Clinical effectiveness of bisphosphonates for prevention of fragility fractures: a systematic review and network meta-analysis

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BACKGROUND

Osteoporosis is characterised by low bone mass and structural deterioration of bone tissue, with a consequent increase in susceptibility to fragility fracture. Fractures cause significant pain, disability and loss of independence and can be fatal.[1]

OBJECTIVE

To assess the relative efficacy of bisphosphonates (alendronate, risedronate, ibandronate and zoledronate) for the treatment of Osteoporosis using a network meta-analysis (NMA).

METHODS

- Systematic literature review conducted using PRISMA guidelines.

Outcome measures

- Number of vertebral, non-vertebral, hip and wrist fractures.
- Percentage change in femoral neck bone mineral density (BMD).

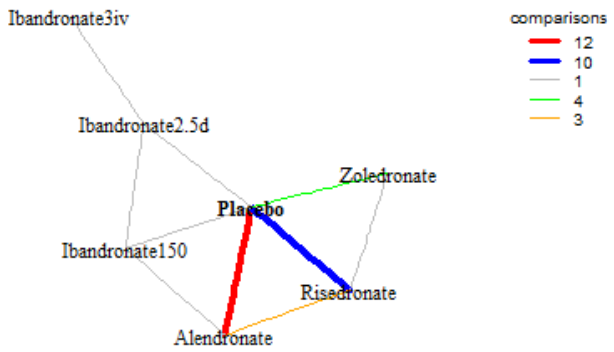
Statistical Analysis

- Bayesian network meta-analysis using WinBUGS [2] software .
- Random effects model to allow for potential heterogeneity in treatment effects between studies.
- Bisphosphonate class effect (treatment effects are assumed to arise from a common distribution).

RESULTS

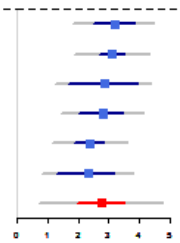
46 RCTs were identified. 27 RCTS provided fracture data and 35 RCTs provided BMD data for the network meta-analysis

Network of evidence (femoral neck BMD)



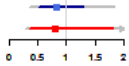
Femoral neck BMD

Treatment	TE *	(95% CrI)	rank †
Zoledronate	3.20	(2.51,3.85)	2(1,5)
Alendronate	3.11	(2.68,3.52)	2(1,4)
Ibandronate 3 mg iv	2.86	(1.69,3.94)	3(1,6)
Ibandronate 150 mg monthly	2.79	(2.04,3.48)	4(1,6)
Risedronate	2.36	(1.90,2.84)	5(3,6)
Ibandronate 2.5 mg daily	2.35	(1.31,3.18)	5(3,6)
Class effect	2.78	(1.97,3.51)	



Fracture outcomes

Treatment	HR	(95% CrI)	rank †
Vertebral			
Zoledronate	0.42	(0.29,0.55)	2(1,5)
Alendronate	0.45	(0.36,0.57)	3(1,5)
Ibandronate.2.5mg.daily	0.46	(0.34,0.64)	3(1,5)
Ibandronate.150.mg.monthly	0.46	(0.28,0.71)	3(1,5)
Risedronate	0.50	(0.39,0.64)	4(1,5)
Class effect	0.45	(0.21,0.97)	
Non-vertebral			
Risedronate	0.72	(0.54,0.89)	2(1,5)
Zoledronate	0.75	(0.61,0.90)	2(1,5)
Alendronate	0.80	(0.65,0.93)	3(1,5)
Ibandronate.150.mg.monthly	0.80	(0.53,1.36)	3(1,6)
Ibandronate.2.5.mg.daily	0.90	(0.67,1.35)	5(1,6)
Class effect	0.79	(0.39,1.64)	
Hip			
Alendronate	0.78	(0.44,1.28)	2(1,5)
Risedronate	0.81	(0.49,1.32)	2(1,5)
Ibandronate.150.mg.monthly	0.86	(0.43,2.00)	3(1,5)
Zoledronate	0.92	(0.55,1.61)	4(1,5)
Class effect	0.85	(0.39,1.85)	
Wrist			
Risedronate	0.76	(0.45,1.24)	2(1,4)
Ibandronate.150.mg.monthly	0.82	(0.41,1.89)	2(1,4)
Alendronate	0.83	(0.51,1.29)	2(1,4)
Class effect	0.81	(0.35,1.81)	



*TE represents the percentage change in BMD for a study of average duration (1.8 years).
†Median rank and 95% CrI.
Treatment effects and 95% CrI are plotted in blue, class effect in red.
95% prediction intervals (PrI) are plotted in grey.

CONCLUSIONS

- All treatments were associated with beneficial effects on fractures and femoral neck BMD relative to placebo.
- Ranking of treatments varied by outcome, although treatment effects were broadly similar within outcome.
- Meta-regression revealed no evidence of differential treatment effects with respect to age and gender.
- There was no evidence of inconsistency of evidence using a node-splitting approach.

REFERENCES

[1] World Health Organization. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis: Report of World Health Organization study group. WHO Technical Report Series 843. 1994.
[2] 4: Lunn DJ, Thomas A, Best N, Spiegelhalter D. WinBUGS – a Bayesian modelling framework: concepts, structure and extensibility. Statistics and Computing 2000; 10: 325-337.

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