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Background: Antibiotic-impregnated bone cement is infrequently used in the United States for primary total hip arthroplasty because of concerns about cost, performance, and the possible development of antibiotic resistance and because it has been approved only for use in revision arthroplasty after infection. The purpose of this study was to model the use of antibiotic-impregnated bone cement in primary total hip arthroplasty for the treatment of osteoarthritis to determine whether use of the cement is cost-effective when compared with the use of cement without antibiotics.

Methods: To evaluate the cost-effectiveness of each strategy, we used a Markov decision model to tabulate costs and quality-adjusted life years (QALYs) accumulated by each patient. Rates of revision due to infection and aseptic loosening were estimated from data in the Norwegian Arthroplasty Register and were used to determine the probability of undergoing a revision arthroplasty because of either infection or aseptic loosening. The primary outcome measure was either all revisions or revision due to infection. Perioperative mortality rates, utilities, and disutilities were estimated from data in the arthroplasty literature. Costs for primary arthroplasty were estimated from data on in-hospital resource use in the literature. The additional cost of using antibiotic-impregnated bone cement ($600) was then added to the average cost of the initial procedure ($21,654).

Results: When all revisions were considered to be the primary outcome measure, the use of antibiotic-impregnated bone cement was found to result in a decrease in overall cost of $200 per patient. When revision due to infection was considered to be the primary outcome measure, the use of the cement was found to have an incremental cost-effectiveness ratio of $37,355 per QALY compared with cement without antibiotics; this cost-effectiveness compares favorably with that of accepted medical procedures. When only revision due to infection was considered, it was found that the additional cost of the antibiotic-impregnated bone cement would need to exceed $650 or the average patient age would need to be greater than seventy-one years before its cost would exceed $50,000 per QALY gained.

Conclusions: When revision due to either infection or aseptic loosening is considered to be the primary outcome, the use of antibiotic-impregnated bone cement results in an overall cost decrease. When only revision due to infection is considered, the model is strongly influenced by the cost of the cement and the average age of the patients. With few patients less than seventy years of age undergoing total hip arthroplasty with cement in the United States, the use of antibiotic-impregnated bone cement in primary total hip arthroplasty may be of limited value unless its cost is substantially reduced.

Level of Evidence: Economic and decision analysis, Level II. See Instructions to Authors for a complete description of levels of evidence.

Deep infection following total hip arthroplasty is a devastating complication that can require costly revision surgery and reduce a patient's functional status. Several methods to reduce the incidence of infection, including improved surgical technique, improved perioperative preparation, and use of prophylactic antibiotics, have been introduced since

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the 1960s[1,2]. These changes have been credited with reducing the infection rate associated with total hip arthroplasty from nearly 10% to between 0.5% and 2%[1,2].

The use of antibiotic-impregnated bone cement has been advocated as one method to further reduce the need for revision surgery following primary total hip arthroplasty[3]. Large registry databases, such as the Norwegian Arthroplasty Register and the Swedish Arthroplasty Register, have shown a decreased rate of revision surgery in patients who received both perioperative intravenous antibiotics and antibiotic-impregnated bone cement at the time of primary total hip arthroplasty[4-7]. Proponents of the use of antibiotic-impregnated bone cement in the United States point to these data as evidence that it should be used in all primary procedures involving use of cement[8]. Opponents of the use of antibiotic-impregnated bone cement frequently cite its cost as the primary concern, especially given the already low rates of infection and revision[9]. Other concerns include the possible development of antibiotic resistance, allergic reactions, and possible compromise of the mechanical properties of the cement from the admixture of antibiotics[10-12]. Also, since antibiotic-impregnated bone cement has been approved by the United States Food and Drug Administration only for second-stage reimplantation after revision due to infection, use of antibiotic-impregnated bone cement in primary total hip arthroplasty represents an off-label usage in the United States.

