

Prevalence of Medication-Related Risks for Falls and Osteoporosis at a Hospital Network: A Post-hoc Analysis

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Received: September 16, 2015 Revised: January 1, 2016
Accepted: January 9, 2016
Published online: April 13, 2016

ABSTRACT

AIM: PRO-OSTEO Extend 1 was an osteoporosis management study at a Victorian Healthcare service. This post-hoc analysis examined comorbidities and drug-related risks for falls and osteoporosis, and analysed the accuracy of the medication subcomponent of the falls risk assessment tool used at the service. The secondary aim of this analysis was to evaluate the impact of proton pump inhibitors on the success of anti-osteoporosis therapies.

MATERIAL AND METHODS: This analysis was part of a two year retrospective cohort study. The falls risk assessment tool medication subsection results, completed by nursing staff, were compared to scores given by the data collection pharmacist based on medical history notes using Mann-Whitney *U* test. The impact of proton pump inhibitors use on active osteoporosis therapy in patients admitted after a fall was analysed using the Fisher Exact test. Prevalence of medical and medication-related risk factors for osteoporosis and falls was compared between patients with fractures without osteoporosis treatment at admission and patient who were excluded from the primary study due to active osteoporosis therapy, or admission after a fall without a fracture.

RESULTS: The falls risk assessment tool completion rate was approximately 80%, with accuracy below 50% $P < 0.001$. Medications which increase osteoporosis and falls risk were prevalent, with high use of benzodiazepines, opioids, serotonin reuptake inhibitors antidepressants and proton pump inhibitors. The impact of proton

pump inhibitors carried a 14% increased relative risk of a fracture in this cohort ($P = 0.218$). There was also high prevalence of pre-existing fractures, pulmonary disease, heart failure and strokes in the study population.

CONCLUSION: Falls risk assessment in relation to medication use is frequently inaccurate and is not done at all for a significant proportion of patients. The use proton pump inhibitors and medication-related risks for falls and osteoporosis treatment can be improved with potential for hospital pharmacists to contribute to the risk reduction strategies.

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Key Words: Osteoporosis; Falls risk assessment tool; Proton pump inhibitors; Bisphosphonates; Minimal-trauma fractures; Hospital

Banakh I. Prevalence of Medication-Related Risks for Falls and Osteoporosis at a Hospital Network: A Post-hoc Analysis. *International Journal of Orthopaedics* 2016; 3(2): 528-534 Available from: URL: <http://www.ghrnet.org/index.php/ijo/article/view/1607>

INTRODUCTION

Falls and fractures account for a large number of Emergency Department presentations across Australian hospitals, with nearly 250 hospital admissions per day for fractures alone^[1]. Medication-related causes for these admissions are not systematically examined or managed during hospitalisation, despite the available tools and pathways for medical and nursing staff^[2]. Screening tools were added to pathways and introduced into hospital practice due to numerous studies indicating that multiple drug classes have a significant contribution to the risk of falls, presentations to hospitals, morbidity and mortality^[2-8]. PRO-OSTEO Extend 1 study was conducted at a Victorian Healthcare Service during 2012-2014 periods, examining the effects of a pharmacist-driven approach to osteoporosis management across a minimal-trauma

fracture population^[9]. The aim of the primary study intervention was to improve the level of osteoporosis assessment and treatment among patients admitted to the healthcare service with minimal-trauma fractures utilising clinical pharmacists' contributions to a multidisciplinary approach. A post-hoc analysis of the osteoporosis management study was carried out to examine patients' past medical histories for the prevalence of conditions and medications that contribute to falls and osteoporosis risk in an Australian setting, as well as to audit the use of the Peninsula Health Falls Risk Assessment Tool (FRAT)^[10]. The use of such a tool by nursing staff on admission has been shown to be reliable and easy to administer in subacute settings and it is included in multiple hospital treatment pathways^[10]. This analysis assessed the accuracy of use of the FRAT in relation to the medication-related falls risk assessment by nursing staff, as well as the completion rate of the FRAT among patients admitted due to falls in both the acute and subacute settings as this aspect of FRAT use has not been thoroughly reviewed in the past.

