

1 **Abstract**

2 *Introduction*

3 Osteoporosis is a common condition among the elderly population, and is associated with an  
4 increased risk of fracture. One of the most common fragility fractures involve the distal radius,  
5 and are associated with risk of subsequent fragility fracture. Early treatment with  
6 bisphosphonates has been suggested to decrease the population hip fracture burden. However,  
7 there have been no prior economic evaluations of the routine treatment of distal radius fracture  
8 patients with bisphosphonates, or the implications on hip fracture rate reduction.

9 *Methods*

10 Age specific distal radius fracture incidence, age specific hip fracture rates after distal radius  
11 fracture with and without risendronate treatment, cost of risendronate treatment, risk of atypical  
12 femur fracture with bisphosphonate treatment, and cost of hip fracture treatment were obtained  
13 from the literature. A unique stochastic Markov chain decision tree model was constructed from  
14 derived estimates. The results were evaluated with comparative statistics, and a one-way  
15 threshold analysis performed to identify the break-even cost of bisphosphonate treatment.

16 *Results*

17 Routine treatment of the current population of all women over the age of 65 suffering a distal  
18 radius fracture with bisphosphonates would avoid 94,888 lifetime hip fractures at the cost of  
19 19,464 atypical femur fractures and \$19,502,834,240, or on average \$2,186,617,527 annually,  
20 which translates to costs of \$205,534 per hip fracture avoided. The breakeven price point of  
21 annual bisphosphonate therapy after distal radius fracture for prevention of hip fractures would  
22 be approximately \$70 for therapy annually.

23 *Conclusion*

24 Routine treatment of all women over 65 suffering distal radius fracture with bisphosphonates  
25 would result in a significant reduction in the overall hip fracture burden, however at a substantial  
26 cost of over a \$2 billion dollars annually. To optimize efficiency of treatment either patients may  
27 be selectively treated, or the cost of annual bisphosphonate treatment should be reduced to cost-  
28 effective margins.

29

30 **Introduction**

31 Osteoporosis is a common condition among the elderly, and has an increasing prevalence due to  
32 the growing elderly population. Over 50% of men and women over the age of 80 meet  
33 diagnostic criteria for osteoporosis. (1) The disease burden of osteoporosis manifests itself as  
34 fragility fractures, which poses both significant social and economic implications. (2-4) One of  
35 the most common fragility fractures involve the distal radius, which is often the index fracture  
36 among patients suffering from osteoporosis. (5,6) Prior fracture of the distal radius is associated  
37 with significant increased risk of subsequent fragility fracture. (3,7-11)

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39 Bisphosphonates have emerged as a treatment for fragility fracture prevention in osteoporotic  
40 patients. Bisphosphonate therapy has demonstrated promise of significantly reducing the rate  
41 fractures in high risk patients, and in the appropriate patients can play an important role in long-  
42 term management of osteoporosis. (12-16) Early initiation of treatment with bisphosphonates  
43 after fragility fracture has been suggested as a means of population hip fracture burden reduction.  
44 (17-19) Some studies have suggested that broad utilization of bisphosphonates in the elderly and  
45 routine use after fragility fractures is cost effective. (12,20) In particular, distal radius fractures  
46 have been targeted as a point of intervention for osteoporosis treatment. (8,21) However, there  
47 have been no prior economic evaluations of the routine treatment of distal radius fracture patients  
48 with bisphosphonates, and the implications on hip fracture rate reduction.

49

50 **Methods**

51 *Overview*

52 We evaluated the economic implications of routine prescription of risendronate after distal radius

53 fracture. We utilized a Markov chain cohort decision model based on outcomes and state  
54 transition probabilities obtained from the literature. Markov modeling allows the ability to  
55 follow a cohort or single patient through different states of health over fixed intervals of time,  
56 where the patient may either stay in a given health state or transition to another one, accruing  
57 outcomes at each interval. (22,23) The decision analysis was conducted with Monte Carlo  
58 simulation with cycle length of 1 year of a cohort representative of the US population  
59 distribution using TreeAge Pro (TreeAge Pro 2013, TreeAge Software, Williamstown, MA).  
60 Monte Carlo simulations, or stochastic simulations, rely on repeat sampling of probabilities to  
61 obtain distributions of outcomes; using this method with a Markov chain decision model allows  
62 simulation of individual patients across the model, incorporating variability at each point of  
63 probability and providing representative cohort wide outcomes. (24)

64

#### 65 *Data*

66 Literature estimates of age specific distal radius fracture incidence and age specific hip fracture  
67 rates after distal radius fracture with and without risendronate treatment were obtained.  
68 (9,15,25,26) The risk of atypical femur fracture with bisphosphonate treatment were also  
69 obtained. (27)

70

71 The direct costs of hip fracture management were from the average reimbursements for DRG  
72 482 and CPT 27245 obtained from public Medicare databases, and anesthesia reimbursements  
73 for CPT 01230 for a one hour case from the Medicare pricer. The cost of risendronate treatment  
74 was obtained from the literature.

