

For reprint orders, please contact: reprints@futuremedicine.com

The need for economic evaluation in osteoarthritis

“...with regard to the medico-economic pressure, it is essential to develop effective treatments and also efficient strategies.”

AGING
HEALTH

Osteoarthritis (OA) is the most common form of joint disease and the leading cause of pain and physical disability in older people. It is an important disease in our aging society and ranks among the top five causes of disability [1]. The condition is associated with a high health economic burden, especially with regard to direct and indirect costs, as well as loss of health-related quality of life [2,3].

The traditional management of OA is mainly symptomatic. At present, a lot of pharmacological, nonpharmacological or surgical treatments are available for patients with knee or hip OA [4–6]. Pharmacological treatments include acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs; i.e., traditional NSAID or COX-II inhibitor), or symptomatic slow-acting drugs (e.g., glucosamine sulfate, chondroitin sulfate and hyaluronic acid). Nonpharmacological treatments include exercises, physiotherapy, patient education or weight loss. Surgery includes joint replacement and osteotomy.

“Deciding which health and public interventions should be funded is an important task for society.”

The direct cost of some of these treatments can be substantial [7]. However, other costs, including the cost for the prevention or the treatment of an adverse event could be quite expensive. For example, co-prescription of gastroprotective agents to prevent NSAID-related gastropathy is a common practice for patients requiring chronic treatment with nonselective NSAIDs [8]. Gastroprotective agents include proton pump inhibitors, histamine H₂ receptor antagonists, misoprostol and, in some cases, antacids. The costs of treating or preventing nonselective NSAID-related gastropathy comprise not only the use of gastroprotective agents, but also hospitalizations and visits to emergency departments for gastrointestinal complications or visits to gastroenterologists and general practitioners.

The costs of dealing with these adverse events are substantial; for example, the iatrogenic costs associated with NSAIDs have been estimated at between £32 and £70 (US \$49.0 and \$107.1) for each patient prescribed an NSAID in the UK, and the total effect on the NHS in the UK was estimated to be between £166 million (US \$254.0 million) and £367 million (US \$561.5 million) per year [9].

In most countries, it is presumed that good care is at least partly influenced by the funds available [10]. Deciding which health and public interventions should be funded is an important task for society. To make the best use of resources, some have argued that consistent decision rules based on a fixed cost for a given amount of benefit should be used [11]. Economic evaluation in OA could be of particular interest to help allocate scarce resources efficiently. Unfortunately, although health economic analyses have been widely used in other diseases, relatively few data are available for OA. The available economic evaluations are mainly pragmatic studies [12–17] or economic modeling studies (e.g., with the Markov model) [18–26]. On the other hand, these cost-effectiveness evaluations in OA using the Markov model (e.g., with anti-inflammatory drugs or with surgery) mainly take into account adverse events, assuming an equal symptomatic effect between treatments [18–26]. Economic evaluation taking into account the effectiveness of different strategies could then be of great interest. However, it should be acknowledged that the most important information for economic modeling (e.g., utility and quality-adjusted life years [QALYs]) has not frequently been collected in OA trials [27]. Consequently, we recommend assessing utility scores in all new clinical trials.

As a point of interest, a lot of trials investigating OA, have assessed health-related quality of life using specific instruments, such as the Women on the Move Against Cancer (WOMAC) or the Lequesne index. As is now recognized, these data cannot be used in cost-effectiveness analyses.



Olivier
Bruyère[†]

[†]Author for correspondence:
Department of Public Health,
Epidemiology & Health
Economics, University of Liege,
Liege, Belgium
Tel.: +32 4366 2581
Fax: +32 4366 2812
olivier.bruyere@ulg.ac.be



Jean-Yves
Reginster

Department of Public Health,
Epidemiology & Health
Economics, University of Liege,
Liege, Belgium
Tel.: +32 4270 3257
Fax: +32 4270 3253
jyreginster@ulg.ac.be

future
medicine part of fsg

However, some authors have developed and estimated a prediction model using linear regression to map the specific health-related quality of life instrument (i.e., the WOMAC) into health utility scores [28,29]. The methodology used to estimate utility from WOMAC has been proposed by Grootendorst in 2007 [29]; however, it should be noted that a recent paper seems to suggest that the actual QALYs could differ from those predicted on the basis of mapping (e.g., with the Grootendorst estimation) [30]. Utility estimates could be used to calculate QALY that could then be used in cost–effectiveness analysis to assess the Incremental Cost Effectiveness Ratio (ICER), which is a measure of the additional cost per unit of health gain. However, it should be acknowledged that such economic studies using utility assessment from specific instruments could only be considered as preliminary and that more sophisticated economic modeling should be developed that could also take into account data related to the natural history of OA.

