Final Report

Investigators: Dr R Clifton-Bligh, Ms V Travers, Dr J Center, Dr T Nguyen, Dr Y Selecki, Dr N Pocock, Prof M Kotowicz, Prof M Seibel, Prof J Eisman

Executive Summary

- We tested the hypothesis that routine inclusion of actuarial fracture risk (using a calculation tool derived by Garvan Institute) in bone density reports would increase initiation of appropriate osteoporosis treatment to patients at high risk of fracture.
- A novel data capture web-based platform was used to assess GP decisions to treat patients for osteoporosis when provided with actuarial fracture risk (displayed graphically) compared to "usual" BMD reports that also included whether a given patient met PBS criteria for treatment or not.
- Our primary endpoint indicated that when GPs were provided with advice in real-time that a patient met PBS criteria for subsidized osteoporosis therapy, then intention to commence osteoporosis treatment was high (70%).
- Contrary to our hypothesis, we did not find that routine inclusion of actuarial fracture risk in bone density reports had any additional stimulus to commencing osteoporosis treatment.
- There was a strong correlation between PBS criteria for osteoporosis treatment and an actuarial ten-year fracture risk of ≥20%.
- We are conducting additional analyses from qualitative surveys to assess GP preference for graphical display of actuarial fracture risk.

Introduction

Osteoporosis is the condition of bone fragility that leads to fracture after minimal trauma. It is a common, chronic and debilitating disease, affecting 23% women and 6% men aged 50 and over (1) – i.e. more than one million Australians (2). Fractures are associated with substantial morbidity and mortality- not just from hip fractures following which 25% will die within 12 months and a further 50% will require a walking aid (3), but also after vertebral and peripheral fractures (4). Despite the availability of effective and safe therapies for osteoporosis, fewer than 30% of women with osteoporosis are offered treatment (5); and even following fragility fracture, fewer than 25% of patients are investigated or treated for osteoporosis (6). One of the major barriers to appropriate treatment of this devastating disease is an apparent failure to recognize the magnitude of risk involved (7, 8).

The recent availability of Fracture Risk Calculators offers an opportunity to overcome this barrier, specifically by facilitating appropriate risk recognition by GPs and their patients. One such web-based calculators being widely used by Osteoporosis specialists in Australia is the Garvan Fracture Risk Calculator, developed in 2008 using data from the Dubbo Osteoporosis Epidemiology Study, which incorporates four clinical risk factors (age, gender, number of fractures after age 50y and number of falls in past 12 months) and BMD (9). Fracture risk-based guidelines for treatment have already been developed in the United States by the National Osteoporosis Foundation (10), and in the United Kingdom by the National Osteoporosis Guidelines Group (11), however, the translation of these guidelines into treatment outcomes has not yet been studied.

In this study, we used a novel interaction platform to assess GP decisions to treat patients for osteoporosis in response to Fracture Risk (displayed graphically) compared to "usual" BMD reports. **We hypothesized that routine inclusion of Fracture Risk (using a calculation tool derived by Garvan Institute) in bone density reports would increase initiation of appropriate osteoporosis treatment to patients at high risk of fracture.**

Subjects and Methods

The study population was General Practitioners from targeted practices from Sydney metropolitan region. A cluster-randomised, cross-over study design was employed such that GPs were initially randomized (by practice) either to the "intervention" group (receiving workshop on Fracture Risk Calculators, and provision of FRC-based bone density reports for duration of study) or the "control" group (no workshop, standard BMD reports). Participating GPs remained in their original randomised group for 6 months before crossing over to the other group for the final 6 months.

The web-based Fracture Risk Calculator ("active" treatment) was used by GPs during real-time patient consultation – i.e. when a patient was seen with bone density results. The GP would enter BMD data together with other variables used in the Garvan Fracture Risk calculation: patient age, gender, history of fragility fracture, and number of falls in the preceding 12 months. Concomitant use of oral corticosteroids was also recorded, since this is a separate PBS criterion for treatment. The Calculator would then graphically display fracture risk for use during the consultation, together with advice as to whether the patient met PBS-criteria for subsidized osteoporosis therapy. The GP would then be prompted to answer two questions: (a) was the patient already on osteoporosis treatment?; (b) and, if not, would the GP intend commencing this patient on osteoporosis treatment?

A similar web-based Placebo calculator was used by GPs in the "placebo" group again during real-time consultation. The GP would enter BMD data together with patient age, gender, history of fragility fracture, falls and concomitant use of oral corticosteroids. The Placebo calculator would then indicate whether the patient met PBS-criteria for subsidized osteoporosis therapy, but would not provide fracture risk. Once again, the GP would be prompted to answer two questions: (a) was the patient already on osteoporosis treatment?; (b) and, if not, would the GP intend commencing this patient on osteoporosis treatment?