The purpose of this study was to employ a decision analytic model that accounts for competing risks, benefits, and costs to assess the cost-effectiveness of the use of antibiotic-impregnated bone cement for primary total hip arthroplasty. Specifically, we sought to answer the question of whether the up-front cost of using antibiotic-impregnated bone cement in all patients undergoing total hip arthroplasty would be justified by the expected decrease in future revisions.

Materials and Methods

Markov decision analysis was used to model the clinical scenario of deciding whether to use antibiotic-impregnated bone cement or standard polymethylmethacrylate bone cement without antibiotics for primary total hip arthroplasty. Markov models are useful when decision problems involve competing risks over time, or when the timing of events is important, as is the case with revision surgery after primary total hip arthroplasty[13]. Assumptions in the model regarding revision rates, costs, utilities, mortality risks, and all other parameters were drawn from the literature and are described in detail below.

Model Design

The design of the Markov model is illustrated schematically in Figure 1 and in detail in the Appendix. The decision tree represents the potential clinical course of hypothetical patients in the scenario modeled (i.e., the decision to use antibiotic-impregnated bone cement or conventional cement). The decision tree includes five main health states, and the arrows between the health states represent chance events that can occur over time. The five health states in this model are: well after total hip arthroplasty with antibiotic-impregnated bone cement, well after total hip arthroplasty without antibiotic-impregnated bone cement, well after aseptic revision, well after revision due to infection, and death. Over the course of the simulation, hypothetical patients transition from one health state to another on the basis of transition probabilities associated with each chance event modeled. Patients who are well after total hip arthroplasty can transition to any of the other health states during each time cycle of the model (one year). Transition probabilities can change over time (e.g., the risk of death from all causes increases with the patient's age). The model continues to cycle until all hypothetical patients eventually reach the death state.

Each health state is assigned a utility. Utilities are defined as a measure of how a patient defines the value of a specific health state. Utility values are typically scaled from 0 (death) to 1 (perfect health)[13]. The value of time in a given health state is measured in quality-adjusted life years (QALYs), which are calculated as the time in the health state multiplied by the utility assigned to the health state (years × utility = QALY). Costs associated with each strategy are calculated on the basis of the occurrence of events in the model, such as the cost of undergoing an aseptic revision when transitioning to the "well after aseptic revision" health state. The model then tabulates the total utilities and costs accumulated by a hypothetical cohort of patients during their simulated life span (before they transition to the death state) for both the antibiotic-impregnated-cement and standard-cement strategies[14]. All costs and utilities are discounted at a standard rate of 3% per year. The cost-effectiveness of using antibiotic-impregnated bone cement is expressed as the ratio of additional costs attributable to this strategy to the additional benefits (QALYs). The model was designed with use of decision analysis software (TreeAge Pro 2005; TreeAge Software, Williamstown, Massachusetts).

Model Assumptions and Parameters

In constructing the decision model, we used the following general assumptions: (1) all patients are undergoing primary total hip arthroplasty for the treatment of osteoarthritis, and a cemented femoral stem is used in all cases; (2) each patient can undergo only one revision during his or her lifetime; (3) revision due to a documented infection is performed as a two-stage procedure, in which the prosthesis is removed, the patient is treated with intravenous antibiotics for six weeks, and a new prosthesis is then implanted; and (4) the use of antibiotic-impregnated bone cement does not affect the utility (value) of the different health states modeled. The parameters of the model are discussed below.

Patient Population

The age of the patients in the model was set at sixty-eight years to coincide with the average age reported in the Norwegian Arthroplasty Register from 1987 to 2004[5]. Patients were assumed to be of average health for their age and to be undergoing total hip arthroplasty because of degenerative arthritis and not a fracture.