In a cost–effectiveness analysis, the incremental cost and incremental effect could be represented visually using the incremental cost–effectiveness plane [31]. The horizontal axis divides the plane according to incremental cost (positive above, negative below) and the vertical axis divides the plane according to incremental effect (positive to the right, negative to the left). This divides the incremental cost–effectiveness plane into four quadrants (FIGURE 1). Each quadrant has a different implication for the decision. If the ICER fell in the southeast quadrant (more effective, less costly), the experimental intervention is always considered cost–effective and called dominant over the alternative. Interventions falling in the northwest (less effective, more costly) are never considered cost–effective, and are thus inferior. Finally, if the ICER fell in the northeast or the southwest quadrant, trade-offs between

costs and effects would need to be considered. These two quadrants represent the situation where the experimental treatment or intervention may be cost effective compared with the control, depending upon the value at which the ICER is considered good value for money. For economic analyses the northeast quadrant and the southwest quadrant could be considered to be of equal value.

“However, it seems that the appropriate threshold for cost–effectiveness may be dependant on the context of a situation, including risk of morality, especially in OA.”

The remaining question is the threshold below which the ICER could be considered as good value for money. Unfortunately, there is no clear answer. For many years, the figure of US \$50,000 per QALY has been proposed as an acceptable cut-off [32]. Others proposed a graded approach to the adoption of interventions. Interventions that cost less than \$20,000 per QALY were seen as having strong evidence for adoption, and those costing more than \$100,000 per QALY having weak evidence for adoption [33]. However, it seems that the appropriate threshold for cost–effectiveness may be dependant on the context of a situation, including risk of morality, especially in OA [34].

In an OA economic model, the long-term structure-modifying effect of some products could be of major importance. Indeed, some treatments (e.g., glucosamine sulfate, chondroitin sulfate and diacerein) were suggested to reduce the structural progression of the joint, as assessed on a radiograph [35]. Since it has been shown that a highest decrease in joint space width or a greatest loss of cartilage over time is associated with an increased need for joint surgery [36,37], we believe that the structural effect of such products should be included as a long-term potential effect in OA economic models. Consequently, the Markov model should not only be restricted to the time of treatment but should also take into account the outcomes after treatment discontinuation.

In conclusion, with regard to the medico-economic pressure, it is essential to develop effective treatments and also efficient strategies. In OA, economic evaluations are likely to be of paramount importance for this purpose and, consequently, need to be developed.

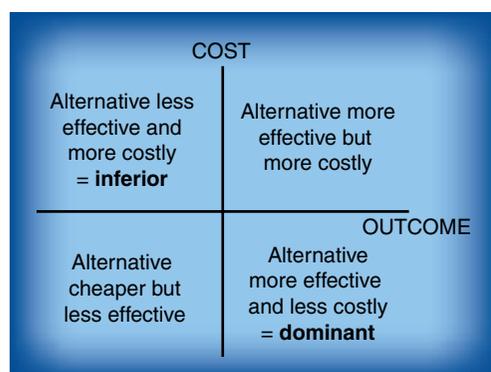


Figure 1. Cost–effectiveness plane.

Financial & competing interests disclosure

This work was supported by an ESCEO-Amgen grant received by Olivier Bruyere from the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis. Olivier Bruyere receives grants, fees or has been reimbursed for attending meetings from MSD, GlaxoSmithKline, Rottapharm, Servier, Theramex, Galapagos and IBSA. He also gives advices to the European Food Safety Authority and the European Society on Clinical and Economic Aspects of Osteoporosis and Osteoarthritis. Jean-Yves Reginster has received consulting fees or payments for participating in advisory boards for: Servier, Novartis, Negma, Lilly, Wyeth, Amgen, GlaxoSmithKline, Roche, Merckle, Nycomed, NPS, Theramex and UCB. He has

received lecture fees when speaking at the invitation of: Merck Sharp and Dohme, Lilly, Rottapharm, IBSA, Genevrier, Novartis, Servier, Roche, GlaxoSmithKline, Teijin, Teva, Ebewee Pharma, Zodiac, Analis, Theramex, Nycomed and Novo-Nordisk; and grant support from: Bristol Myers Squibb, Merck Sharp & Dohme, Rottapharm, Teva, Lilly, Novartis, Roche, GlaxoSmithKline, Amgen and Servier. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.