The secondary aim of the post-hoc analysis was to examine the impact of proton pump inhibitors (PPIs) on the success of osteoporosis treatments on prevention of fractures in patients admitted to the service on active therapy after a fall. The use of PPIs has been reported to reduce the effectiveness of bisphosphonates in preventing further fractures; however, these reports have been inconsistent and the precautionary recommendations to avoid the combinations to reduce the risk of treatment failure have not been adhered to at a local level of practice due to the questionable level of significance of the drug interaction^[11-14]. Hence, this post-hoc analysis aimed to investigate the potential impact of this drug-related interaction on the success of treatment after hospital admission for a fall.

MATERIAL AND METHODS

The PRO-OSTEO Extend 1 study method is described elsewhere, but briefly, the study was a retrospective cohort study measuring rates of osteoporosis assessment and treatment for patients admitted with minimal-trauma fractures. The study was conducted over a 2 year period across one of south-east healthcare networks in Melbourne, as an extension of a pilot study that was carried out in 2010^[9,15]. The study sites included three rehabilitation facilities as well as two acute hospitals. The healthcare service consists of a dedicated age-care and orthopaedics ward, with an orthopaedics surgical, an aged-care and a combination of an ortho-geriatric review teams. Patients were included in the primary study if they had a minimal-trauma fracture (MTF) and survived to discharge. Patients were excluded from the primary study if they had an admission for a fall without a fracture, a non-minimal-trauma fracture or had a MTF but either died during the admission or if they were receiving active osteoporosis therapy prior to admission. Active therapy was defined as bisphosphonates, strontium ranelate, denosumab or teriparatide. The duration of therapy prior to incident admission was not examined as this information is not routinely documented in patient histories at tertiary centres. Patients who were excluded from the primary study due to osteoporosis therapy use were included in the post-hoc analysis to determine the impact of PPI therapy on the success of osteoporosis treatment after a fall. In this post-hoc analysis, treatment failure was considered to be admission after a fall with minimal-trauma fracture while on the active therapy.

Digitised medical records of patients admitted to the Peninsula

Health service with a diagnosis of fall and/or fracture were reviewed for use of drugs that are established as risk factors for either osteoporosis development or falls, or both^[2-8]. The medical risk factors that patients were screened for included: heart failure, chronic obstructive pulmonary disease (COPD), cerebrovascular accident (CVA) or transient ischaemic attack (TIA), epilepsy, dementia, Parkinson's disease, chronic inflammatory conditions such as rheumatoid arthritis, smoking history, excessive alcohol consumption, and body mass index (BMI) above 30 or below 20 as recorded in medical histories by medical, nursing, pharmacy and allied health staff^[16,17]. Medication related risk factors that were screened for included: PPIs, antidepressants, antipsychotics, antihypertensives, loop diuretics (frusemide), anticholinergic medications, antiepileptics, thyroxine, aromatase inhibitors, gonadotrophin releasing hormone receptor agonists, androgen antagonists and warfarin^[2-8,17,18].

As part of this post-hoc analysis the use of the FRAT was reviewed in relation to the completion of the medications risk subsection for all patients screened for the primary study, with exception of paediatric (< 18 years of age) and non-minimal-trauma admissions (see Figure 1). The FRAT is composed of four sections including: history of recent falls, medications, psychological and cognitive status. The medications subsection assists clinicians, primarily nurses, to evaluate how patients' medications contribute to the individual risk of falls with a score of 1 to 4. A score of 1 indicates that no medications are in use that increase the risk of falls, a score of 2,3 and 4 equate to 1,2 and more than 2 drugs in use that increase the risk of falls respectively^[10]. The first FRAT score recorded in patients' medical notes, the indicator of medications used in preadmission period, was used for the purpose of this study. It was compared to the FRAT score as assessed by a pharmacist based on medication records from the medical and or ambulance notes and if available from the medication reconciliation forms.