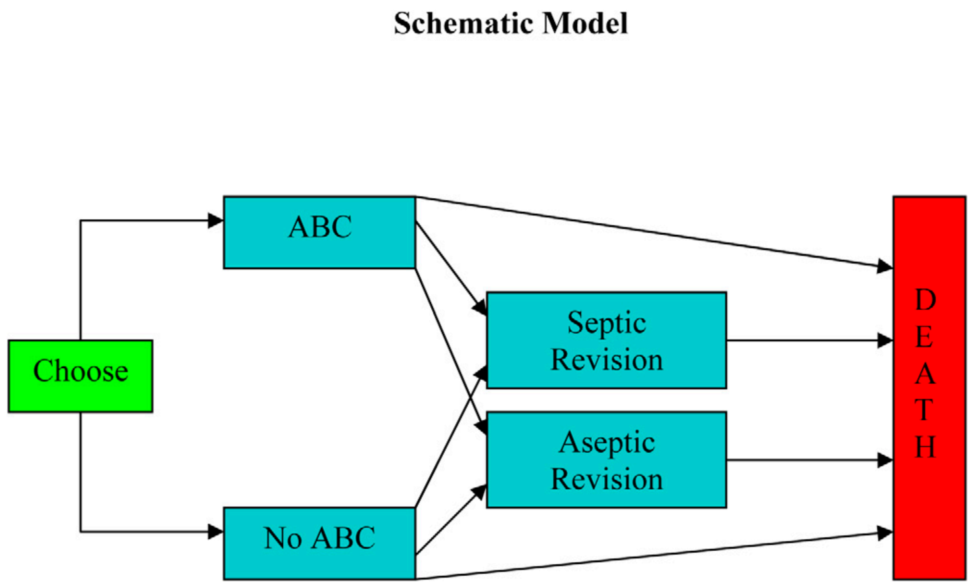

Fig. 1

Clinical pathway of patients assumed to have hip arthritis for which medical management has failed. Each patient receives a total hip arthroplasty with or without antibiotic-impregnated bone cement (ABC). When patients survive the operation, they are assumed to stay well until they die of other causes or need a revision. When they have a revision and survive, they are assumed to stay well with that revision until they die from other causes. The model continues until all patients reach the death state.

Revision Rates

Revision rates were based on a recent study on the difference in revision rates, as reported to the Norwegian Arthroplasty Register, between patients who had received systemic antibiotics and antibiotic-impregnated bone cement at the time of primary total hip arthroplasty and patients who had received systemic antibiotics only[4,5]. The results in that study were divided into revisions due to a documented infection (positive cultures) and aseptic revisions (negative cultures). The rate of revision was slightly higher in the first several years after the arthroplasty, but a linear rate of revision was assumed for the model. This approach provides a more conservative estimate of the cost-effectiveness of antibiotic-impregnated bone cement because revision costs are shifted further into the future and therefore discounted. The ten-year revision rates were converted into yearly rates of both revisions due to infection and those due to aseptic loosening. For patients treated with antibiotic-impregnated bone cement, the rate of revision due to infection was set at 0.04% per year and the rate of revision due to aseptic loosening was set at 0.31% per year (Table I). The revision rates for the group treated with standard bone cement were then determined by multiplying the revision rates for the group treated with antibiotic-impregnated cement by the increased risk of revision in subgroups in which antibiotic-impregnated bone cement was not used. The relative risk of revision due to infection was set at 1.8 and the relative risk of aseptic revision was set at 1.3 for the standard-cement branch (Table I). The rates of infection and aseptic loosening used in the model are on the low end of rates reported in the literature[7,15], again providing a conservative estimate of the cost-effectiveness of antibiotic-impregnated bone cement.

Mortality Rates

The age-specific probability of death from all causes was estimated from U.S. Life Tables from 2002. The risk of death increased as the hypothetical patients cycled through the model, and the probability of death was set at 100% at age 101 to terminate the simulation. The risk of perioperative death for patients treated with primary total hip arthroplasty was set at 0.23% on the basis of data from the Norwegian Arthroplasty Register[5]. Revisions were assumed to be associated with the same mortality risk.

Utilities

Laupacis et al. used the time-trade-off technique to determine utility scores for patients before and after primary total hip arthroplasty[16]. These patients had a mean age of sixty-four years, and the utility value averaged 0.80 two years after the total hip arthroplasty. Rorabeck et al. found a similar result using the time-trade-off technique[17]. These data were used to assign a utility value of 0.80 for patients who had undergone primary total hip arthroplasty in our model (Table I).

