Impact of Compliance and Other Factors on Fracture Risk for Osteoporosis in Postmenopausal Women in Hungary

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INTRODUCTION

- Osteoporosis is a condition characterized by low bone mass & microarchitectural deterioration of bone tissue and thus an increase in bone fragility and the risk of fractures.
- The economic burden of osteoporosis is substantial and costs are expected to increase in the future due to higher incidence of fractures and demographic changes.
- Patients with prior fractures face an increased risk of sustaining subsequent fractures & the goal of intervention is hence to prevent the first fracture (1), mainly hip & vertebral fractures that are associated with the largest costs & reduction in quality of life for patients (2).
- However, compliance with osteoporosis drugs is frequently very low, leading to increased fracture risk.

OBJECTIVE

- Examine the factors associated with fracture risk in women with postmenopausal osteoporosis (PMO) in Hungary, with key interest in compliance.

METHODS

Study Population

- This retrospective analysis used patients' attendance data from the National Health Insurance Fund Administration (NHIFA) containing detailed provision data (medicine, out- and inpatient services) from the whole Hungarian population.
- Subjects were females, ≥50 years old with a diagnosis of osteoporosis (ICD-10 codes, M80 or 81), who started an osteoporosis drug prescription between Jan 2004 and Jan 2011.

Study Design

- The relationship between all factors (covariates) & fracture risk was assessed using Cox proportional hazard models extended to model recurrent events with the Andersen-Gill method (i.e. considering multiple fracture events & not only first fracture) and estimating 95% confidence intervals.
- Covariates, determined based on a 36-month period before the index date (i.e. the start of the analysis period), were:
  1. **Compliance:** 2 models were used: MPR was divided a) into 2 categories, compliant (MPR≥80%) and non-compliant (MPR<80%) and b) into 3 categories, compliant to oral drugs (MPR≥80%), compliant to injectable drugs (MPR≥80%) and non-compliant (MPR<80%), with non-compliant being the reference category in both models
  2. **Age:** 10-year age groups using the 50-59 age group as the reference category
  3. **Diagnosis cohorts:** Osteoporosis diagnosis was grouped into primary & secondary prevention (i.e. patients with diagnosis of osteoporosis with no prior fracture & with pathological fracture, respectively), with primary prevention being the reference category
  4. **Co-medication:** 3 groups were used: no co-medication, 1 other therapy and 2 or more other therapies, with no co-medication being the reference category
  5. **Prior fractures:** Prevalence of fractures at index date, with no prior fracture being the reference category
  6. **Fractures during analysis period:** Prevalence of fractures during the analysis period in patients with no fractures at the time of the analysis vs that in patients with ≥1 fracture

RESULTS

- 223,068 patients were analysed and 128,610 matched inclusion criteria for the fracture risk analysis, with 139,604 observations (no. of index dates in the analysis).
- Characteristics of the patients at these index dates are described in **Table 1**.

Table 1. Patient characteristics used in the analysis

	No. of observations (%)
Age (years)	
Total	139,604 (100.0)
50-59	29,634 (21.2)
60-69	45,706 (32.7)
70-79	44,593 (32.0)
80-89	18,708 (13.4)
≥90	963 (0.7)
Compliance	
Non-compliant	74,956 (53.7)
Compliant	64,648 (46.3)
Diagnosis cohorts	
Primary	94,048 (67.4)
Secondary	45,556 (32.6)
Co-medication	
No co-medication	82,507 (59.1)
With 1 co-medication	39,079 (28.0)
With ≥2 co-medications	18,018 (12.9)
Prior fractures	
No prior fracture	115,097 (82.4)
With 1 fracture	17,585 (12.6)
With 2 fractures	4,513 (3.2)
With ≥3 fractures	2,409 (1.7)

- **Table 2** summarizes the fracture risk analysis for each covariate.
- Patients older than 70 years had an increase in fracture risk of 31% for the 70-79 age group and 76% for the 80+ age group compared to patients aged 50-59 years old.
- Prior fractures were associated with 81% and with 215% increased risks of a new fracture in patients with 1 and 2+ prior fractures, respectively, compared with patients with no prior fractures.
- A relationship was found between any co-medication and fracture risk, with a 15% increase with 1 co-medication and a 36% increase with 2+ co-medications compared to none.