Patients who met the inclusion criteria for PRO-OSTEO Extend 1 study were compared to the cohort that was excluded to identify any additional differences beyond the exclusion criteria that contributed to patients' management and outcomes.

PRO-OSTEO Extend 1 study received human ethics review exemption due to the audit nature of the study.

Statistics

Continuous variables were analysed using the Student's *t*-test, while binomial variables were analysed using χ^2 and Fisher exact test methods with a 2-sided α set at a significance level of 0.05. Medications risk FRAT score differences between nurse assessed and pharmacist assessed scores were analysed using the Mann-Whitney *U* test with a 2-sided α set at a significance level of 0.05. The impact of PPI therapy on treatment outcomes was assessed using Fisher Exact test with a one-sided α set 0.05 for significance. Study results were analysed using SPSS Computer Program, version 19.0. Chicago, IL: SPSS Inc.

RESULTS

Over the two-year study period 560 patient admissions met the inclusion criteria and 305 admissions met the exclusion criteria for PRO-OSTEO Extend 1 study^[9]. As part of this post-hoc analysis, 32 patients were excluded as the analysis examined adult population after minimal-trauma hospital admission. Baseline patient characteristics for both groups from the parent study are described in Table 1. Patients who met the inclusion criteria for the primary study were younger ($P = 0.027$), more likely to be female ($P = 0.016$) and

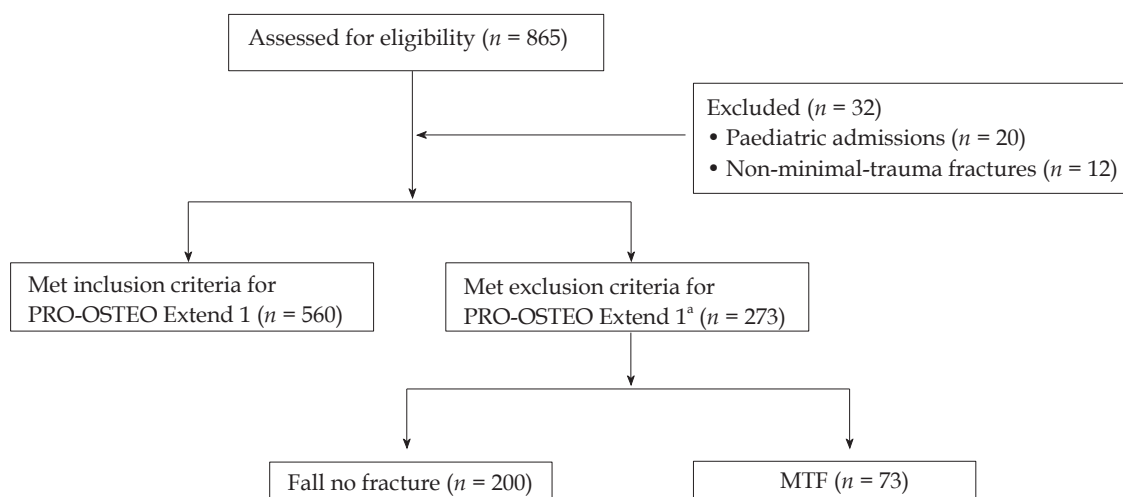


Figure 1 PRO-OSTEO Extend 1 patient flow diagram. MTF = minimal-trauma fracture. ^a273 patients were excluded from the primary study, but were included in this post-hoc analysis due to use of osteoporosis medications prior to hospitalisation or due to mortality during admission.

had a longer length of stay, while older age and male gender, risk factors for higher mortality, contributed to the differences observed as a result of the exclusion criteria of death during admission.

