

Health technology assessment in osteoporosis : new perspectives from adherence and preference studies

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Summary

Osteoporosis is a bone disease leading to increased fracture risk affecting more than one in three women aged over 60 years in western countries. With the rapid development of new anti-osteoporosis medications in a context of limited healthcare resources, it is important to help decision makers to make appropriate and efficient decisions about the use of these medications. Health technology assessment (HTA) aims to assess the medical, social, economic and ethical implications of health technologies, and is therefore extremely useful to inform and guide health policy decisions. In particular, economic evaluations that compare health technologies in terms of costs and outcomes are increasingly used to promote a more rational use of health resources. In recent years, non-adherence with osteoporosis medications has emerged as a critical obstacle in the treatment of osteoporosis but relatively few studies have been conducted to assess the economic implications of poor adherence and to estimate the effectiveness and potential economic value of programs to enhance adherence. To improve medication adherence, understanding the preferences of patients and addressing patients' concerns with treatment would be worthwhile.

The increasing burden of osteoporosis and major recent innovations in osteoporosis care, alongside continuing limitations in healthcare resources, justified further research into the health-economic aspects of treatment of osteoporosis. The aim of this dissertation was therefore to review economic evidence on the treatment of osteoporosis and to provide new perspectives from adherence and preference studies. More specifically, the first part of the thesis reviewed and critically appraised studies about the cost-effectiveness of drugs in postmenopausal women. The second part assessed the economic implications of poor adherence with anti-osteoporosis medications, estimated the potential economic value of improving adherence and reviewed the published literature about interventions to improve adherence. The last part, finally, evaluated the preferences of patients for osteoporosis medication attributes and established how patients trade between these attributes.

Chapter 2 of the thesis provides a general overview of HTA including economic evaluations and reviews the various aspects of HTA in osteoporosis, including epidemiology and burden of disease, and assessment of the cost-effectiveness of recent advances in the treatment of osteoporosis. Chapters 3 and 4 present systematic literature reviews and critical appraisal of cost-effectiveness analyses about different drugs in osteoporosis such as denosumab. These reviews suggest that osteoporotic drugs are generally cost-effective compared to no treatment in postmenopausal women aged over 60-65 years with low bone mass, especially those with prior vertebral fractures. We also observed that quality of reporting is still largely insufficient for several cost-effectiveness articles. In chapter 5, the importance of incorporating

medication adherence in cost-effectiveness analysis in osteoporosis was described, explained and justified.

The next two chapters focus on medication adherence. First, chapter 6 assessed the clinical and economic burden of non-adherence with oral bisphosphonates using a modelling approach. This analysis revealed that poor adherence may reduce the potential benefits of drug therapy observed in clinical trials by approximately fifty percent and doubles the cost per quality-adjusted life-years gained of these medications. In addition, this study suggests that interventions to improve medication adherence have the potential to increase efficiency in allocating healthcare resources. Chapter 7 reviewed and appraised published articles that tested adherence improvement programs, suggesting that several interventions (including education programs, monitoring/supervision, different drug regimens) could represent an effective way to improve adherence.

Finally, chapters 8 and 9 provided evidence on the preferences of patients for osteoporosis medications. Given the burden of poor adherence to oral regimens and the availability of new drug treatment with different routes and timing of administration, understanding the preferences of patients for new administration schemes could be useful for decision-makers and health professionals. In chapter 8, a qualitative research (using the nominal group technique method) was performed to identify most important attributes for drug treatment in osteoporosis. Based on this qualitative research, five important attributes were identified (effectiveness, side effects, mode and frequency of administration and cost) and hence included in the discrete-choice experiment (DCE). Chapter 9 reported the results of the DCE conducting in a sample of 257 Belgian women, revealing that patients have preferences for mode of administration (such as 6-month subcutaneous or oral monthly tablet) and that they are willing to pay or to give up some efficacy for their preferred treatment options. A substantial heterogeneity was also observed for most parameters underlining the importance of shared decision-making and taking into account individual preferences.

The findings of this dissertation can have several implications for decision making, clinical practice and future/further research. First, the review of economic evidence about anti-osteoporosis drugs could help decision makers to efficiently allocate healthcare resources. Second, this dissertation raises awareness about the urgent need to improve adherence among those patients that have deliberately chosen for a drug regimen, after having been well-informed on the pros and cons per treatment option, and the potential economic value of improving adherence. Decision makers and clinicians have to tackle the problem of poor adherence and set up interventions/programs to improve adherence. Third, information about patients' preferences may help physicians to improve patient satisfaction and adherence with

therapy while the substantial heterogeneity in patients' preferences for medication attributes highlights the importance to take into account individual preferences into shared decision-making to improve osteoporosis care. Finally, this dissertation could give several directions for future/further research including the importance to improve the quality of reporting of economic evaluations but also to incorporate medication adherence in cost-effectiveness analyses, the need to develop (cost-) effective interventions to enhance adherence, and the importance to understand and incorporate patients' preferences in clinical and policy decisions.