

Development and Validation of a Markov Microsimulation Model for the Economic Evaluation of Treatments in Osteoporosis

Mickaël Hiligsmann, MPH, MSc,^{1,2} Olivier Ethgen, PhD,² Olivier Bruyère, PhD,² Florent Richy, PhD,² Henry-Jean Gathon, PhD,¹ Jean-Yves Reginster, MD, PhD²

¹Department of Economics, University of Liège, Liège, Belgium; ²Department of Public Health, Epidemiology and Health Economics, University of Liège, Liège, Belgium

ABSTRACT

Objective: Markov models are increasingly used in economic evaluations of treatments for osteoporosis. Most of the existing evaluations are cohort-based Markov models missing comprehensive memory management and versatility. In this article, we describe and validate an original Markov microsimulation model to accurately assess the cost-effectiveness of prevention and treatment of osteoporosis.

Methods: We developed a Markov microsimulation model with a lifetime horizon and a direct health-care cost perspective. The patient history was recorded and was used in calculations of transition probabilities, utilities, and costs. To test the internal consistency of the model, we carried out an example calculation for alendronate therapy. Then, external consistency was investigated by comparing absolute lifetime risk of fracture estimates with epidemiologic data.

Results: For women at age 70 years, with a twofold increase in the fracture risk of the average population, the costs per quality-adjusted

life-year gained for alendronate therapy versus no treatment were estimated at €9105 and €15,325, respectively, under full and realistic adherence assumptions. All the sensitivity analyses in terms of model parameters and modeling assumptions were coherent with expected conclusions and absolute lifetime risk of fracture estimates were within the range of previous estimates, which confirmed both internal and external consistency of the model.

Conclusion: Microsimulation models present some major advantages over cohort-based models, increasing the reliability of the results and being largely compatible with the existing state of the art, evidence-based literature. The developed model appears to be a valid model for use in economic evaluations in osteoporosis.

Keywords: cost-effectiveness, Markov model, microsimulation, modeling, osteoporosis.

Introduction

Osteoporosis is an increasingly major health problem around the world. It is a disease characterized by low bone mass with micro-architectural disruption and increased skeletal fragility, leading to increased fracture risk. Osteoporotic fractures results in significant morbidity, mortality [1], and reductions in quality of life [2,3]. They also impose a huge financial burden on health-care systems. Moreover, with an aging population and increasing life expectancy, their consequences are expected to increase in the future.

In the cost-constrained environment of health care, economic evaluation of various diagnostic and treatment strategies is commonly used to help allocate resources in the most efficient manner [4–6]. Modeling is an important tool of economic evaluation by its ability to: extrapolate results from one trial; combine multiple sources of data; generalize results from one context to another; define research strategy; and delineate areas of uncertainty [7]. Nevertheless, models have limitations related to the quality of the assumptions and the data utilized [8,9]. Thus, models should be designed and conducted to reflect the complexity of the real world [9].

During the past decade, significant improvements were achieved in the field of pharmacoeconomic assessment of

osteoporotic interventions [6,10]. However, remaining limitations relate to the effects of drugs on nonvertebral, nonhip fractures, the assessment of adherence to treatment, and also the failure to appropriately consider a lifetime horizon. Moreover, most of the models are cohort-based [11], thereby limited in their ability to deal simultaneously and accurately with the complex interactions of patient, intervention, and clinical events. Specifically, this approach is limited by the “memoryless” feature of the process, which is known as the Markov assumption [12]. This assumption means that once a patient has moved from one state to another, the model will have “no memory” regarding where the patient came from. When transition probabilities depend on prior events (such as in osteoporosis), this dependence or “memory” should be reflected in the model [13]. In many cohort models, “post-fracture states” have therefore been used for persistent changes in transition probabilities and utilities after hip and vertebral fractures. Nevertheless, future events are potentially inaccurately estimated by this approach [14].

Examples of the weaknesses of this approach follow. First, because of the desire to avoid an unmanageable number of health states, cohort models have restricted the number of disease states and transitions between them. For example, it has been frequently assumed that patients who have had a hip fracture cannot experience any future nonhip fracture [11]. This does not reflect realistic clinical perspectives because patients can definitely have other fractures after a nonfatal hip fracture. Additionally, patients in “postfracture state” might have a previous history of one, two, or more prior fractures but may be assigned the same transition probabilities, costs, and utility. This is also inconsistent with epidemiologic studies. Various studies have

Address correspondence to: Mickaël Hiligsmann, Department of Public Health, Epidemiology and Health Economics, University of Liège, Avenue de l'hôpital 3, Bat B23, 4000, Liège, Belgium. E-mail: m.hiligsmann@ulg.ac.be