The following comorbidities were more common amongst the cohort that met the exclusion criteria: prevalent fractures, COPD, heart failure and CVA/TIA, as well as medications known to increase the risk for osteoporosis and falls (see table 1)^[16,17]. However, the included group had significantly more patients with inflammatory conditions ($P < 0.001$) and extremes of BMI ($P = 0.008$). The rates of current smoking, previous smoking and excessive alcohol consumption history were similar between the groups. The medication FRAT scores between included and excluded groups were of 2.9 versus 3.3 respectively ($P < 0.001$). The differences were due to the comorbidities, which frequently require the use of medications such as frusemide, corticosteroids and antidepressants, increasing the risk of falls and fractures.

The overall study population had a large exposure to medications that are identified as risk factors for osteoporosis development with approximately 10% of patients on thyroxine and corticosteroids, over 20% on selective serotonin reuptake inhibitors (SSRIs) and serotonin and noradrenaline reuptake inhibitors (SNRIs), and over 40% of patients on PPIs. While the excluded cohort had a greater prevalence of risk factors for osteoporosis and falls, this group also had a significantly higher rate of cholecalciferol and calcium use ($P < 0.001$), which is likely to have been influenced by the exclusion criteria of active therapy use in combination with these supplements.

FRAT tool analysis

A significant proportion of patients in both groups had no FRAT completed during their admission, 18.8% in the included group compared with 21.3% in the excluded group. There was a large contribution to these results from low use of FRAT in the Emergency Departments at the two acute sites. When medication FRAT scores were completed, the first score recorded was accurate in 47.9% of patients in the included group and 33.7% of the excluded group ($P < 0.001$). The average difference between the first recorded medication FRAT score and the pharmacist reviewed scores for the entire study population was 0.7, 2.6 versus 3.3 respectively ($P < 0.001$). The majority of patients had their medication risk underestimated by 1 or 2 points, whereas

overestimation was less frequent (see Figure 2).

PPIs and osteoporosis treatment success

Amongst patients excluded from the primary study, 73 patients sustained a minimal-trauma fracture (MTF) and 200 did not have a fracture following a fall. Patients who had a fracture were older, more likely to be a female, with an extra 8 days of hospitalisation ($P = 0.004$). These patients also had more than triple the mortality rate, 34.2% (25 out of 73) compared to 11% (22 out of 200), $P < 0.001$. Mortality occurred mostly during the incident admission in the fracture group, while among patients without a fracture after a fall deaths occurred in the post-discharge period, but still within the high risk period of the first 12 months after admission. Patients with a MTF were also more than twice as likely to have a prevalent fracture ($P < 0.001$), were more likely to have heart failure ($P = 0.001$) and inflammatory conditions ($P = 0.003$). Dementia was more prevalent in the MTF group, but the difference did not reach statistical significance ($P = 0.166$) (see Table 2). Over 75% of patients with fractures were on active osteoporosis treatments, but they were also more likely to be on PPIs, 42.5% versus 7.5% in the non-fracture cohort ($P = 0.014$). The fracture population also had a higher exposure to medications that contribute to falls and fractures, including frusemide, corticosteroids, benzodiazepines and opioids. The FRAT score difference was low (0.4), but it was statistically significant ($P = 0.045$).

Amongst patients on active osteoporosis treatment, the addition of a PPI increased the relative risk of a fracture by 14%, but the result did not reach statistical significance ($p = 0.218$). When stratified by active therapy, PPI combination with a bisphosphonate treatment increased the risk of treatment failure by 39% (RR = 1.39, $P = 0.077$), whereas for strontium ranelate and for denosumab the number of patients included in the study were too low to provide an indication of an effect on treatment success. When individual bisphosphonates were examined, no individual bisphosphonate stood out as the most effected, alendronate ($P = 0.596$), risedronate ($P = 0.265$), zoledronate ($P = 0.100$). The number of patients using zoledronate was small likely as a result of a more recent registration for osteoporosis indication with the Therapeutic Goods Administration and addition to the Pharmaceutical Benefits Scheme for subsidisation. Another contributor to the lower use of zoledronic acid is the challenge in organising an intravenous infusion for

Table 1 Baseline characteristics of patients screened for PRO-OSTEO Extend 1 study¹.