Importantly, both web-based tools were designed to capture GP data entries (and prompt responses) **all via a secure portal with data stored on a central server.** This significantly increased the speed and ease with which data was collected and stored for the study – i.e. GPs entered data directly onto the web-based FRC tool, and these data were sent directly to the investigators' server for later analysis.

We recruited **n=58** GPs into the study (of whom 5 withdrew during the study), from **8 different medical practices**. Pre-study questionnaires were collected, answering questions relevant to interpretation of study endpoints (full/part time GP, estimated number of patients 70 years and older seen in the GP practice, estimated number of BMD scans ordered per month, estimated number of patients commenced on osteoporosis treatment per month). Every GP in each medical practice was personally visited by the principal investigator (RCB) and the study co-ordinator at recruitment and to facilitate training in the study tool; a second 'workshop' visit was scheduled for every GP after 3 months of using the "Fracture Risk Calculator" (FRC) tool, in order to reinforce learning about the use of the tool outputs in decision-making for osteoporosis treatments. Four medical practices (n= 29 GPs) were initially randomized to the FRC group and the other four practices (n= 29 GPs) to the "placebo" (PBO) group.

The study was approved by the Northern Area Health Service Human Research Ethics Committee.

Results

During the study, **n=911 data entries** were received. Each data entry represented a unique decision by the GP, in real-time consultation, whether osteoporosis treatment would be recommended based upon BMD reports displayed according to actuarial Fracture Risk vs standard BMD report, together with indication as to whether patient met criteria for PBS-subsidized therapy. Demographics of this patient data entered by participating GPs are shown in **Table 1**, according to whether the GP was randomized to be shown actuarial fracture risk of not: patients entered by GPs using the FRC tool were slightly older, and more likely to have had a fracture and to have fallen more than once, compared to patients entered by GPs using the placebo tool. However, as shown in **Table 2**, actuarial fracture risk was similar for both groups (i.e. regardless of whether the GP was shown the risk or not).

From 911 entries, 223 patients were already on some form of potent osteoporosis treatment (oral or intravenous bisphosphonate, hormone replacement therapy, or denosumab). As shown in **Table 3**, patients on existing treatment were more likely to have had at least one fracture, and to have fallen, that those patients who were not yet on treatment. Also as expected, the majority of these treated patients had actuarial fracture risk estimates of ≥20% (**Table 4** and **Fig. 1**) – i.e. existing strategies were correctly identifying patients at highest risk of fracture for treatment. These data also validated the web-based interactive design and data capture methods.

From 688 patients who were treatment naive, 316 entries were provided by GPs during the 6 months they were randomized to the "active" group and 372 entries from GPs during the 6 months they were randomized to the "placebo" group.

In preliminary analysis of the primary endpoint, for patients with a ten-year fracture risk of ≥20% there was no difference in treatment intention between the active (70.1%) and placebo (69.9) groups (Fig. 2, P = 0.17).

Four pre-specified secondary analyses were performed. We examined treatment intention by GPs according to fracture risk gradient (divided into equal octiles) to show that a decision to treat for osteoporosis increased above a threshold fracture risk of about 15%, regardless of whether the GPs were aware of the actuarial risk ("active" group) or not ("placebo" group)(**Fig. 3A**). We then examined treatment intention by GPs for patients with a ten-year hip fracture risk of ≥3%, and showed no difference between the active (58.3%) and placebo (65.5%) groups (**Fig. 3B**, P = 0.17). We also found no differences in treatment intention by GPs for patients with an existing history of fragility fracture (**Fig. 3C**, P = 0.07) or those who qualified for PBS-subsidized therapy (**Fig. 3D**, P = 0.27).

Fig. 4 shows the proportion of patients treated by GPs according to randomized allocation to FRC or PBO, by age deciles.

Conclusions

Our study is the first to examine whether provision of fracture risk estimates (using the Garvan Fracture Risk Calculator) to GPs affects the decision to treat a patient for osteoporosis. Our primary endpoint indicated that GPs had a very high intention to treat patients at high fracture risk, regardless of whether that actuarial fracture risk was known to the GP at the time. Importantly, both "active" and "placebo" groups received advice in real-time as to whether a patient met PBS criteria for subsidized osteoporosis therapy: this is likely to have biased treatment intention upwards in both groups. Indeed, previous studies have indicated that only about 20% of patients with an osteoporotic fracture receive treatment in primary care (12). Nevertheless, our study points to the value of providing prompted advice towards treatment at the very least for patients who qualify for PBS therapies. Our results are broadly consistent with a recent GP-based study that found that 70% of subjects >70 y with a diagnosis of osteoporosis were prescribed bone-active treatments (13).