There are few studies in the orthopaedic literature in which functional outcome was measured following aseptic revision of a total hip arthroplasty, and we found no studies in which a utility score was directly determined for patients who had undergone that procedure. Hozack et al. used scores on the Short Form-36 (SF-36) to compare patients treated with primary total hip arthroplasty with those treated with aseptic revision total hip arthroplasty[18]. The patients who underwent revision had lower scores in every category postoperatively, despite having had similar preoperative scores. The utility value

TABLE I Markov Model Variables

Variable	Value	Reference
Rate of revision due to infection with antibiotic cement	0.4% over 10 years	5
Aseptic revision rate with antibiotic cement	3.1% over 10 years	5
Relative risk of revision due to infection with regular cement	1.8 × baseline rate	5
Relative risk of aseptic revision with regular cement	1.3 × baseline rate	5
Probability of death from all causes	U.S. 2002 life tables	
Probability of death from total hip arthroplasty	0.23% increased risk	5
Cost of primary total hip arthroplasty	$21,654	21
Increased cost of aseptic revision	1.6 × baseline cost	21
Increased cost of revision due to infection	4.44 × baseline cost	21
Additional cost of antibiotic cement	$600	
Utility of primary total hip arthroplasty	0.80	16
Utility of aseptic revision	0.72 (10% decrease)	18
Utility of revision due to infection	0.64 (20% decrease)	
Disutility of total hip arthroplasty	−0.1	
Disutility of aseptic revision	−0.12 (20% more)	
Disutility of revision due to infection	−0.20	
Discount rate per year	3% for cost and utilities	

for aseptic revision was conservatively estimated to be 10% lower than that for primary total hip arthroplasty ($0.80 \times 90\% = 0.72$). Comparative functional outcome data following revision due to infection were not identified in the literature, and a conservative estimate of a 20% decrease in utility was assigned to the patients treated with that procedure ($0.80 \times 80\% = 0.64$).

Disutilities

Disutilities are a measure of the transient lower quality of life associated with undesirable events[13]. They were used in this model to represent the temporary health state of a patient in the perioperative period, when patients have increased pain and decreased mobility, as well as the potential for other complications (Table I). The disutility is assessed as a one-time toll within the model, and the assigned amount is deducted from the patient's accumulated QALYs at the time that they undergo one of the procedures. The disutility for primary total hip arthroplasty was set at −0.1, which is the equivalent of deducting just over five weeks of perfect health. The disutility for aseptic revision was set at −0.12, a slight increase to account for the increase in complexity of a typical revision procedure. For revisions due to infection, the assigned disutility was −0.20, which takes into consideration that the majority of patients undergo a two-stage procedure and thus spend a longer period of time in an undesirable health state.

Costs

All cost estimates are in 2002 U.S. dollars. Cost estimates for primary total hip arthroplasty were obtained from the orthopaedic literature as well as from the National Inpatient Survey (NIS) data. These estimates accounted for the costs associated with the procedure and the acute hospitalization. Surgeons' fees, costs for a rehabilitation stay, and lost wages due to missed workdays were not included. Estimates ranged from $12,846 to $31,000 for a primary total hip arthroplasty[19,20]. The cost assigned to a primary total hip arthroplasty in our model was $21,654, which was based on studies, published in 2005, by Bozic et al., who estimated the hospital resources used for primary total hip arthroplasties, aseptic revisions, and revisions due to infections[21,22].

In the literature, estimates of the increase in cost for aseptic revisions, as compared with the cost for primary arthroplasty, have ranged from 20% to 60%[22], although in many reports it is unclear whether revisions due to infection were included in the estimate. In our model, the cost of an aseptic revision was estimated to be $34,866, as reported by Bozic et al.[21].

Cost estimates for revisions due to infection were based on the assumption that the majority of patients were treated with a two-stage revision, with intravenous antibiotics administered during the period between the removal of the prosthesis and the revision implant procedure. The cost assigned to revisions due to infection in the model was $96,166, on the basis of the data reported by Bozic et al.[21].