Criteria	Patients who met inclusion criteria (n = 560)	Patients who met exclusion criteria (n = 273)	Significance
Age mean (years)	77.5	80	0.027
median (IQR)	82 (19.0)	85 (13.5)	
> 65 years (%)	456 (81.4)	239 (87.5)	0.026
Gender			
Females (%)	399 (71.2)	172 (63.0)	0.016
Males (%)	161 (28.8)	101 (37.0)	
LOS mean (days)	21	18	0.053
median (IQR)	2 (3)	4 (24)	
Previous fracture (%)	161 (28.8)	93 (34.1)	0.118
Dementia (%)	131 (23.4)	73 (26.7)	0.292
COPD (%)	85 (15.2)	53 (19.4)	0.123
CCF (%)	78 (13.9)	45 (16.5)	0.329
CVA/TIA (%)	106 (18.9)	70 (25.6)	0.026
Inflammatory diseases (%)	104 (18.6)	20 (7.3)	<0.001
<20 BMI >30 (%)	71 (12.7)	18 (6.6)	0.008
Smokers (%)	53 (9.5)	19 (7.0)	0.227
Ex-smokers (%)	74 (13.2)	36 (13.2)	1
Alcohol abuse(%)	83 (14.8)	32 (11.7)	0.223
Osteoporosis risk factor distribution			
PPI use (%)	240 (42.9)	120 (44.0)	0.764
SSRI use (%)	105 (18.8)	66 (24.2)	0.069
SNRI (%)	38 (6.8)	14 (5.1)	0.353
Frusemide use (%)	55 (9.8)	56 (31.5)	<0.001
Corticosteroid use (oral) (%)	53 (9.5)	39 (14.3)	0.037
Warfarin use (%)	65 (11.6)	35 (12.8)	0.613
Thyroxine use (%)	54 (11.4)	25 (9.2)	0.319
Average number of drugs that contribute to falls	2.2	2.7	0.001
Benzodiazepines(%)	146 (26.1)	102 (37.4)	0.001
Opioids (%)	114 (20.4)	66 (24.2)	0.209
TCAs (%)	39 (7.0)	12 (4.4)	0.147
Antipsychotics (%)	58 (10.4)	36 (13.2)	0.226
Antihypertensives (%)	296 (52.9)	167 (61.2)	0.023
Antiepileptic drugs (%)	53 (9.5)	33 (12.1)	0.243
Preadmission osteoporosis therapy			
Vitamin D supplements (%)	190 (33.9)	130 (47.6)	<0.001
Calcium supplements (%)	107 (19.1)	85 (31.1)	<0.001
Active therapy:			
Bisphosphonates (%)	0 (0.0)	79 (28.9)	<0.001
Strontium ranelate(%)	0 (0.0)	6 (2.2)	<0.001
Denosumab(%)	0 (0.0)	6 (2.2)	<0.001
Raloxifene(%)	12 (2.1)	1 (0.4)	0.052
Calcitriol(%)	3 (0.5)	2 (0.7)	0.73
Nandrolone(%)	1 (0.1)	0 (0.0)	0.485
FRAT scores			
FRAT incomplete for admission(%)	105 (18.8)	58 (21.3)	0.394
FRAT score completed correctly(%)	268 (47.9)	92 (33.7)	<0.001
Average correct score	2.9	3.3	<0.001

¹Patients with non-minimal trauma and paediatric admissions were not included in this post-hoc analysis. LOS: Length of stay; PPI: Proton pump inhibitors; SSRIs: Selective serotonin reuptake inhibitors; SNRIs: Serotonin noradrenaline reuptake inhibitor; TCAs: Tricyclic antidepressants; CCF: Congestive cardiac failure; CVA: Cerebrovascular accident; TIA: Transient ischaemic attack; COPD: Chronic obstructive pulmonary disease. Inflammatory disease include rheumatoid arthritis, polymyalgia rheumatic, ulcerative colitis and sarcoidosis.

patients in the community settings.