#### 75 *Model*

76 A unique stochastic Markov chain decision tree model was constructed from derived estimates.  
77 The tree was analyzed with a modified Monte Carlo simulation of a cohort of women 65 and  
78 older based of 2012 US population estimates. (28) The results were evaluated with comparative  
79 statistics, and a one-way threshold analysis performed to identify the break-even cost of  
80 bisphosphonate treatment.

81

## 82 **Results**

83 Our model predicts 357,656 lifetime hip fractures after incidence of distal radius fracture in the  
84 cohort of all females aged over 65 in the US. In the same cohort of patients routinely treated  
85 with bisphosphonates after distal radius fracture, the number of hip fractures was predicted at  
86 262,767 over the lifetime of the cohort, and was also associated with 19,464 atypical femur  
87 fractures (Figure 1).

88 The direct costs of hip fractures associated with routine non-treatment of osteoporosis after distal  
89 radius fracture was \$4,165,256,788 over the lifetime of the cohort, or \$466,131,380 on average  
90 annually. The direct costs of hip fractures, atypical fractures, and routine use of bisphosphonates  
91 over the lifetime of the same cohort was \$23,668,091,028, or \$2,652,748,908 on average  
92 annually (Figure 2). The difference in cost is significant at  $\alpha=0.95$ .

93

## 94 *Sensitivity Analysis*

95 One way sensitivity analysis was performed varying the cost of bisphosphonates to identify the  
96 threshold at which routine bisphosphonate use after distal radius fracture became cost neutral.  
97 We found that the breakeven price point of annual bisphosphonate therapy after distal radius  
98 fracture for prevention of hip fractures would be approximately \$70 for therapy annually.

**100 Discussion**

101 Osteoporosis is a population health concern that particularly with the growing elderly population  
102 has tremendous clinical and economic implications. (2,3) Bisphosphonate therapy has been  
103 suggested as a means of helping manage the burden of fragility fractures in the elderly. Despite  
104 their beneficial impact on the prevention of fragility fractures, bisphosphonates are also  
105 associated with rare but concerning atypical femoral shaft fractures. (27,29,30) While these  
106 fractures occur sporadically, they do offset the disease and economic benefits that may be  
107 accrued from avoiding fragility fractures. Furthermore bisphosphonate therapy in and of itself  
108 can be expensive. Utilization of bisphosphonates in post-menopausal women with DEXA  
109 positive osteoporosis is considered to be cost effective, and even more aggressive routine  
110 utilization of bisphosphonates after index fragility fracture has been suggested. (8,16,21)

111

112 Here we present the first economic model evaluating wide-spread utilization of bisphosphonate  
113 therapy after distal radius fracture. Routine treatment of the current population of all women over  
114 the age of 65 suffering a distal radius fracture with bisphosphonates would avoid 94,888 lifetime  
115 hip fractures at the cost of 19,464 atypical femur fractures and \$19,502,834,240, or on average  
116 \$2,186,617,527 annually, which translates to costs of \$205,534 per hip fracture avoided. So  
117 while significant risk reduction of hip fractures may be achieved with bisphosphonate use, this  
118 comes at a significant cost. We found the primary driver of the economic imbalance with routine  
119 bisphosphonate utilization in our model is the cost of the therapy itself, with some contribution  
120 from the incidence of atypical femur fractures. Driving the cost of therapy down towards the  
121 breakeven point of \$70 annually would help avoid excess cost. Also selecting patients for

122 therapy that may be at lower risk for atypical femur fracture, i.e. with anatomy consistent with  
123 larger neck-shaft angles, may reduce the consequent burden of “bisphosphonate fractures.”  
124 However given the significant excess cost per fracture prevented, we would not recommend  
125 routine prescription of bisphosphonate therapy after distal radius fracture, but instead follow-up  
126 with DEXA for evaluation of osteoporosis status prior to any pharmacological therapy.  
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128 **References**

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