It is known that treatment decisions by GPs are heavily dependent upon PBS criteria (13). It is highly likely therefore that our study simply identified this adherence by GPs to PBS criteria for osteoporosis treatment. The similarity of treatment intention between the groups also speaks to the strength of existing PBS criteria for osteoporosis treatments. GPs prescribing to PBS standards are providing treatment to patients at high risk of fragility fracture. In essence, the PBS criteria are already de facto approximations to actuarial fracture risk of ≥20% (estimated using the Garvan FRC).

It is unknown whether a change to Fracture Risk-based treatment strategies would benefit Australian healthcare. The primary perceived advantage of Fracture Risk over existing PBS-criteria is that FRC includes age and BMD as continuous variables (rather than categorical cut-offs of 70 years of age, or BMD T-scores ≤ -2.5). FRC also includes the number of fragility fractures (rather than "yes" or "no" in PBS), and the number of falls (not included in PBS). **Arguably, the similarity of treatment intention shown in our study for GPs using either Fracture Risk or standard BMD reports indicates that either approach would be suitable for providing effective osteoporosis treatment to those at risk of fracture.** We are currently analysing qualitative data regarding GP preference on the use of the Fracture Risk Calculator.

In summary, our study identified that treatment intention for osteoporosis was not different for GPs provided with actuarial fracture risk compared to standard BMD results. Further research is needed to determine whether communication of actuarial fracture risk affects patient decisions to start and/or continue osteoporosis treatments.

References

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Table 1: demographic data entered by participating GPs, according to whether randomized to being shown risk (FRC group) or not (placebo group)

Factor	Not shown risk (PBO)	Shown Risk (FRC)	P-value
n	487	424	
sex = Women (%)	437 (89.7)	344 (81.1)	<0.001
age (mean (sd))	67.86 (10.40)	70.54 (10.04)	<0.001
age (%)			<0.001
50-59	119 (24.4)	59 (13.9)	
60-69	141 (29.0)	125 (29.5)	
70-79	161 (33.1)	160 (37.7)	
80-89	66 (13.6)	80 (18.9)	
fractures (%)			0.007
0	337 (69.2)	248 (58.5)	
1	112 (23.0)	139 (32.8)	
2	26 (5.3)	25 (5.9)	
3	12 (2.5)	12 (2.8)	
falls (%)			0.004
0	345 (70.8)	276 (65.1)	
1	104 (21.4)	83 (19.6)	
2	22 (4.5)	43 (10.1)	
3	16 (3.3)	22 (5.2)	
bmd.available = Yes (%)	456 (93.6)	391 (92.2)	0.481
Corticosteroids = Yes (%)	19 (3.9)	31 (7.3)	0.035
weight (mean (sd))	65.75 (13.77)	70.06 (16.89)	0.27
Prior treatment = Yes (%)	115 (23.6)	108 (25.5)	0.566

Table 2: actuarial fracture risk calculated using the Garvan Fracture Risk Calculator according to randomized allocation

Factor	Not shown risk (PBO)	Shown Risk (FRC)	P-value
n	487	424	
5-year risk of hip fracture (mean (sd))	6.60 (13.13)	6.47 (11.69)	0.879
5-year risk of any osteoporotic fracture (mean (sd))	14.42 (14.40)	15.76 (13.54)	0.15
10-year risk of hip fracture (mean (sd))	11.02 (17.89)	11.14 (15.86)	0.918
10-year risk of any osteoporotic fracture (mean (sd))	25.74 (19.54)	28.24 (19.06)	0.052

Table 3: demographic data according to baseline treatment status.

Factor	Not on existing treatment	On existing treatment	P-value
n	621	290	
sex = Women (%)	528 (85.0)	253 (87.2)	0.43
age (mean (sd))	68.74 (10.46)	69.89 (9.98)	0.117
ageg (%)			0.405
50-59	130 (20.9)	48 (16.6)	
60-69	177 (28.5)	89 (30.7)	
70-79	219 (35.3)	102 (35.2)	
80-89	95 (15.3)	51 (17.6)	
fractures (%)			<0.001
0	454 (73.1)	131 (45.2)	
1	121 (19.5)	130 (44.8)	
2	29 (4.7)	22 (7.6)	
3	17 (2.7)	7 (2.4)	
falls (%)			<0.001
0	477 (76.8)	144 (49.7)	
1	88 (14.2)	99 (34.1)	
2	36 (5.8)	29 (10.0)	
3	20 (3.2)	18 (6.2)	
bmd.available = Yes (%)	579 (93.2)	268 (92.4)	0.754
Corticosteroids = Yes (%)	27 (4.3)	23 (7.9)	0.04
weight (mean (sd))	69.17 (15.23)	65.69 (16.08)	0.398

Table 4: actuarial fracture risk according to baseline treatment status.