Bibliography

Papers of special note have been highlighted as:

• of interest

•• of considerable interest

- Murray CJ, Lopez AD: Global mortality, disability, and the contribution of risk factors: Global Burden of Disease Study. *Lancet* 349(9063), 1436–1442 (1997).
- Reginster JY: The prevalence and burden of arthritis. *Rheumatology (Oxford)* 41(Suppl. 1), 3–6 (2002).
- Rabenda V, Manette C, Lemmens R *et al.*: Prevalence and impact of osteoarthritis and osteoporosis on health-related quality of life among active subjects. *Aging Clin. Exp. Res.* 19(1), 55–60 (2007).
- Bruyere O, Burlet N, Delmas PD, Rizzoli R, Cooper C, Reginster JY: Evaluation of symptomatic slow-acting drugs in osteoarthritis using the GRADE system. *BMC Musculoskelet. Disord.* 9, 165 (2008).
- Zhang W, Moskowitz RW, Nuki G *et al.*: OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. *Osteoarthritis Cartilage* 16(2), 137–162 (2008).
- Jordan KM, Arden NK, Doherty M *et al.*: EULAR Recommendations 2003: an evidence based approach to the management of knee osteoarthritis: Report of a Task Force of the Standing Committee for International Clinical Studies Including Therapeutic Trials (ESCISIT). *Ann. Rheum. Dis.* 62(12), 1145–1155 (2003).
- Rabenda V, Manette C, Lemmens R *et al.*: Direct and indirect costs attributable to osteoarthritis in active subjects. *J. Rheumatol.* 33(6), 1152–1158 (2006).
- Rabenda V, Burlet N, Belaiche J *et al.*: Determinants of gastro-protective drugs co-prescription during treatment with nonselective NSAIDs: a prospective survey of 2197 patients recruited in primary care. *Osteoarthritis Cartilage* 14(7), 625–630 (2006).
- Moore R, Phillips C: Cost of NSAID adverse effects to the UK National Health Service. *J. Med. Econ.* 2, 45–55 (1999).
- Andrews G, Simonella L, Lapsley H, Sanderson K, March L: Evidence-based medicine is affordable: the cost-effectiveness of current compared with optimal treatment in rheumatoid and osteoarthritis. *J. Rheumatol.* 33(4), 671–680 (2006).
- Johannesson M, O'Connor RM: Cost-utility analysis from a societal perspective. *Health Policy* 39(3), 241–253 (1997).
- Outlines how to use cost-utility analysis from a societal perspective and the arguments that could be made for using data, such as a model for economic evaluation of healthcare.**
- Thomas KS, Miller P, Doherty M *et al.*: Cost effectiveness of a two-year home exercise program for the treatment of knee pain. *Arthritis Rheum.* 53(3), 388–394 (2005).
- Mazieres B, Bard H, Ligier M, Bru I, d'Orsay GG, Le Pen C: Medicoeconomic evaluation of hyaluronic acid for knee osteoarthritis in everyday practice: the MESSAGE study. *Joint Bone Spine* 74(5), 453–460 (2007).
- Pope JE, Prashker M, Anderson J: The efficacy and cost effectiveness of N of 1 studies with diclofenac compared with standard treatment with nonsteroidal antiinflammatory drugs in osteoarthritis. *J. Rheumatol.* 31(1), 140–149 (2004).
- Russo P, Capone A, Attanasio E *et al.*: Pharmacoutilization and costs of osteoarthritis: changes induced by the introduction of a cyclooxygenase-2 inhibitor into clinical practice. *Rheumatology (Oxford)* 42(7), 879–887 (2003).
- Castelnuovo E, Cross P, Mt-Isa S, Spencer A, Underwood M: Cost-effectiveness of advising the use of topical or oral ibuprofen for knee pain; the TOIB study [ISRCTN: 79353052]. *Rheumatology (Oxford)* 47(7), 1077–1081 (2008).
- Coupe VM, Veenhof C, van Tulder MW *et al.*: The cost effectiveness of behavioural graded activity in patients with osteoarthritis of hip and/or knee. *Ann. Rheum. Dis.* 66(2), 215–221 (2007).
- Marshall JK, Pellissier JM, Attard CL, Kong SX, Marentette MA: Incremental cost-effectiveness analysis comparing rofecoxib with nonselective NSAIDs in osteoarthritis: Ontario Ministry of Health perspective. *Pharmacoeconomics* 19(10), 1039–1049 (2001).
- Contreras-Hernandez I, Mould-Quevedo JF *et al.*: Cost-effectiveness analysis for joint pain treatment in patients with osteoarthritis treated at the Instituto Mexicano del Seguro Social (IMSS): Comparison of nonsteroidal anti-inflammatory drugs (NSAIDs) vs cyclooxygenase-2 selective inhibitors. *Cost Eff. Resour. Alloc.* 6, 21 (2008).
- Koskinen E, Eskelinen A, Paavolainen P, Pulkkinen P, Remes V: Comparison of survival and cost-effectiveness between unicompartmental arthroplasty and total knee arthroplasty in patients with primary osteoarthritis: a follow-up study of 50,493 knee replacements from the Finnish Arthroplasty Register. *Acta Orthop.* 79(4), 499–507 (2008).
- SooHoo NF, Sharifi H, Kominski G, Lieberman JR: Cost-effectiveness analysis of unicompartmental knee arthroplasty as an alternative to total knee arthroplasty for unicompartmental osteoarthritis. *J. Bone Joint Surg. Am.* 88(9), 1975–1982 (2006).
- Moore A, Phillips C, Hunsche E, Pellissier J, Crespi S: Economic evaluation of etoricoxib versus non-selective NSAIDs in the treatment of osteoarthritis and rheumatoid arthritis patients in the UK. *Pharmacoeconomics* 22(10), 643–660 (2004).
- Tavakoli M: Modelling therapeutic strategies in the treatment of osteoarthritis: an economic evaluation of meloxicam versus diclofenac and piroxicam. *Pharmacoeconomics* 21(6), 443–454 (2003).

