based protocols are now considered largely ineffective in reducing the osteoporosis management gap.

Using a network approach, the Kaiser Southern California Healthy Bones Program linked electronic medical records of 620,000 fracture patients with guidelines for osteoporosis management. Compared to historical data, the implementation of this program resulted in a significant increase in referrals for bone densitometry and prescriptions of anti-osteoporotic therapies. In addition, hip fracture numbers had decreased by an average of 37% [35]. Finally, direct patient interventions [36] or coordinated fracture services involving specialists, dedicated fracture coordinators, and primary care physicians [37–42] appear to be even more effective in detecting and managing patients with incident osteoporotic fractures. However, none of the previous studies adopted a controlled design selection and hence significant bias cannot be excluded.

In the present study, patient characteristics at baseline were similar in the intervention and control groups. In particular, relevant risk factors for osteoporotic fracture such as age, body weight, prevalent non-vertebral fracture status, family history, glucocorticoid use, smoking/ alcohol use, and falls risk were not significantly different between groups. While BMD was not included in the current analysis, prior studies have shown BMD and body weight to independently confer similar risks in regards to osteoporotic fracture [43, 44]. In fact, BMD may be substituted with body weight when calculating individual fracture risk [45]. While BMI and the proportion of women were higher in the MTF group, multivariable regression analyses revealed that the intervention effect remained unchanged after adjustment for these confounders. Also, groups did not differ when stratified by major vs. minor index fracture. However, as shown in Table 1, there were more patients with incident hip fractures in the MTF than in the control group, while the proportion of patients with wrist fractures was similar in both groups. Previous studies indicate that among survivors of an initial hip fracture the risk of a subsequent hip fracture is significantly increased [46, 47]. In contrast, the 10-year risk of refracture in patients with an initial wrist facture was found to be lower than that following other osteoporotic fractures [48]. At study completion, there were fewer hip and wrist fractures in the MTF than in the control group (Table 2), indicating that the intervention was effective despite the inclusion of patients with more severe osteoporosis at baseline.

The incidence of refracture over 4 years was reduced by more than 80%, and the time to fracture was on average prolonged by 10 months in patients managed by the MTF program. The results indicate that early intervention after an index fracture significantly reduces the frequency of subsequent fractures and hence disease burden. The overall refracture rate in the MTF group is similar to the 5.2% refracture rate reported in a dedicated fracture liaison program in Scotland [47], although this latter study had no control group to which refracture rates could have been compared. Our refracture rate without intervention of 19.7% over 4 years is comparable to a refracture rate of 19.4% over the same time interval reported by Johnell et al. [49], indicating our control data is comparable to that seen elsewhere.

Randomized controlled trials (RCTs) into the effect of oral anti-resorptives such as bisphosphonates, raloxifene, and strontium ranelate have demonstrated a reduction in non-vertebral fracture risk by 15–35%, with more pronounced effects in older patients and in those with more severe osteoporosis [16, 50]. In the present study, the effect of the intervention program on non-vertebral refracture rates was considerably greater than what has been described in RCTs. This difference in fracture reduction may in part be attributable to the relative small number of events in both groups, and to potential biases due the non-randomized observational nature of our study. However, the two groups included in the final analyses were balanced for baseline anthropometric, socio-economic, and clinical risk factors, and there was no evidence for selective inclusion or attrition of specific subgroups. Also, the intervention effect was more pronounced in older patients (Fig. 3). Hence, it appears that other factors associated with the MTF program co-determine its effect on refracture

rates. Recent studies have demonstrated that drug compliance is a major factor in the anti-fracture efficacy of oral treatments for osteoporosis [51–53]. While we have no reliable data on therapeutic persistence and adherence in the control group, we have established via Medicare records that persistence and adherence to medication was high in the MTF group of patients. In addition, patients attending the MTF program were repeatedly educated about their disease and motivated to engage in physical and outdoor activities. All of these factors have been shown to amplify compliance and drug efficacy, and are therefore likely contributors to the observed effects. Therefore, while the low refracture rates in the MTF group are likely due to high compliance rates, patient education and changes in lifestyle, the reasons for the high re-fracture rate in the control group appear to reside largely in the beliefs and decisions of these patients and their primary physicians.

More than two thirds of patients in the control group received no treatment at all, or calcium and vitamin D supplements only. One third was commenced on triple therapy by their primary care physician. These proportions are comparable to other published data, and are consistent with the known under-treatment of patients with osteoporosis even after a major disease complication has occurred [17]. Among patients receiving no treatment at all, one out of ten subjects suffered a new fracture within 4 years, while those receiving calcium and vitamin D supplements refractured at a rate of 40% within 4 years. This difference in refracture rates, although clearly based on small numbers, may reflect a perception of higher risk by the treating physician in those commenced on calcium and vitamin D, as compared to those patients not being treated at all. This observation is further compatible with evidence indicating that in patients with prior osteoporotic fractures, supplementation with calcium and/or vitamin D alone is not effective to prevent further fractures [52–54]. Finally, our results suggest that compared to standard care, management by a coordinated intervention program is associated with better long-term outcomes even in those patients receiving effective pharmacotherapy.

Strengths and limitations of the study

The intervention focused on younger community-living individuals with recent *non-vertebral* osteoporotic fractures. This has three important implications: firstly, as the remaining lifetime risk of refracture is higher in younger patients, the long-term effect of an intervention to reduce this risk will be greater in younger than in elderly populations. Secondly, however, we have little data on vertebral fractures, which are more common in osteoporosis and may follow a different refracture pattern. Of note, however, there were no vertebral refractures in the MTF group. Thirdly, while our study population is representative of the age-specific demographics of western industrialized countries, our results cannot be extrapolated to elderly or frail populations, as health care conditions in these patients differ from those of community-dwelling individuals.

Patients were not randomized for ethical reasons. Although the two groups were comparable in regards to most baseline characteristics, making a selection bias on the basis of anthropometric, clinical, or socioeconomic factors unlikely, self-selection bias in MTF group cannot be excluded. In particular, patients in the MTF group had more severe osteoporosis which would tend to increase compliance with therapy. Indeed, while we have no data in the control group, it is likely that the MTF group was more adherent to their medication than patients in the control group. On the other hand, such differences would be expected as a true intervention effect.

Compared to other reports of system-level care, a relatively large number of patients elected follow-up with their primary care physicians, despite the fact that the MTF service was free. This may in part be due to the strong advocacy for primary care in Australia, particularly in regards to chronic diseases. Another important factor affecting patient attendance rates was the waiting time between index fracture and appointment with the MTF service: longer intervals were associated with lower attendance rates.

Some data was gathered from electronic patient files and we cannot exclude that individual patients from the control group received treatment in hospitals outside our network. However, most patients live within 5 km of the referral center so that treatment outside the network seems unlikely to be a major confounding factor. Finally, while the available demographic and clinical data were similar for both groups, we have no information in the control group on other important variables which may affect fracture risk, such as dietary calcium intake, vitamin D, PTH and sex hormone levels, physical activity, and, in particular, BMD. The latter may have been higher in the MTF group along with a higher body weight and BMI, although multivariable-adjusted regression analyses seem to indicate that the intervention effect was not affected by body weight or BMI.

In summary, the current study demonstrates that following a minimal trauma fracture, refracture rates over 4 years are high among untreated patients. Targeted and co-ordinated intervention following a fragility fracture, and continued clinical follow-up results in a more than 80% reduction in the risk of further fracture.

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Conflicts of interest None.

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