Factor	Not on existing treatment	On existing treatment	P-value
n	621	290	
5-year risk of hip fracture (mean (sd))	5.23 (11.08)	9.35 (14.66)	<0.001
5-year risk of any osteoporotic fracture (mean (sd))	13.13 (13.34)	19.14 (14.55)	<0.001
10-year risk of hip fracture (mean (sd))	8.93 (15.48)	15.67 (19.00)	<0.001
10-year risk of any osteoporotic fracture (mean (sd))	23.67 (18.48)	33.85 (19.38)	<0.001

Figure 1. Actuarial fracture risks, calculated using the Garvan Fracture Risk Calculator, for patients already on bone-active treatments. On *left* is shown proportions of subjects with ten-year risk of osteoporotic fracture of <10%, 10-15%, 15-20% and >20%, in those attending GP practices randomized to use the Fracture Risk Calculator (FRC). On *right* is shown proportions of subjects with fracture risks <10%, 10-15%, 15-20% and >20%, in those attending GP practices randomized to use standard BMD reports. As expected, the majority of patients already on bone-active treatment in either group had actuarial fracture risks of >20%.

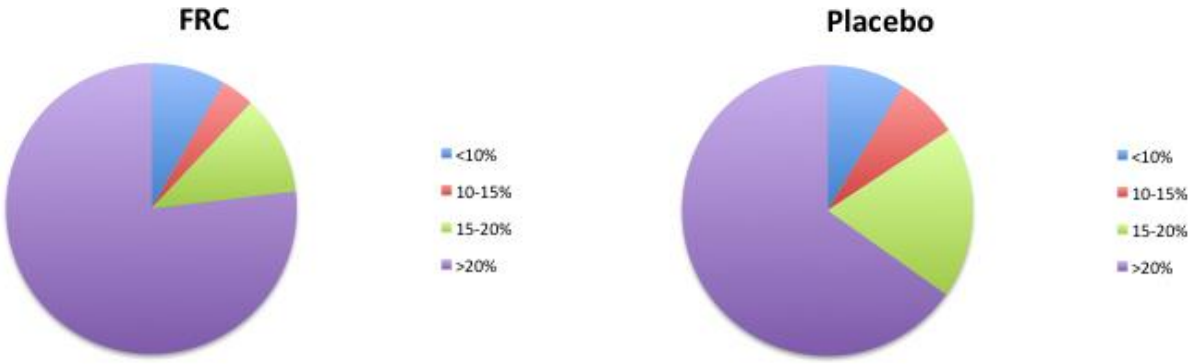

Figure 2. Primary end-point of study: decision to treat with bone-active drugs according to ten-year risk of osteoporotic fracture risk of <20% or ≥20%, for GPs randomized to use the FRC tool compared to placebo group using standard BMD reports. No significant difference was found between the groups, and for both the decision to treat patients at high risk was ~70%.