The additional cost of using antibiotic-impregnated bone cement was estimated by calculating the difference between the cost of standard polymethylmethacrylate bone cement and the cost of commercially available premixed gentamicin antibiotic-impregnated bone cement. Gentamicin antibiotic-impregnated bone cement is the cement that has been studied the most often, and its beneficial effects have been shown by data in both the Swedish and the Norwegian Arthroplasty Register[5,6]. The estimated cost of a 40-g packet of antibiotic-impregnated bone cement at our institution is approximately $365, and standard bone cement costs approximately $65. It was estimated that two packets of cement are used on the average, resulting in an additional cost of $600 per primary total hip arthroplasty.

Analysis

Cost-effectiveness analysis is a useful tool for evaluating medical interventions when one strategy is more costly but also more effective[14]. If a treatment strategy is more costly and less effective, it is said to be dominated by the alternative treatment strategy and should never be chosen[13]. Similarly, if a strategy is less costly and more effective, it should always be chosen. The measure of a treatment's cost-effectiveness is expressed as an incremental cost-effectiveness ratio[13], which is calculated by dividing the difference in cost between the two strategies by the difference in effectiveness (i.e., the net cost divided by net benefit). The unit of measure for effectiveness in this analysis is QALYs, resulting in a ratio expressed in dollars per QALY. Although no specific dollar value has been universally agreed on as the threshold for cost-effectiveness, a medical intervention is generally considered to be cost-effective if the incremental cost-effectiveness ratio is ≤$50,000 per QALY[13]. The incremental cost-effectiveness ratio was determined for this model by calculating the difference between the costs accumulated by the patients treated with the antibiotic-impregnated bone cement and those accumulated by the patients treated with the standard bone cement. This dollar amount was then divided by the difference in accumulated QALYs between the two strategies. A second analysis was performed with use of the same methods but with the relative risk of aseptic revision set at one to evaluate the cost-effectiveness of antibiotic-impregnated bone cement when only documented infections are considered as outcomes. By analyzing revisions due to documented infection separately, we could compare the minimal expected benefit from antibiotic-impregnated bone cement with the maximal benefit that could be expected when all revisions were considered in the model.

Sensitivity analysis was then performed on each of the parameters within the model. Sensitivity analysis is used to evaluate how the outcome of the model might change when cost, benefit, or risk assumptions are varied over a plausible range of values. For example, if the cost of a primary total hip arthroplasty is evaluated over the range reported in the literature ($12,846 to $31,000), we can determine whether uncertainty surrounding the true cost of total hip arthroplasty substantially weakens the conclusions drawn from the model.

Source of Funding
No external funding source was used for this study.

Results

When all revisions (those due to infection or aseptic loosening) were considered to be the primary outcome measure, the use of antibiotic-impregnated bone cement for primary total hip arthroplasty was found to be less costly and more effective (dominant), resulting in an overall cost decrease of $200 per patient. When only revision due to infection was considered to be the primary outcome measure, the use of antibiotic-impregnated bone cement was found to have an incremental cost-effectiveness ratio of $37,355 per QALY, which suggests that it is a cost-effective strategy if all of the model parameters remain constant (Table II).

TABLE II Total Cost and QALYs

Primary Outcome Measure/Cement Type	Cost	QALYs	Cost per QALY	Incremental Cost-Effectiveness Ratio
All revisions				
Antibiotic cement	$23,900	9.454	$2533	Dominant
Regular cement	$24,100	9.439	$2551	—
Revisions due to infection				
Antibiotic cement	$23,900	9.454	$2533	$37,355
Regular cement	$23,700	9.445	$2509	—

Revision Rates

Sensitivity analysis revealed that the relative risk of aseptic revision after the use of standard bone cement would need to be <1.2 before the use of antibiotic-impregnated bone cement was no longer the dominant strategy (Table III). Antibiotic-impregnated bone cement remained cost-effective (<$50,000 per QALY) until the relative risk of aseptic revision after the use of standard bone cement was <1.0—i.e., antibiotic-impregnated bone cement would need to be associated with an increased risk of the patient requiring aseptic revision before it would no longer be a cost-effective strategy.