DISCUSSION

The PRO-OSTEO Extend 1 study has shown that the falls population treated at one of the Victorian Healthcare Services is similar to others¹⁹, and carries a significant medication-related burden in relation to medications that increase the risk of falls, with an average of more than 3 drugs per patient. This study has identified that PPI therapy was strongly associated with increased fracture rate, combined use with active osteoporosis treatment and a trend towards reduced treatment efficacy. This post-hoc analysis also showed that a significant proportion of patients

admitted after a fall and or fracture do not have any medication risk assessment completed as indicated by their medical records, and for over 50% who do have a FRAT completed, the medication risk is frequently underestimated. Prolonged stay at the acute and transfer to the subacute care settings increased the likelihood of FRAT use in this study, but only by 2.4% over an average of extra 3 days of hospitalisation. The underestimation of risk leads to reduced implementation of falls reduction strategies and the lack of risk factor modification during admission and on discharge from hospitals and rehabilitation sites. However, even when drug risks are identified, not all of them can be modified. A patient with stage 3 or 4 heart failure and fluid overload cannot forgo their diuretic therapy, nor can a patient with fragile inflammatory condition

Table 2 Baseline characteristics of patients excluded from PRO-OSTEO Extend 1 study by fracture status on admission.

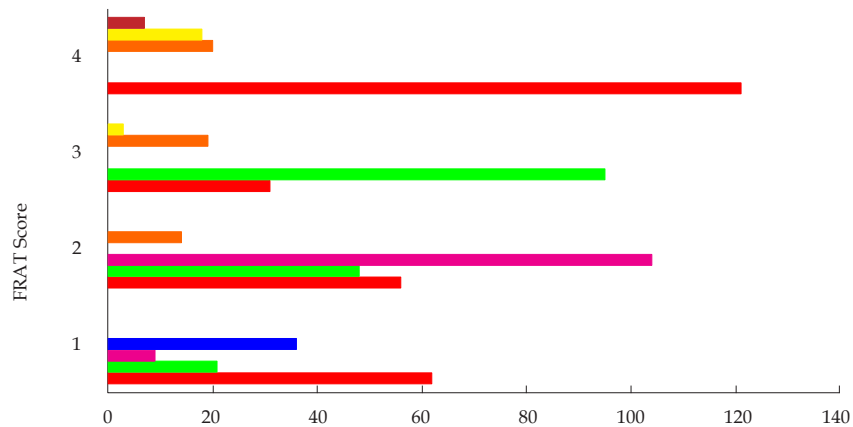
Criteria	Minimal-trauma fracture (n = 73)	Fall without fracture (n = 200)	Significance
Age mean (years)	83.3	78.7	0.008
> 65 years (%)	66 (90.4)	173 (86.5)	0.386
Gender			
Females (%)	54 (74.0)	120 (60.0)	0.871
Males (%)	19 (26.0)	80 (40.0)	
LOS mean (days)	23.8	15.8	0.004
Previous fracture (%)	40 (54.8)	57 (26.5)	<0.001
Dementia (%)	24 (32.9)	49 (24.5)	0.166
COPD (%)	17 (23.3)	36 (18.0)	0.328
CCF (%)	21 (28.8)	24 (12.0)	0.001
CVA/TIA (%)	14 (19.2)	56 (28.0)	0.14
Inflammatory diseases (%)	11 (15.1)	9 (4.5)	0.003
< 20 BMI > 30 (%)	5 (6.8)	13 (6.5)	0.918
Smokers (%)	2 (2.7)	17 (8.5)	0.098
Ex-smokers (%)	9 (12.3)	27 (13.5)	0.8
Alcohol abuse (%)	1 (1.4)	29 (14.5)	0.002
Risk factor distribution			
PPI use (%)	41 (56.2)	79 (39.5)	0.014
SSRI use (%)	22 (30.1)	44 (22.0)	0.165
SNRI (%)	3 (4.1)	11 (5.5)	0.645
Furosemide use (%)	30 (41.1)	56 (28.0)	0.039
Corticosteroid use (%)	19 (26.0)	20 (10.0)	0.001
Warfarin use (%)	5 (6.8)	30 (15.0)	0.075
Thyroxine use (%)	10 (13.7)	15 (7.5)	0.116
Average number of drugs that contribute to falls	3.0	2.6	0.065
Benzodiazepines (%)	34 (46.6)	68 (34.0)	0.057
Opioids (%)	23 (31.5)	43 (21.5)	0.087
TCAs (%)	4 (5.5)	8 (4.0)	0.598
Antipsychotics (%)	11 (15.1)	25 (12.5)	0.579
Antihypertensives (%)	50 (68.5)	117 (58.5)	0.134
Antiepileptic drugs (%)	7 (9.6)	26 (13.0)	0.444
Preadmission osteoporosis therapy use			
Vitamin D supplements (%)	51 (69.9)	79 (39.5)	<0.001
Calcium supplements (%)	41 (56.2)	44 (22.0)	<0.001
Active therapy	55 (75.3)	39 (19.5)	<0.001
Bisphosphonates (%)	46 (63)	33 (16.5)	<0.001
Strontium ranelate (%)	4 (5.5)	2 (1.0)	0.025
Denosumab (%)	5 (6.8)	1 (0.5)	0.002
Raloxifene (%)	0 (0.0)	1 (0.5)	0.545
Calcitriol (%)	0 (0.0)	2 (1.0)	0.391
FRAT scores			
FRAT incomplete for admission (%)	5 (6.8)	52 (26.2)	0.001
FRAT score completed correctly (%)	26 (35.3)	57 (28.7)	0.258
Average correct score	3.6	3.2	0.045
On any active treatment and PPI (%)	31 (42.5)	15 (7.5)	0.218
On bisphosphonate and PPI (%)	26 (35.6)	12 (6.0)	0.077
On denosumab and PPI (%)	2 (2.7)	1 (0.5)	0.5
On strontium and PPI (%)	3 (4.1)	2 (1.0)	0.667

