# PREDICTORS OF DISCONTINUITY AND FAILURES OF THERAPY WITH BISPHOSPHONATES: RESULTS FROM A LARGE POPULATION-BASED COHORT STUDY

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**Background**. Randomised clinical trials (RCT) have consistently shown that long-term treatment with bisphosphonates (BP) improves bone mineral density and reduces the risk of fracture. Patients enrolled in RCT, however, achieve very high, and almost optimal, compliance, while in the clinical practice compliance is really impaired. Recent observational studies have reported rates of one-year BP refill compliance (RC) ranging from 44% to 71%. Poor RC resulted in suboptimal improvement of bone density, in increasing risk of fracture, and in worsening the cost-effectiveness profile of therapy. **Methods**. All the 11,863 women resident in Lombardy aged 45 years or over who during 2003 received for the first time at least one prescription for BP entered into the study and were followed until December 2005 recording both bisphosphonate dispensations and hospitalisations for fractures and gastrointestinal (GI)-related events. Multi-state models, with in-treatment and treatment-free periods, as transient states, and both fractures and GI-related events, as competing causes of failure, were fitted to the data. The effect of several covariates on transition rates between states were estimated. **Results**. At entry, the included women had mean age of 72 years. Alendronate administered once-weekly was the main first-choice treatment. In average, RC was only 27%. Significant negative prognostic factors for treatment discontinuation were use of alendronate at once-daily dosing, and low RC during follow-up. The risk of fracture was significantly higher for women who at cohort entry were aged more than 75 years and for those who already experienced at least an episode of fracture. Negative prognostic factors for fracture occurrence during follow-up were use of corticosteroids, switching between drugs, low RC and high rate of BP discontinuation. Compared with women who were exposed to once-weekly dosing, those who experienced once-daily dosing had a two-fold risk of GI-related events. **Conclusions**. Persistent use of bisphosphonates decreases the risk of both treatment discontinuation and osteoporotic fractures in clinical practice. The extension of the dosing regimen from once-daily to once-weekly reduces the risk of treatment discontinuation, improves the safety profile of bisphosphonates, and does not affect the efficacy of therapy.