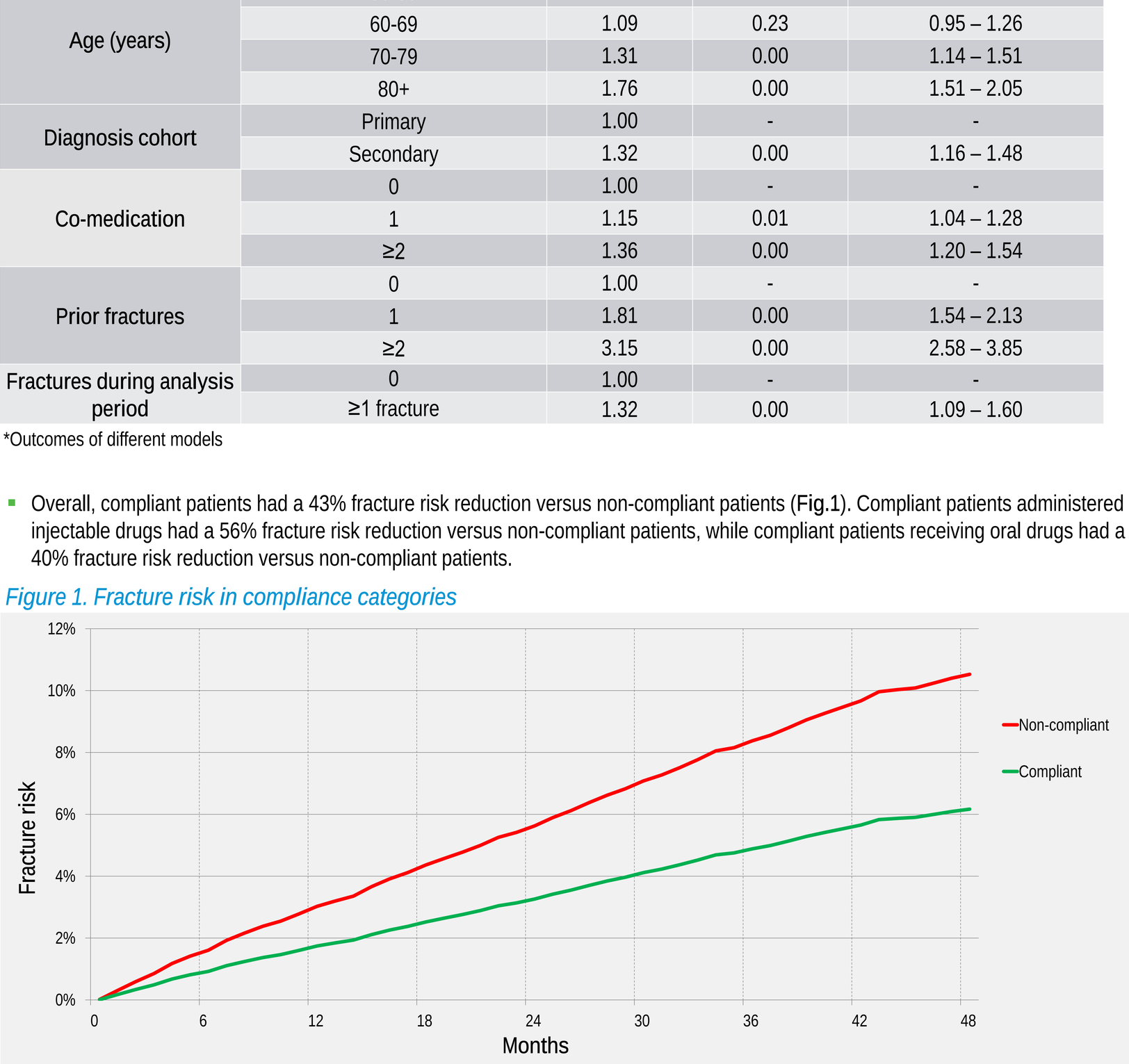
Table 2. Relative fracture risk by each covariate using the Andersen-Gill method

Covariate	Category		RR	p-value	95% Confidence interval
Compliance	Non-compliant		1.00	-	-
	Compliant	All drugs	0.57	0.00	0.49 – 0.66
		Oral drugs*	0.60	0.00	0.51 – 0.71
		Injectable drugs*	0.44	0.00	0.30 – 0.64
Age (years)	50-59		1.00	-	-
	60-69		1.09	0.23	0.95 – 1.26
	70-79		1.31	0.00	1.14 – 1.51
	80+		1.76	0.00	1.51 – 2.05
Diagnosis cohort	Primary		1.00	-	-
	Secondary		1.32	0.00	1.16 – 1.48
Co-medication	0		1.00	-	-
	1		1.15	0.01	1.04 – 1.28
	≥2		1.36	0.00	1.20 – 1.54
Prior fractures	0		1.00	-	-
	1		1.81	0.00	1.54 – 2.13
	≥2		3.15	0.00	2.58 – 3.85
Fractures during analysis period	0		1.00	-	-
	≥1 fracture		1.32	0.00	1.09 – 1.60

*Outcomes of different models

- Overall, compliant patients had a 43% fracture risk reduction versus non-compliant patients (**Fig.1**). Compliant patients administered injectable drugs had a 56% fracture risk reduction versus non-compliant patients, while compliant patients receiving oral drugs had a 40% fracture risk reduction versus non-compliant patients.

Figure 1. Fracture risk in compliance categories



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DISCLOSURE

- This study was sponsored by Amgen (Europe) GmbH and GlaxoSmithKline.
- M. Intorcia and E. Psachoulia are employees and shareholders of Amgen; P. Lakatos has received consulting, research and speaker fees and grants from many companies with drugs for bone diseases, including Amgen; E. Kovács, Z. Lang and E. Tóth are employees of Healthware Ltd and conducted this research under contract to Amgen.

CONCLUSIONS

- Age, any co-medication and prior fractures were associated with an increased relative risk of fracture.
- Compliance, however, was associated with protection against fracture (reduction of relative fracture risk), with injectable drugs providing greater risk reduction than oral drugs.
- Main limitation of this analysis is that it was not possible to adjust for some important confounding factors, e.g. BMD T-scores, as this information was not available.

ISPOR 15th Annual European Meeting, Berlin, Germany; November 3–7, 2012