10.1111/j.1524-4733.2008.00497.x

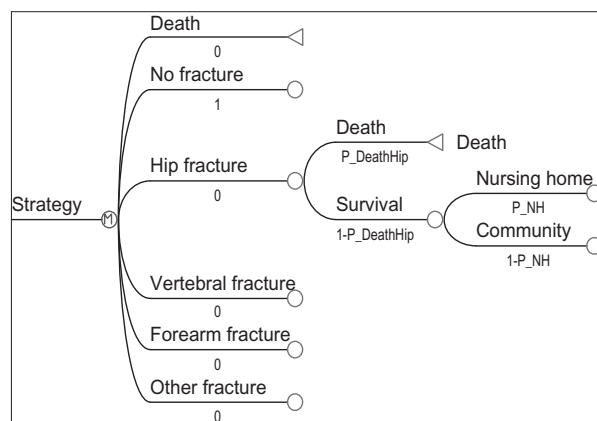


Figure 1 Markov model structure for each strategy. P_DeathHip and P_NH are, respectively, probabilities of death in the year after hip fracture and probabilities of being admitted to a nursing home after hip fracture for surviving patients.

shown a relationship between utility values and the number and location of prior fractures [15–18]; thus, if a model fails to record all the prior fractures, the utility value of patients with multiple prevalent fractures will be overestimated. Moreover, prior fractures were also shown to dramatically increase the risk of subsequent fractures [19,20] and there should be a record of all fractures to accurately assess this increased risk. Third, the residential status of a patient, defined as community- or nursing home dwelling, may affect long-term costs. The failure to track residential status will, for example, inappropriately add costs to a patient with an incident fracture who already lives in a nursing home [14].

Microsimulation models address the above weaknesses and have the potential to be more accurate than cohort models. Their use has increased dramatically with the speed of computing technology and they now begin to supplant cohort models in health-care technology assessment [21]. In the setting of osteoporosis, a Monte Carlo microsimulation identifies individual subjects to track their characteristics and individual disease histories [22]. Factors such as prior fracture and current residential status are used to calculate transition probabilities, utility values, and costs. Therefore, microsimulation models require no restrictive assumptions regarding patient movement to health states and allow assessing the impact of prior fractures without creating a large, incomprehensible and unmanageable number of health states. The infrequent use of microsimulation in osteoporosis is due to the greater variance in results because of random variation in individual outcomes, and of the much greater detail required for data sets (to be modeled) than would be required for cohort-based models. These factors have been proposed as the rationale for supporting the use of cohort-based approaches [23]. Potential drawbacks with microsimulation models include the computation burden when the joint uncertainty in all parameters is assessed using probabilistic sensitivity analysis [12].

We believe that there is value in developing microsimulation models in the field of osteoporosis [23]. The objective of this study was therefore to develop and validate a new Markov microsimulation model for the assessment of the cost-effectiveness of the prevention and treatment in osteoporosis. In this article, we present the model and we validate it through an empirical illustration.

Methods

The developed model was constructed using decision analysis software (TreeAgePro 2006 Suite, release 0.4, TreeAge Software, Inc., Williamstown, MA).

Model Structure

Because osteoporosis is a chronic disease characterized by a recurrence of events and when the fracture risk is continuous over time, a Markov modeling technique is appropriate [24]. The structure of the model is shown in Figures 1 and 2. It has been suggested that the model should be kept as simple as possible to be understandable, while capturing the underlying essentials of the process and interventions [13]. Therefore, the model consists of six states: “no fracture,” “death,” “hip fracture,” “vertebral fracture,” “forearm fracture,” and “other fracture.” This last state represents all other osteoporotic fractures [25] (e.g., humerus, pelvis, or distal femur).

The cycle length of the model is 1 year because events rarely occur more than once a year and most of the data sources, such as fracture disability and fracture cost, are calculated on this frequency. The model follows the patients until they are dead or they reach the age of 105 years.

All the transitions between health states other than death are possible. So, in every cycle and regardless of the current state, each individual has a probability of having a fracture based on fracture risk, of having no fracture, or of dying based on mortality rates. If an individual is in a fracture state, she might have a new fracture (all fracture types are possible), or move to the “no fracture” state, or die. If an individual were to die, she would remain in the “death” state for the rest of the simulation.

A branch was created to keep track of residential status (either in the community or in a nursing home) for an individual with a hip fracture because this fracture type is associated with admission to a nursing home. Once a patient enters a nursing home, we assume that he/she will stay there for the rest of his/her life. We also assume a discount rate of 3% for costs and of 1.5% for health benefits for the base-case analysis, as recommended for health economic evaluations in Belgium, the country of reference for the present article [26].

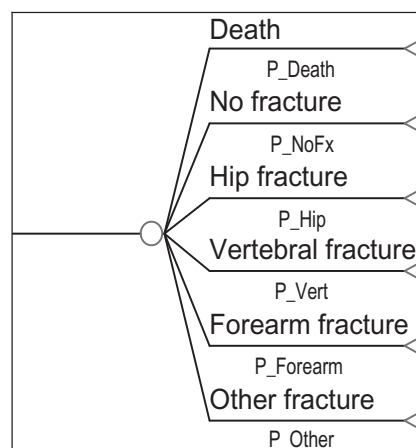


Figure 2 Expanded subtree for all health state other than death. P_Death, P_NoFx, P_Hip, P_Vert, P_Forearm, P_Other are transition probabilities of death, no fracture, hip fracture, vertebral fracture, forearm fracture, and other fractures, respectively. Figure 2 needs to be applied to all health states other than death in Figure 1 (represented by a green circle).

Download English Version:

<https://daneshyari.com/en/article/989727>

Download Persian Version:

<https://daneshyari.com/article/989727>

[Daneshyari.com](https://daneshyari.com)