Modeled cost impact of persistence with bisphosphonate therapy for women with postmenopausal osteoporosis

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INTRODUCTION

In the US, 10 million individuals have osteoporosis while an additional 34 million have low bone mass; 68% are women.[1] Osteoporosis is responsible for more than 1.5 million fractures each year in the US and annual direct expenditures (hospital and nursing home care) are estimated at US$14 billion.[1] Bisphosphonates are currently the most widely used drugs for osteoporosis. Most clinical trials of bisphosphonates demonstrate reduction of fracture risk at 1 year, suggesting that a minimum 1 year of therapy is required to achieve statistically and clinically significant reductions in fracture rate. Patient persistence with bisphosphonates is therefore important if therapy is to yield a clinical benefit (prevent fractures and chronic disability) in patients with osteoporosis. Previous studies have shown that persistence with weekly bisphosphonates is better than with daily dosing regimens yet >50% of patients on the weekly regimen do not persist on therapy at the end of 1 year.[2,3] Previous cost-effectiveness (CE) analyses of bisphosphonate therapy have included limited information on important issues such as the impact of treatment persistence.[4,5] We developed a model to estimate CE of treatment for women with established osteoporosis when persistence was improved.

METHODS

- Markov Model, using 10-year time horizon, up to 5 years of therapy (**Figure 1; Appendix 1**).
- Perspective of the payer.
- Postmenopausal women aged ≥50 years with prevalent radiologic vertebral deformity and hip bone mineral density T-score ≤–2.5.
- Vertebral fracture risk reduction 43%, beginning after 1 year.
- Non-vertebral fracture (hip and wrist) risk reduction 18%, beginning after 1 year.
- Waning fracture benefit following therapy discontinuation based on expected hip bone density loss (0.54%/year).
- Yearly drug cost = US$780 wholesale acquisition cost for weekly bisphosphonate.
- Direct costs for health resources for fracture treatment estimated from literature, discounted at 3% yearly. Utilities derived from the literature, discounted at 3% yearly.
- Baseline persistence: 36% at 1 year, 24% at 2–5 years.[3]
- Transition probabilities based on literature, accounting for impact of increasing age, prior fracture, and mortality.
- Comparators
  - bisphosphonate therapy persistence reported in managed care setting (usual)[3]
  - bisphosphonate therapy with 10% absolute improvement in persistence over usual (increased).
- Sensitivity analyses
  - age <65 years vs ≥65 years
  - absolute improvement in persistence varying from 0–50% above usual.

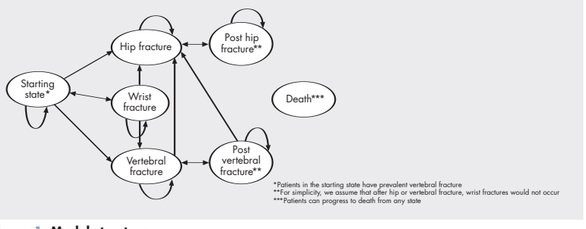

Figure 1. Model structure.

RESULTS

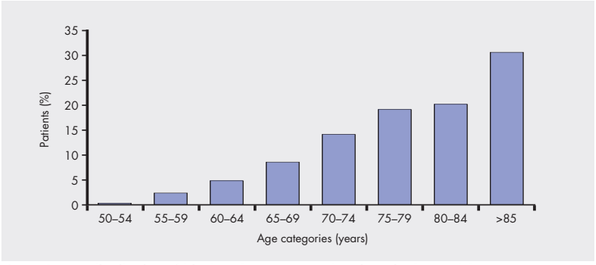

Figure 2. Age distribution of bisphosphonate-treated patients in the model.

- The analysis population was elderly, with a median age of 80 years (**Figure 2**).

Table 1. Fracture and cost per patient.

Outcome	Usual	10% increased persistence
Number of fractures per 1,000 patients treated		
Hip	151	148
Vertebral	238	227
Wrist	73	72
All	462	447
Average costs per patient treated (US$)		
Drug	1,062	1,418
Fracture care	5,841	5,727
Total	6,903	7,146

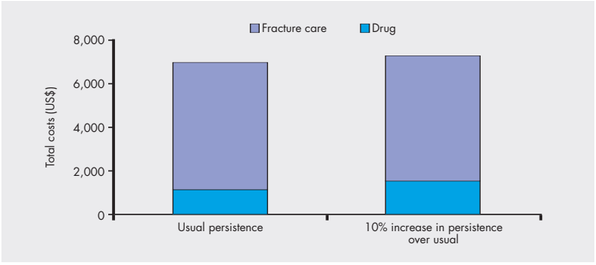

Figure 3. Total healthcare costs per bisphosphonate-treated patients.

