Editor’s Spotlight/Take 5: Prophylactic Fixation Can Be Cost-effective in Preventing a Contralateral Bisphosphonate-associated Femur Fracture

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Most clinicians are familiar with the common article types found in orthopaedic journals: Original studies about treatments and diagnostic tests, as well as synthetic content like meta-analyses. For those looking for guidance on how to read these papers more critically, Clinical Orthopaedics and Related Research® has made some good tools available [1, 2]. But some of the most-fun-to-read (and most-helpful) articles employ less-common study designs, and this month’s CORR® features a good example of exactly this.

A group out of Stanford University led by Julius A. Bishop MD, (with collaborators at Northwestern and Harvard Universities) has created a Markov model that delivered a convincing cost-effectiveness analysis about prophylactic intramedullary nailing of femurs contralateral to atypical bisphosphonate-associated fractures.

I may just have lost a large number of readers … perhaps those who are allergic to unfamiliar or methods-heavy article types, or those who do not rod femurs.

If so, that would be too bad, since Dr. Bishop’s team has engaged with many of the values that we all espouse: Curiosity, a willingness to engage with a challenge (whether as readers, researchers, or surgeons), and the desire to try new tools to solve resistant problems. As such, the article is good reading whether or not you ever plan to run a Markov model or place an intramedullary femoral nail.

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So stay with us here. Markov models in medical research allow us to contemplate a patient in some state of health (let’s say someone who has experienced an atypical femur fracture), factor in elements that may influence the likelihood of future health states arising (such as a contralateral atypical femur fracture in that same patient), and determine the odds that those events will occur over time. The time component is especially important, and that really is what elevates the Markov model over other simulations. Dr. Bishop’s team took this a step further and used the best-available evidence to assign value to each health state as a patient might perceive it, along with the potential costs of treating the health states involved, in order to determine when prophylactic placement of a contralateral intramedullary femoral nail might be cost effective in patients with bisphosphonate-associated femur fractures who vary by age, ethnicity, and other presenting factors.

Their model suggested that prophylactic contralateral femoral fixation is likely to be especially cost effective in Asian patients, as well as those with prodromal pain, changes to femoral geometry, or visible radiographic findings in the contralateral femur, particularly if they are younger.

Since these fractures are uncommon [5], the specific findings here—though
important for those who treat these injuries and those who have them—would not justify covering this topic in our Editor's Spotlight/Take 5 section.

Rather, my reason for introducing you to this work here is that the methodological approach Dr. Bishop’s team used should get us all thinking about how this approach (and others like it) might be used to tackle the large unsolved problems in our specialty. Join me as I visit with Dr. Bishop about this fascinating work—and how it might lead to answers to other clinical questions you may have thought were unanswerable—in the Take 5 interview that follows.

Take Five Interview with Julius A. Bishop MD, senior author of “Prophylactic Fixation Can Be Cost-effective in Preventing a Contra-lateral Bisphosphonate-associated Femur Fracture”

Seth S. Leopold MD: Congratulations on this fascinating study. Markov analysis is an underutilized tool in our specialty; it can give insight on cost-benefit questions like the one you explored as well as on risk-benefit decision-making. Can you explain to readers—who are not methodologists—why this approach is so powerful?

Julius A. Bishop MD: Thank you. As orthopaedic surgeons, many of our interventions involve benefits, harms, and costs that are influenced by multiple variables, take place over a long time span, and can therefore, be difficult to study using most conventional research methodology. Markov analysis is a mathematical modeling technique that has great potential in orthopaedic research because it allows researchers to observe the effects of a particular intervention on a simulated cohort of patients, accounting for multiple treatment strategies, patient variables, potential outcomes, and costs as well as the passage of time.

Dr. Leopold: As you noted, Markov analysis (and decision analysis, more generally) can help us answer unsolved clinical problems that cannot be easily tackled in other ways; what topics in our specialty do you think are ripe for analysis using these tools, and why might decision analysis be the right next step for these clinical questions?

Dr. Bishop: It is clear that there are many opportunities to apply decision analysis in orthopaedics, particularly when a randomized controlled trial is either not feasible or when there is lack of equipoise. Controversial topics or those that have distinct and well-defined treatment strategies and outcomes lend themselves to decision analysis. Promising topics include limb salvage versus amputation for the treatment of severe open lower extremity fractures, prophylactic fixation versus radiation for the treatment of metastatic lesions of the femur, and arthrodesis versus arthroplasty for the treatment of ankle arthritis or degenerative disk disease of the spine.

Dr. Leopold: When you read a decision analysis (whether or not Markov modeling is used), what practical elements help you to know whether it is robust, and why? Remember, your reader here is the hardworking clinician, not the biostatistician.

Dr. Bishop: A critical reader should scrutinize several details of a decision analysis study to determine whether the paper is relevant and robust. In order to be relevant, the model illustrated in the decision tree must fit the reader’s treatment algorithm. The next step is to determine if the outcome probabilities and utilities are sensible and credible. They should be derived rigorously, using the best available evidence. The literature search, an assessment of study quality, and the rationale for assigning probabilities and utilities all should be outlined clearly in the methods section. Furthermore, the reader should pay particular attention to the sensitivity analysis, which is the study of how varying the independent variables used in a model impacts the outcome of the model. If the outcome of the model is stable during a wide range of independent variables, the model is said to be robust. This means that results will not change with small variations in estimates of outcome probability, health states, or costs.

Dr. Leopold: While both decision analyses and cost-effectiveness analyses such as you performed deal with a parameter called the quality-adjusted life year (QALY), they differ in that decision analyses focus on risk-benefit calculations and cost-effectiveness analyses like yours determine how much it costs to deliver one QALY. This will seem like another language to many; can you help translate the key terms here into plain language, and—importantly—help readers to know what a QALY “should” cost?

Dr. Bishop: Quality-adjusted life years are a measure used in health economics that incorporates both quantity and quality of life. One QALY is equal to a year in perfect health. Any
state other than perfect health has a QALY value less than one and death represents a QALY value of zero. There are several techniques by which any health outcome can be assigned a QALY value. Quality-adjusted life years can be incorporated into a decision analysis model to identify the treatment strategy that will improve outcome regardless of cost. A cost effectiveness model is similar but also establishes the cost per QALY for any given treatment strategy. If a particular treatment is more effective (that is, it results in more QALYs) and less expensive than the alternatives, it is obviously better. If the treatment is less effective and more expensive than the alternatives, it is obviously inferior. However, if a particular treatment is more effective but more expensive, or less effective and less expensive, then decision making becomes more complicated, and cost per QALY is important. In the United States, treatments that cost less than USD 50,000 per QALY are generally considered cost effective, those that cost between USD 50,000 and USD 100,000 per QALY are considered possibly cost effective, while those that cost more than USD 100,000 per QALY are often considered not cost effective [3]. As the reader might expect, cost effectiveness analyses in other countries often use different thresholds.

Dr. Leopold: Now that there are better guidelines for the management of osteoporosis that include recommended limitations on duration of bisphosphonate therapy [4], at what point do you think we will stop seeing patients with these atypical femur fractures, or do you think that even with the new guidelines this problem will persist?

Dr. Bishop: The heightened awareness of atypical femur fractures frequently associated with prolonged bisphosphonate therapy has led to limitations on the duration of bisphosphonate therapy and should decrease the number of patients we see with these fractures. However, some patients who present with atypical femur fractures have never been treated with bisphosphonates, so I do not expect the incidence to decrease to zero [5]. When these rare patients present in the future, we will still need a thoughtful and effective treatment strategy for their contralateral side.

References