LOS: Length of stay; PPI: Proton pump inhibitors; SSRIs: Selective serotonin reuptake inhibitors; SNRIs: Serotonin noradrenaline reuptake inhibitors; TCAs: Tricyclic Antidepressants; CCF: Congestive cardiac failure; CVA: Cerebrovascular accident; TIA: Transient ischaemic attack; COPD: Chronic obstructive pulmonary disease. Inflammatory disease include rheumatoid arthritis, polymyalgia rheumatic, ulcerative colitis and sarcoidosis.

be managed without a carefully adjusted dose of corticosteroids. Nevertheless, many patients were using medications that could be stopped or altered, including benzodiazepines and antipsychotics, which are frequently used beyond guideline recommendations^[2,18]. Alarming, these classes were used more frequently in patients with dementia, adding further to the risk of worsening confusion, falls, fractures and mortality amongst an already high risk population, a trend that has been reflected in other studies^[2,19].

The rate of FRAT completion during the study period was lower than the previously reported rates of over 90% for this healthcare network, but within the range reported by other hospitals^[10,20]. The difference may be attributed to the inclusion of acute sites in this study, and especially the fast patient turnover Emergency Departments, which concentrate on the management of the

immediate medical concern rather than the preventative measures or risk assessment. Other reasons for the FRAT score inaccuracies in relation to medications could stem from the lack of availability of a complete medication history on admission, delayed completion of medication reconciliation forms and failure to recognise medications that increase the risk of falls. Nursing staff experience may also influence recognition of some drugs as risk factors for falls and this has been previously identified; however, there was high inter-rater reliability for FRAT from previous research into this tool^[10,20]. Some possible solutions that may reduce medication risk underestimation may come from improving nursing skill mix and patient to nurse ratio, or a greater liaison with ward and Emergency Department pharmacists for medication reconciliation and falls-risk factor modification, as well as provision of education to the



