

Author and year	Sources searched and dates; types of studies	Measures of compliance and persistence	Bisphosphonates covered	Adherence results	Persistence results
Cramer 2007 ¹²⁷	<p>MEDLINE for citations of relevant articles accessible between January 1998 and May 2006</p> <p>Studies were required to contain information of medication-taking practices relating to bisphosphonates and to contain at least one measure of persistence or compliance</p>	<p>Compliance (defined as the extent to which a patient acts in accordance with the prescribed interval and dose as well as dosing regimen) was measured as the medication possession ratio (MPR). This is the number of days' supply received over the length of the follow up.</p> <p>Persistence (defined as the accumulation of time from initiation to discontinuation of therapy) was measured as the number of days of possession without a gap in refills, and the percentage of patients.</p>	<p>Alendronate, risedronate</p> <p>14 reports</p>	<p>Compliance, ranged from 0.59 to 0.81. When comparing compliance with weekly and daily bisphosphonates, the mean Medication Possession Ratio (MPR) was consistently higher for weekly versus daily therapy (0.58 to 0.76 versus 0.46 to 0.64 for patients receiving weekly and daily bisphosphonate therapy respectively).</p>	<p>The percentage of patients persisting with therapy for 1 year ranged from 17.9% to 78.0%. Persistence was also improved in patients receiving weekly bisphosphonates, assessed by both length of persistence (194 to 269 days [weekly] and 134 to 208 days [daily]) and percentage of persistent patients at the end of the follow-up period (35.7% to 69.7% [weekly] and 26.1% to 55.7% [daily]).</p>
Imaz 2010 ¹²⁸	<p>Database of Abstracts of Reviews of Effects (DARE); the Health Technology Assessment Database, the International Science Index web of knowledge, Cochrane, Embase and MEDLINE between May 1, 2006 and March 22, 2009.</p>	<p>Two meta-analyses were performed to obtain the mean of persistence days and the mean MPR, after 1 year of follow-up.</p>	<p>Mainly Alendronate and risedronate. Two studies included ibandronate and two studies HRT</p> <p>15 studies</p>	<p>The pooled MPR mean was 66.9% (95% CI 63.3 to 70.5; five studies) at one year follow-up.</p>	<p>The pooled persistence mean was 184.1 days (95% CI 163.9 to 204.3; five studies) at one year follow-up.</p>

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Kothawala 2007 ¹²⁹	PubMed and Cochrane databases of English-language articles published from January 1, 1990, to February 15, 2006.	Persistence - how long a patient receives therapy after initiating treatment; compliance how correctly, in terms of dose and frequency, a patient takes the available medication; and adherence - a measure that assesses both persistence and compliance.	Twenty-four studies including 14 in bisphosphonates only, but not reported what type.	Pooled adherence rates decreased from 53% (95% CI, 52%-54%) for treatment lasting 1 to 6 months to 43% for treatment lasting 7 to 12 months (95% CI, 38%-49%) or 13 to 24 months (43%; 95% CI, 32%-54%). The pooled refill compliance estimate was 68% (95% CI, 63%-72%) for treatment lasting 7 to 12 months and 68% (95% CI, 67%-69%) for treatment lasting 13 to 24 months. The pooled self-reported compliance rate was 62% (95% CI, 48%-75%) for treatment lasting 1 to 6 months and 66% (95% CI, 45%-81%) for treatment lasting 7 to 12 months.	The pooled database-derived persistence rate was 52% (95% confidence interval [CI], 44%-59%) for treatment lasting 1 to 6 months, 50% (95% CI, 37%-63%) for treatment lasting 7 to 12 months, 42% (95% CI, 20%-68%) for treatment lasting 13 to 24 months, returning to 52% (95% CI, 45%-58%) for treatment lasting more than 24 months. Pooled

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Lee 2011 ¹³⁰	MEDLINE, EMBASE, Biosis and Derwent Drug File for publications (January 1979 to January 2009)	Since adherence was difficult to accurately quantify, preference, compliance and persistence were evaluated.	Alendronate, risedronate 10 studies	Patients' preference and adherence at 12 months were higher with weekly over daily bisphosphonates ($\geq 84\%$ preference for weekly, medication possession ratios (MPR) 60–76% vs. 46–64%; MPR reported for oral bisphosphonates were 68–71% at 12 months. At 2 years, only 43% of patients had MPR $\geq 80\%$ for daily and weekly bisphosphonates	Persistence 12 months 43.6–69.7% weekly vs. 31.7–55.7% daily
Lloyd-Jones 2006 ¹¹⁶	(MEDLINE, EMBASE, CINAHL, Biosis, Cochrane Central Register of Controlled Trials, Science Citation Index, Social Sciences Citation Index) to April 2006		Alendronate, risedronate Seventeen relevant studies were identified.	The most relevant evidence for persistence with oral bisphosphonate therapy comes from the UK PEM studies of alendronate and risedronate. 2920 of the 11,916 patients prescribed alendronate by general practitioners (24.5%) appeared to have discontinued	Evidence from one study in 812 women prescribed alendronate and followed for a mean of ten months, 20.8% had discontinued at two months, and 46.1% by ten months.

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				therapy within a year. The two most common reasons for stopping treatment were dyspeptic conditions (756, 6.3% of the total cohort) and noncompliance (365, 3.0% of the total cohort). 8,245 of 11,742 patients (70.3%) whose treatment status was recorded were still being prescribed risedronate after 6 months	
Mikyas 2014 ¹³¹ Review of studies in men	PubMed, MEDLINE, EMBASE, and Cochrane databases were searched 1 January 1998 to 30 June 2012	Adherence included related terms, such as persistence and compliance;	Alendronate and other treatments 18 studies in men	The percentage of males adherent to bisphosphonates [medication possession ratio (MPR)>0.8] over a 1-year period ranged from 32% to 64%	
Vieira 2013 ¹³²	Systematic review of articles on BPs adherence for treatment of osteoporosis, indexed on MEDLINE (via PubMed) databases, from inception of databases until January 2013	27 studies met the eligibility criteria. Identified studies covered a wide range of aspects regarding adherence and associated factors,	Alendronate, risedronate, ibandronate, zoledronate	Studies in treatments of interest; Cohort study 775 taking zoledronate; 275 taking ibandronate; the proportion of patients with high adherence for the zoledronate and the 2 ibandronate cohorts was 62.8% versus 36.0% and 33.3%. But approximately 30% of patients taking zoledronate did not receive a second infusion.	

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		<p>adherence and fracture, adherence and BPs dosage. The studies were mostly observational. Data not pooled</p>			<p>Cohort study 22,363 new users of an oral BP (alendronate, risedronate, ibandronate): Patients receiving oral BPs on a monthly basis showed higher rates of medication compliance. Overall compliance 43%</p> <p>Cohort study 451,113 new patients: alendronate, etidronate, risedronate: Persistence with therapy declined from 63% at 1 year to 46% at 2 years and 12% at 9 years.</p> <p>RCT 341 postmenopausal women taking -weekly alendronate or monthly ibandronate: MPR ranged from 93% to 100%.</p> <p>Retrospective observational: 2,990 women taking-weekly (alendronate or risedronate) or monthly ibandronate: Patients treated with a monthly regimen were 37% less likely to be non-persistent and were more compliant, with a 5% higher absolute MPR, than women treated with weekly regimens.</p> <p>Cohort study 32,804 patients taking weekly risedronate or weekly alendronate (brand or generic): Patients initiated on weekly oral generic alendronate showed a statistically significant lower persistence to BP therapy compared to patients initiated on weekly oral branded risedronate and weekly oral branded alendronate</p>