When only revisions due to infection were considered, it was found that the relative risk of revision due to infection with the use of standard bone cement had to be <1.7 before the use of antibiotic-impregnated bone cement was no longer a cost-effective strategy. If the relative risk of infection after the use of standard bone cement were >2.4, the use of antibiotic-impregnated bone cement would become the dominant strategy (Table IV).

Utilities

Sensitivity analysis of the utility values assigned to the different health states revealed that, when all revisions are considered to be the primary outcome measure, antibiotic-impregnated bone cement remains the dominant strategy even when the utility of life after a single primary total hip arthroplasty is equal to the utility of life after a revision due to aseptic loosening or infection (Table III). If only revision due to infection is considered as the primary outcome measure, the utility of a revision due to infection would need to be >0.70 (close to the value of life after primary total hip arthroplasty) before the use of antibiotic-impregnated bone cement would no longer be cost-effective (Table IV).

Disutilities

In the sensitivity analysis, the disutility values assigned to the procedures were found to have essentially no effect on the model over a broad range of values. This held true when all revisions were considered to be the primary outcome measure as well as when only revision due to infection was considered to be the primary outcome measure.

Costs

Sensitivity analysis of costs revealed that the model is much more sensitive to cost parameters than it is to the other parameters

TABLE III Sensitivity Analysis with All Revisions as Primary Outcome

Variable	Threshold at Which Antibiotic Cement No Longer Dominant Strategy (Still Cost-Effective, Incremental Cost-Effectiveness Ratio <$50,000 per QALY)	Threshold at Which Antibiotic Cement No Longer Cost-Effective (Incremental Cost-Effectiveness Ratio >$50,000 per QALY)
Cost of antibiotic cement	>$700	>$1500
Cost of total hip arthroplasty	<$17,000	<$0
Cost of revision due to infection	<2.9 × total hip arthroplasty cost	<0
Cost of aseptic revision	<1.1 × total hip arthroplasty cost	<0
Utility of aseptic revision	>0.85	>0.9
Utility of revision due to infection	>1.0	>1.0
Age	>73 yr	>83 yr
Relative risk of aseptic revision	<1.2	<1.0
Relative risk of revision due to infection	<1.6	<0.8

analyzed. When all revisions were considered to be the primary outcome measure, it was found that the cost of a primary total hip arthroplasty would need to be <$17,000 before the use of antibiotic-impregnated bone cement is no longer the dominant strategy. The use of antibiotic-impregnated bone cement remains cost-effective for all possible values of the cost of a primary total hip arthroplasty. The cost of an aseptic revision would need to be <1.1 times the cost of a primary total hip arthroplasty before the use of antibiotic-impregnated bone cement is no longer the dominant strategy. The additional cost of antibiotic-impregnated bone cement would need to be >$700 before the use of antibiotic-impregnated bone cement is no longer the dominant strategy, and the use of antibiotic-impregnated bone cement would remain cost-effective (<$50,000 per QALY) until its additional cost was >$1500 (Table III).

When only revisions due to infection were evaluated, it was found that the cost of a primary total hip arthroplasty would need to be >$35,000 before the use of antibiotic-impregnated bone cement becomes the dominant strategy. The cost of a primary total hip arthroplasty would need to be <$17,000 before the use of antibiotic-impregnated bone cement is not cost-effective. The cost of a revision due to infection would need to be more than seven times the cost of a primary total hip arthroplasty before the use of antibiotic-impregnated bone cement becomes the dominant strategy. The additional cost of using antibiotic-impregnated bone cement would need to be <$400 before the use of antibiotic-impregnated bone cement becomes the dominant strategy. The use of antibiotic-impregnated bone cement remains cost-effective until the additional cost of antibiotic-impregnated bone cement is >$650 (Table IV).