24. Al MJ, Maniadas N, Grijseels EW, Janssen M: Costs and effects of various analgesic treatments for patients with rheumatoid arthritis and osteoarthritis in the Netherlands. *Value Health* 11(4), 589–599 (2008).
25. Loyd M, Rublee D, Jacobs P: An economic model of long-term use of celecoxib in patients with osteoarthritis. *BMC Gastroenterol.* 7, 25 (2007).
26. Kamath CC, Kremers HM, Vanness DJ *et al.*: The cost–effectiveness of acetaminophen, NSAIDs, and selective COX-2 inhibitors in the treatment of symptomatic knee osteoarthritis. *Value Health* 6(2), 144–157 (2003).
27. Ruchlin HS, Insinga RP: A review of health-utility data for osteoarthritis: implications for clinical trial-based evaluation. *Pharmacoeconomics* 26(11), 925–935 (2008).
28. Marshall D, Pericak D, Grootendorst P *et al.*: Validation of a prediction model to estimate health utilities index Mark 3 utility scores from WOMAC index scores in patients with osteoarthritis of the hip. *Value Health* 11(3), 470–477 (2008).
29. Grootendorst P, Marshall D, Pericak D, Bellamy N, Feeny D, Torrance GW: a model to estimate health utilities index mark 3 utility scores from WOMAC index scores in patients with osteoarthritis of the knee. *J. Rheumatol.* 34(3), 534–542 (2007).
- **Relates to the development of a formula to translate Western Ontario and McMaster University Osteoarthritis Index scores, collected in clinical trials of patients with osteoarthritis, into Health Utilities Index Mark 3 utility scores for application in economic evaluation.**
30. Barton GR, Sach TH, Jenkinson C, Avery AJ, Doherty M, Muir KR: Do estimates of cost-utility based on the EQ-5D differ from those based on the mapping of utility scores? *Health Qual. Life Outcomes* 6, 51 (2008).
31. Black WC: The CE plane: a graphic representation of cost–effectiveness. *Med. Decis. Making* 10(3), 212–214 (1990).
32. Hirth RA, Chernew ME, Miller E, Fendrick AM, Weissert WG: Willingness to pay for a quality-adjusted life year: in search of a standard. *Med. Decis. Making* 20(3), 332–342 (2000).
- **Determines the value of a quality-adjusted life year as implied by the value-of-life literature and compares this value with arbitrary thresholds for cost–effectiveness that have come into common use.**
33. Laupacis A, Feeny D, Detsky AS, Tugwell PX: How attractive does a new technology have to be to warrant adoption and utilization? Tentative guidelines for using clinical and economic evaluations. *CMAJ* 146(4), 473–481 (1992).
34. Byrne MM, O'Malley K, Suarez-Almazor ME: Willingness to pay per quality-adjusted life year in a study of knee osteoarthritis. *Med. Decis. Making* 25(6), 655–666 (2005).
35. Bruyere O, Reginster JY: Glucosamine and chondroitin sulfate as therapeutic agents for knee and hip osteoarthritis. *Drugs Aging* 24(7), 573–580 (2007).
36. Cicuttini FM, Jones G, Forbes A, Wluka AE: Rate of cartilage loss at two years predicts subsequent total knee arthroplasty: a prospective study. *Ann. Rheum. Dis.* 63(9), 1124–1127 (2004).
37. Bruyere O, Richey F, Reginster JY: Three year joint space narrowing predicts long term incidence of knee surgery in patients with osteoarthritis: an eight year prospective follow up study. *Ann. Rheum. Dis.* 64(12), 1727–1730 (2005).

Affiliations

- Olivier Bruyère
Department of Public Health, Epidemiology & Health Economics, University of Liege, Liege, Belgium
Tel.: +32 4366 2581
Fax: +32 4366 2812
olivier.bruyere@ulg.ac.be
- Jean-Yves Reginster
Department of Public Health, Epidemiology & Health Economics, University of Liege, Liege, Belgium
Tel.: +32 4270 3257
Fax: +32 4270 3253
jyreginster@ulg.ac.be