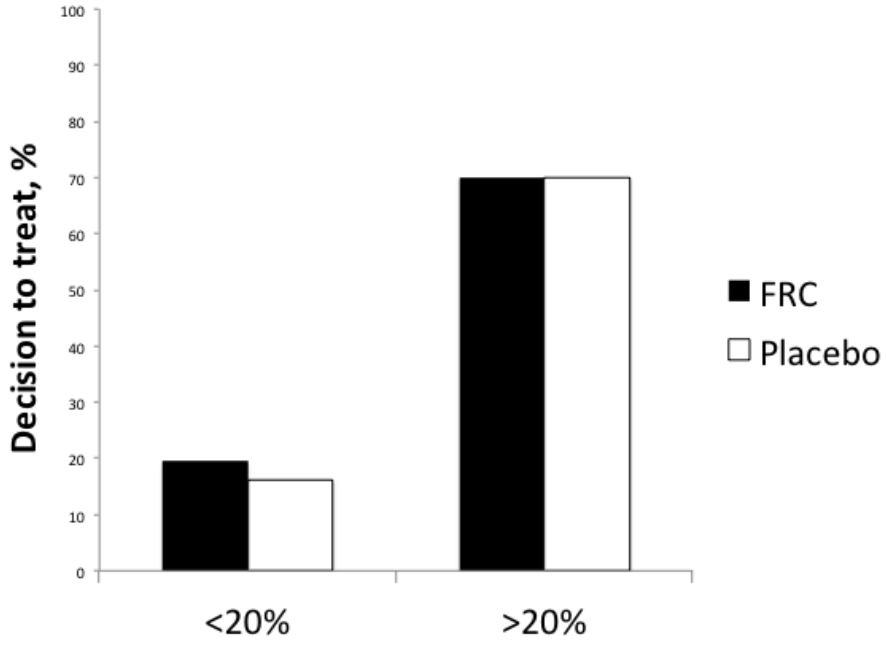

Figure 3. (A) Decision to treat according to octiles of actuarial fracture risk. **(B)** Decision to treat according to actuarial ten-year risk of hip fracture <3% or ≥3%. **(C)** Decision to treat according to history of prevalent osteoporotic fracture. **(D)** Decision to treat according to whether or not patients met PBS-criteria for osteoporosis therapy.

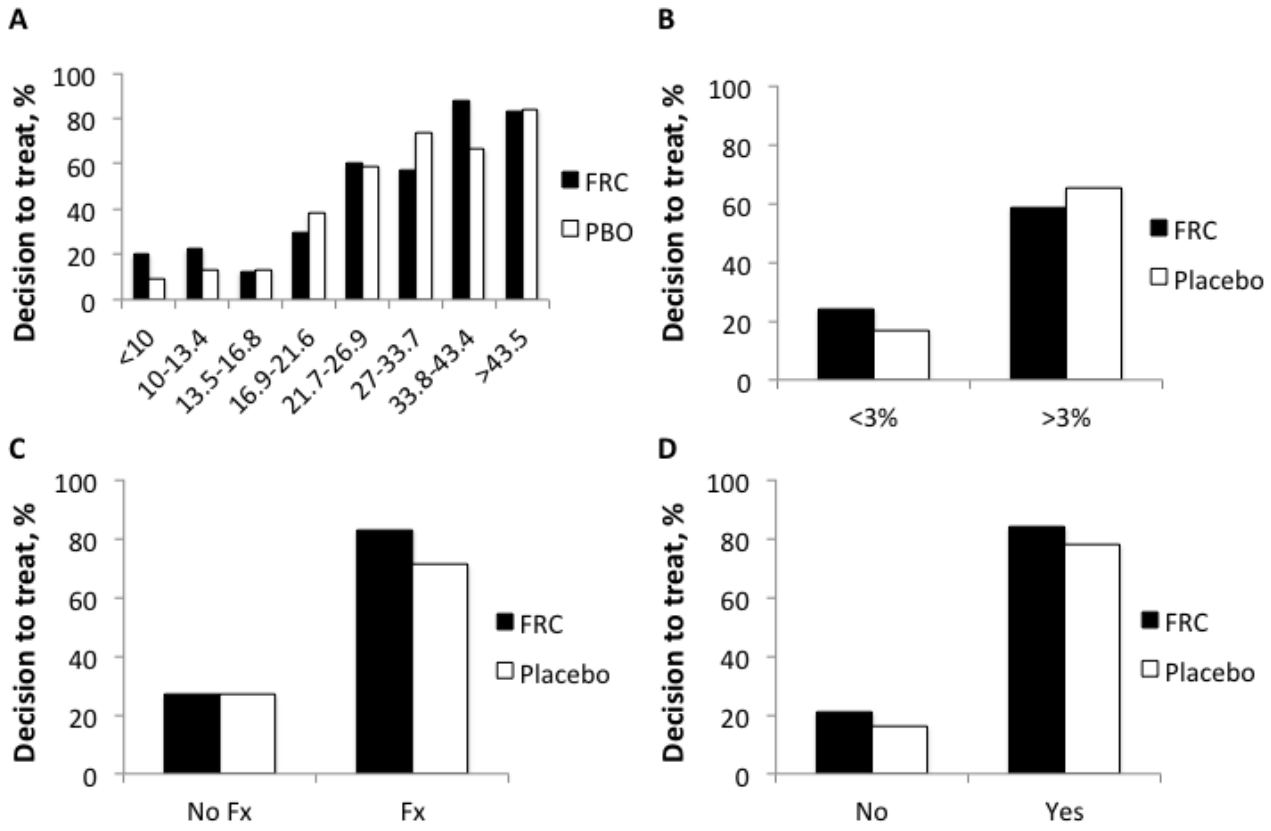

Figure 4. Number and proportion of patients treated by GPs according to randomized allocation to FRC (risk shown) or PBO (risk not shown), by age deciles.