Age

The average age of the patients within the model also influenced the outcome. As the average age at surgery becomes older, patients are less likely to live long enough to need a revision, so the use of antibiotic-impregnated bone cement becomes less cost-effective. When all revisions were considered as the primary outcome, it was found that the average age of patients would need to be greater than seventy-three years before the use of antibiotic-impregnated bone cement is no longer the dominant

TABLE IV Sensitivity Analysis with Only Revisions Due to Infection as Primary Outcome

Variable	Threshold at Which Antibiotic Cement Becomes the Dominant Strategy (Less Costly, More Effective)*	Threshold at Which Antibiotic Cement No Longer Cost-Effective (Incremental Cost-Effectiveness Ratio >$50,000 per QALY)*
Cost of antibiotic cement	<$400	>$650
Cost of total hip arthroplasty	>$35,000	<$17,000
Cost of revision due to infection	>7.3 × cost of primary total hip arthroplasty	<3.5
Cost of aseptic revision	NA	NA
Utility of aseptic revision	NA	NA
Utility of revision due to infection	<0	>0.7
Age	<46 yr	>71 yr
Relative risk of revision due to infection	>2.4	<1.7

*NA = not applicable.

strategy. The use of antibiotic-impregnated bone cement remains cost-effective until the average age of the patients is greater than eighty-three years (Table III).

When only revisions due to infection were considered, it was found that the average age of the patients needs to be less than forty-six years before the use of antibiotic-impregnated bone cement becomes the dominant strategy. The use of antibiotic-impregnated bone cement remains cost-effective until the average age of patients exceeds seventy-one years (Table IV).

Age and Cost

Age and cost were the two parameters in the model that had the greatest influence on the outcome, with changes over a reasonable range of values. Two-way sensitivity analysis was performed on these parameters to demonstrate their interaction with each other.

When all revisions were considered to be the primary outcome measure, it was found that the cost has to decrease substantially as the average age of the population increases. For example, if the average age is eighty-five, the cost of antibiotic-impregnated bone cement must be <$500 per case to remain a cost-saving strategy. The range for cost-effectiveness (<$50,000 per QALY) is much broader, as demonstrated in the Appendix.

When only revisions due to infection were used as the primary outcome measure, the parameters were much tighter. With an average age of seventy years, the cost of antibiotic-impregnated bone cement would need to be <$350 per case to provide cost-savings. If the average age increases to eighty-five years, the cost of antibiotic-impregnated bone cement would need to be <$200 to provide cost-savings and would need to be <$400 per case to remain cost-effective (see Appendix).

Discussion

This decision model demonstrated that the off-label use of antibiotic-impregnated bone cement is a strategy that is very dependent on the average age of the patients as well as the cost of the antibiotic-impregnated bone cement that is being used. This model showed antibiotic-impregnated bone cement to be cost-effective when the patient population is young (less than seventy-one years old) and the cost of the cement is low (<$650). With the cost of antibiotic-impregnated bone cement still being relatively high in the United States and most American patients under the age of seventy being treated with an uncemented femoral stem, use of antibiotic-impregnated bone cement in primary total hip arthroplasty may be of limited value at this time.

The model is quite sensitive to changes in key parameters when only revision due to documented infection is considered to be the primary outcome measure. The cost of antibiotic-impregnated bone cement in this setting only needs to exceed $650 before it becomes cost-inefficient to use it for all primary total hip arthroplasties. Similarly, if the use of antibiotic-impregnated bone cement does not reduce the risk of deep infection by at least 70%, then it is no longer a cost-effective intervention. It is important to keep in mind that the infection rates used in the model were very low (0.7% over ten years for patients treated with standard bone cement and 0.4% over ten years for those treated with antibiotic-impregnated bone cement) compared with some rates reported in the literature[7]. If infection rates are actually higher, the use of antibiotic-impregnated bone cement would be a more cost-effective option over a wider range of assumptions regarding costs and outcomes. Also, the risk of infection was assumed to be a linear function over time, as opposed to an exponential function with the majority of infections occurring within two years after the initial arthroplasty. The assumption of linearity results in a more conservative estimate of the cost-effectiveness of antibiotic-impregnated bone cement by displacing the costs and utility declines associated with revision into the future. The use of antibiotic-impregnated bone cement would become more cost-effective if more infections occurred within two years, which is likely the case given that the antibiotics are generally fully eluted within four weeks.