	1	2	3	4
Overestimated score by 3 points	0	0	0	7
Overestimated score by 2 points	0	0	3	18
Overestimated score by 1 points	0	14	19	20
Underestimated score by 3 points	36	0	0	0
Underestimated score by 2 points	9	104	0	0
Underestimated score by 1 points	21	48	95	0
Correctly scored	62	56	31	121

Figure 2 Medication FRAT scores accuracy, recorded versus pharmacist reviewed scores.

healthcare staff^[20]. However, these responsibilities and tasks require sufficient time allocation and smaller clinician to patient ratios for appropriate service delivery for falls patients, as recommended by staffing standards^[20,21].

One of the risk factor mitigation approaches is the review of long-term PPI use. PPIs have been identified in previous studies and systematic reviews as independent contributors to development of osteoporosis^[8,22-25], as well as in several studies, as attenuators of bisphosphonate activity in patients on treatment for osteoporosis^[8,11,23,24]. This post-hoc analysis of effects of PPIs on treatment success was highly limited by the number of patients identified as being on active therapy, but the relative risk increase is in-line with the most recent large meta-analysis results^[25]. The other limitation is the lack of documentation of duration and adherence to active therapy and PPI use prior to hospitalisation and temporal relation between the PPI therapy initiation in relation to active therapy. This is of importance in identifying patients who may have been suffering from bisphosphonate induced oesophagitis and gastritis, or exacerbation of underlying reflux, in which case bisphosphonate cessation would be more appropriate than adding a PPI. The lack of documentation of adherence to and duration of anti-osteoporosis treatment also limits the interpretation of effect on treatment outcomes, as treatment failure may simply be due to non-adherence to therapy or insufficient duration of treatment prior to event. However, despite the limitation of documentation of order of drug therapy initiation, the effects on the bisphosphonate class of therapy by PPIs are sufficiently large enough in this post-hoc analysis to see a reasonable trend on effect of PPIs, and when combined with other studies the results should add to caution in the use of the combination of treatments, in addition to the precautions from the oral bisphosphonate induced oesophagitis and gastritis. A recent review of drug induced osteoporosis recommends avoidance of PPI therapy with bisphosphonates, with consideration for change to lower potency histamine-2 receptor antagonists as an alternative

treatment option^[24].

Unlike the study limitation in evaluation of PPI impact on osteoporosis treatment success, the study size was significantly greater than the one used in the past for evaluation of the use of the FRAT, and provides a better reflection on the use of the tool across an entire healthcare service.

CONCLUSION

This post-hoc analysis of PRO-OSTEO Extend 1 indicates that there is a large prevalence of medical and medication-related risk factors for falls and osteoporosis, with an average of more than 3 drugs per patient that contribute to the risk of falls. The analysis also indicates that the medication-related falls risk on completion of the FRAT is significantly underestimated, and that the use of the falls assessment tool is lower than previously reported among a high risk population with significant comorbidity burden. Proton pump inhibitor use was associated with greater fracture rates and trended towards bisphosphonate treatment failure, and as such should be reviewed in both hospital and community settings. Both of these outcomes could be improved through liaison with hospital pharmacists.

Disclosure summary: This study was funded through the Roche Research Grant on ‘Safety and Quality’-ROC1301 via the Society of Hospital Pharmacists of Australia.

ACKNOWLEDGMENTS

Sarah Chao (Co-investigator and Pharmacy Manager Rehabilitation, Aged and Palliative Care Services at Peninsula Health), Dr. Steven Morris (former Director of Endocrinology at Peninsula Health), Skip Lam (Director of Pharmacy at Peninsula Health), Ben Leung (Deputy Director of Pharmacy at Peninsula Health) and Alice

Lam (Senior Clinical Pharmacy Services Manager) for the support provided in organising and conducting this study.

CONFLICT OF INTERESTS

The authors declare no conflicts of interest.

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