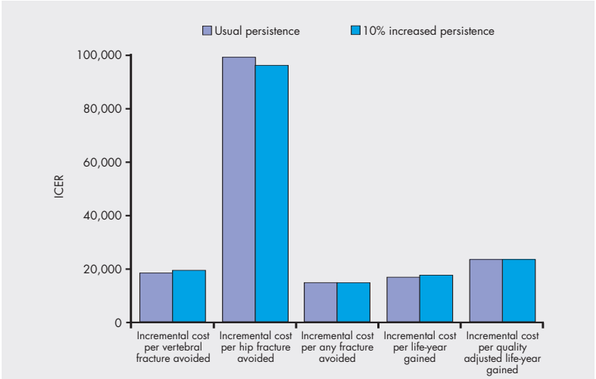

Figure 4. ICERs for selected endpoints.

- The incremental cost-effectiveness ratios (ICERs) for selected endpoints were similar with 10% improved persistence and with usual persistence (**Figure 4**).

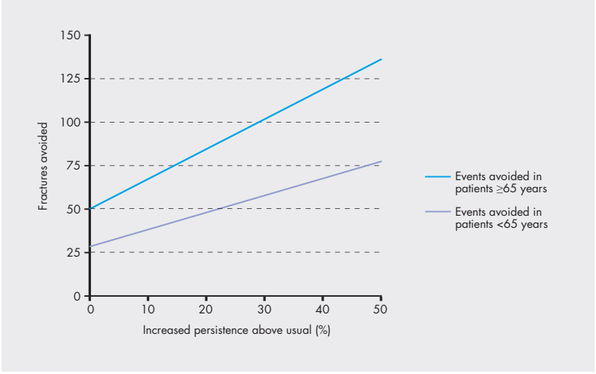

Figure 5. Sensitivity analyses: fractures avoided per 1,000 patients as persistence increases above usual.

- A greater fracture benefit is seen with greater persistence; the benefit is greatest among the elderly (**Figure 5**).

DISCUSSION

- Based on treating a population of high risk women (T-score <–2.5 and previous vertebral fracture)
  - a conservative improvement in persistence of 10% was selected to approximately match differences observed for weekly bisphosphonate regimens compared to daily dosing[2,3]
  - small increments in persistence have noted effects on numbers of fractures averted
  - increased drug costs due to increased persistence are largely offset by reduced numbers of fractures and their attendant costs
  - thus, an improvement in persistence with bisphosphonate therapy can result in 3.2% fewer fractures with little economic impact to payers (3.5% greater cost)
  - within our model's parameters, improved persistence reduces incremental costs per hip fracture avoided and does not substantially change incremental costs per vertebral fracture avoided or other ICERs
  - greater than 10% improvements in persistence may positively impact patient outcomes and ICERs; further investigation is needed.

CONCLUSIONS

- Greater clinical benefit can be expected when persistence is improved.
- Increased persistence maintains acceptable ICERs, by US standards.
- Bisphosphonate regimens that potentially increase persistence are warranted.

REFERENCES

1. National Institutes of Health. Osteoporosis and Related Bone Diseases National Resource Center. Accessed November 12, 2004.
2. Cramer JA, et al. J Bone Miner Res 2004;19(Suppl. 1):S448.
3. Utilization characteristics associated with bisphosphonate therapy: Ingenix II. Data on file – Roche.
4. Johnell O, et al. Pharmacoeconomics 2003;21:305–14.
5. Grima DT, et al. Pharmacol Ther 2002;27:448–55.

Appendix 1. Functional parameters.

Parameter	Source
Bisphosphonate efficacy	Kanis JA, et al. Health Technology Assessment 2002;6:29
Residual effect of therapy	Bagger YZ, et al. Bone 2003;33:301–7
Population demographics	2002 US Census; US Census Bureau 2002
Initial transition probabilities	Black DM, et al. J Bone Miner Res 1999;14:821–8 Kanis JA, et al. Osteoporos Int 2000;11:669–74 Kanis JA, et al. Osteoporos Int 2001;12:356–61
Fracture transition probabilities	Kloztbeucher CM, et al. J Bone Miner Res 2000;15:721–39
Mortality probabilities	US National Vital Statistics Reports, 2003 Johnell O, et al. Osteoporos Int 2004;15:38–42
Utilities	Brazier JE, et al. Osteoporos Int 2002;13:768–76 Tosteson ANA, et al. Osteoporos Int 2001;12:1042–9
Drug costs	Wholesale Acquisition Cost (WAC); Redbook 2005
Medical care costs	Eddy DM, et al. Osteoporos Int 1998;(Suppl. 4) (Costs adjusted to 2004 dollars using the Medical Consumer Price Index)

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