
Systematic review and meta-analysis of real-world adherence to drug therapy for osteoporosis

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CRD summary

This review assessed patient adherence to drug therapy for osteoporosis. The authors concluded that up to one half of patients fail to take medication as directed and this pattern occurred shortly after treatment initiation. Variations within the included studies, unclear study quality, and other methodological limitations in the review process, mean that the reliability of this conclusion is questionable.

Authors' objectives

To assess patient adherence to drug therapy for osteoporosis in real-world settings.

Searching

PubMed and the Cochrane Library were searched from January 1990 to February 2006 for published English-language studies. Search terms were reported. The reference lists of included papers were scanned to identify further articles of interest.

Study selection

Observational studies assessing pharmacological drug adherence in patients with osteoporosis were eligible for inclusion in the review.

The outcomes of interest were grouped according to standardised definitions: persistence (how long a patient received therapy after initiating treatment); compliance (how correctly, in terms of dose and frequency, patients took their medication); and adherence (a combined measure of persistence and compliance).

In the included studies: bisphosphonates were the most frequently assessed drug; treatment duration ranged from one month to over 24 months; and a higher proportion of included patients were new users.

Two independent reviewers were involved in reviewing a 10% random sample of studies for inclusion in the review.

Assessment of study quality

The authors did not state that they assessed validity.

Data extraction

Persistence was measured as the cumulative percentage of patients who continued therapy over a set period of time, and from discontinuation rates. Data were derived from administrative databases and self report; these were analysed separately. Many studies measured persistence as a function of gap between refills.

Compliance data were extracted as the percentage of patients who reported following the dosing recommendations, or from pharmacy claims (refill compliance) that provided the mean percentage of doses available at a given time.

Adherence data were extracted as the percentage of patients achieving a predefined medication possession ratio threshold (80% or 66%). Estimates were presented along with 95% confidence intervals.

The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis

Outcome rates were pooled in a random-effects meta analysis. Sub-group analyses were conducted to explore the influence of treatment duration, medication type, dosing frequency, measurement method, baseline bone mineral

density, age, new versus prior users, and switching or restarting medications.

Results of the review

Twenty-four observational studies (n=384,242 patients) were included in the review.

Persistence: In six studies (n=106,961 patients), the pooled persistence estimate from administrative database information ranged from 52% (95% confidence interval (CI):44 to 59) for treatment lasting one to six months, to 42% (95% CI: 20 to 68) for treatment lasting 13 to 24 months, after which time the rate returned to 52% (95% CI: 45 to 58). Pooled estimates from self-reported data (13 studies, n=7,230 patients) were higher, ranging from 89% (95% CI: 77 to 95%) for treatment lasting one to six months, to 68% (95% CI: 60 to 75) for treatment lasting longer than 24 months. Self reported rates were lower amongst new users, and rates increased as the gap between refills widened over a period of 30 to 120 days.

Compliance: In seven studies (n=321,734 patients) the pooled refill compliance rate was 68% at both seven to 12 months (95% CI: 63 to 72) and at 13 to 24 months (95% CI: 67 to 69). The pooled estimate from self-reported data (four studies) was 62% (95% CI: 48 to 75) of patients following the recommended instructions within six months of starting treatment.

Adherence: In six studies (n=264,432 patients), the pooled estimate of patients (achieving an medication possession ratio higher than 66% (one study) and higher than 80% (five studies) as the measure of good adherence) ranged from 53% (95% CI: 52 to 54) for treatment lasting one to six months, to 43% (95% CI: 32 to 54%) for treatment lasting 13 to 24 months. Pooled adherence rates were lower amongst new users.

Subgroup analyses showed higher rates of persistence (using various measures) arising from bone mineral density testing, use of bisphosphonates, switch or restarting medication, and weekly dosing schedules. Increased refill compliance was also noted from bone mineral density testing, switching medications, and weekly dosing schedules.

Authors' conclusions

One third to one half of patients being treated with pharmacological drugs for osteoporosis did not take their medication as directed and this pattern occurred shortly after the initiation of treatment.

CRD commentary

This review addressed a clear question that was supported by broad, but potentially reproducible, inclusion criteria. The search strategy appeared to access some relevant sources, but this was largely limited to electronic databases of published English-language articles. It is possible that relevant studies may have been missed, and that publication and language biases may have been introduced. There was no reported assessment of study quality, so it was difficult to interpret the strength of the authors' conclusions. The transparency of the data extraction process was not clear, and the independent sampling of studies for inclusion in the review cannot fully rule out the possibility of errors and bias in the selection process. The authors acknowledged that there was variation amongst the included studies. Heterogeneity was not formally assessed, but some account was taken for variation in the chosen method of synthesis. The authors declared some potential conflicts of interest in terms of employment and consultancy services connected with the pharmaceutical industry. Their conclusions reflect the evidence presented, but due to the methodological limitations identified above, the extent to which the conclusions are reliable is unclear.

Implications of the review for practice and research

Practice: The authors stated that the implications of poor drug adherence in patients with osteoporosis means that increased risks of fractures and hospitalisations are likely.

Research: The authors stated that prospective trials are needed to assess the relationship between adherence and patient outcomes, using a combination of measures and longer term follow-up. Further research should also aim to standardise terms and definitions, allowing the effective comparison of interventions to improve patient adherence.

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