Age also strongly influenced the results of the model. In the analysis in which all revisions were considered to be the primary outcome measure, the use of antibiotic-impregnated bone cement was found to cross the $50,000 per QALY threshold when the age of the patients undergoing the primary total hip arthroplasty was greater than eighty-three years. The average age was lower when only revision due to infection was considered as the primary outcome measure, with an average age of greater than seventy-one being the threshold. With the majority of total hip arthroplasty implants in the United States being uncemented, the average age for the use of a cemented prosthesis may be above these thresholds. If the true average age for the use of cement is higher than the thresholds noted above, then perhaps the use of antibiotic-impregnated bone cement is not justified in that population.

The results of this model were more stable over a broader range of parameter estimates when all revisions were considered to be the primary outcome measure. Those analyses demonstrated that the cost of using antibiotic-impregnated bone cement would need to be >$1500 before it becomes cost-inefficient, which is well above the current cost estimates.

A potential concern is that antibiotic-impregnated bone cement has been shown to decrease the rate of aseptic revisions as well as revisions due to infection[5]. One potential explanation is that a low-grade infection that is not detectable by culture is the cause of some aseptic revisions[5]. The reason for the decrease in aseptic revisions is not entirely clear, which is why we also evaluated the model with only revisions due to infection as the outcome measure.

Limitations of the model are generally related to the quality of the data that are used to evaluate the efficacy of antibiotic-impregnated bone cement. The estimations of the revision rates used in this model were based on data from registers, which could have introduced bias into the data. The Norwegian and Swedish Arthroplasty Registers have continued to show a substantial difference in infection rates with the use of antibiotic-impregnated bone cement[5,6], but to date no high-quality randomized controlled trials have been performed to evaluate the efficacy of antibiotic-impregnated bone cement[23,24], probably because of the large number of patients and extended follow-up that would be needed for such an investigation.

Other concerns about the use of antibiotic-impregnated bone cement are the potentials for an allergic reaction as well as for the development of antibiotic-resistant organisms[10,12]. To our knowledge, no allergic reactions have been documented to date, but gentamicin, which rarely causes allergic reactions, has been the antibiotic primarily used in bone cement in Europe. The possibility of an allergic reaction may become greater if other antibiotics such as the cephalosporins are used. Although antibiotic resistance is a theoretical concern, there have not been reports of a greater percentage of resistant infections in Europe, where antibiotic-impregnated bone cement is used extensively. These concerns certainly warrant continued surveillance, but currently there is no evidence that should deter one from using antibiotic-impregnated bone cement for primary total hip arthroplasty on those grounds.

In summary, the off-label use of antibiotic-impregnated bone cement for primary total hip arthroplasty with cement appears to be a cost-effective strategy if the patient population is young and the cost of the cement is relatively low. This may limit the usefulness of antibiotic-impregnated bone cement in primary total hip arthroplasty in the United States, given its current cost and the older average age of patients being treated with cemented femoral stems. In our model, we evaluated costs from a hospital resource-use perspective, which was chosen to determine if the additional up-front cost of antibiotic-impregnated bone cement was justified by a future decrease in costs for revisions. The results can potentially be used by surgeons and policy-makers to help decide whether the use of antibiotic-impregnated bone cement for primary total hip arthroplasty is justified in view of the additional costs, current infection rates, and average age of the population in which a cemented prosthesis is used.

Appendix

eA A figure showing the Markov model and figures demonstrating the results of the sensitivity analyses of age versus cost are available with the electronic versions of this article, on our web site at jbjs.org (go to the article citation and click on "Supplementary Material") and on our quarterly CD/DVD (call our subscription department, at 781-449-9780, to order the CD or DVD). ■

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