ARTICLE

How to Evaluate Pharmacoeconomic Data: The Example of Enoxaparin in Acute Coronary Syndromes

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ABSTRACT

The purpose of this article is to help pharmacists understand the process by which they should evaluate new drugs for inclusion in the formulary, specifically for determining whether the benefit is worth the risk and cost. A cost-effectiveness evaluation of enoxaparin for the treatment of acute coronary syndromes is used as an example. The ESSENCE trial demonstrated that the risk for the composite endpoint of death, myocardial infarction or recurrent angina in patients presenting with unstable angina or non-Q-wave myocardial infarction was lower, for up to 1 year after the index event, among patients treated with enoxaparin than among those who received standard heparin therapy. A pharmacoeconomic study for the Canadian population of the ESSENCE trial showed that treatment with enoxaparin resulted in an annual cost saving of approximately $1,485 per patient treated. A critical appraisal of these 2 studies demonstrates that both were well designed and valid and that their results should be taken into consideration for current clinical practice.

Key words: pharmacoeconomic analysis, enoxaparin, acute coronary syndromes

RÉSUMÉ

L'objectif de cet article est d'aider les pharmaciens à comprendre la démarche qu'ils devraient suivre pour évaluer l'inscription d'un nouveau médicament au formulaire, plus particulièrement pour déterminer si l'avantage l'emporte sur le risque et le coût. Une analyse coût-efficacité de l'énoxaparine dans le traitement des syndromes coronariens aigus a été utilisée à titre d'exemple. L'essai ESSENCE a démontré que le risque combiné de mortalité globale, d'infarctus du myocarde ou d'angine récidivante chez les patients souffrant d'angine instable ou d'infarctus du myocarde sans onde Q était plus faible chez les patients traités à l'énoxaparine que chez ceux ayant reçu de l'héparine standard, et ce, jusqu'à une année après l'événement indicateur. Une étude pharmacoéconomique de la population canadienne de l'essai ESSENCE a montré que le traitement à l'énoxaparine avait entraîné des économies annuelles d'environ 1 485 $ par patient traité. Une évaluation critique de ces deux études a démontré leur rigueur et leur validité et que leurs résultats devraient être considérés dans la pratique clinique actuelle.

Mots clés : étude pharmacoéconomique, énoxaparine, syndromes coronariens aigus

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INTRODUCTION

When a new drug comes on the market, not only must the benefits and risks of the therapy be weighed, but it must also be determined whether the benefits are worth the health care resources consumed. Because of the importance of this decision, pharmacoeconomic evaluations should be performed in accordance with published recommendations, such as the *Guidelines for Economic Evaluation of Pharmaceuticals: Canada*.[1]

The purpose of this article is to help pharmacists understand the process by which they should evaluate new drugs for inclusion in the formulary, specifically how they can determine whether the benefits associated with such drugs are worth the risks and expense. The cost-effectiveness evaluation of enoxaparin in acute coronary syndromes is used to demonstrate the evaluation process. Enoxaparin, a low-molecular-weight heparin, has recently been approved in Canada for use in acute coronary syndromes. It is also indicated for prophylaxis against

deep vein thrombosis after surgery and for the treatment of deep vein thrombosis and pulmonary embolism.

PRINCIPLES OF PHARMACOECONOMICS

Efficacy, effectiveness, and efficiency are 3 facets to be considered when evaluating the benefits of a drug. Efficacy reflects the benefits of a treatment under the ideal conditions usually present in a clinical trial.[2] Effectiveness refers to the benefits associated with a drug being used in clinical practice. Efficiency encompasses not only the results of using a drug but also its costs. Thus, pharmacoeconomic studies try to determine drug efficiency by comparing the costs and consequences of pharmaceutical products with those of relevant alternatives. These studies are pertinent to the decision-making process when trying to balance the costs of specific alternatives with their respective differences in clinical outcome.

There are 5 primary types of pharmacoeconomic analysis: cost–consequence analysis, cost–benefit analysis, cost-effectiveness analysis, cost–utility analysis, and cost-minimization analysis.[1-3] Each type of analysis entails a comparison of the costs and therapeutic consequences of different drugs or treatments in treating a particular medical condition or, in some cases, various conditions. The type of analysis chosen for an economic study depends on the question being asked. The 5 types of analysis differ primarily in terms of how therapeutic consequences are measured. The therapeutic outcome can be measured in monetary terms (cost–benefit analyses), physical units (cost–consequence and cost-effectiveness analyses), or measures of quality of life (cost–utility analysis), or the therapeutic consequences can be assumed to be equal, as in cost-minimization analyses (Table 1).[2]

Table 1. Types of Pharmacoeconomic Analyses

Type of analysis	Description	Cost Unit	Therapeutic Outcomes Unit	Comments
Cost–consequence analysis	Costs and consequences of the drug compared with one or more relevant alternatives and simply listed in disaggregated form	Monetary	Physical units such as life years gained, cases successfully treated, blood pressure (as millimetres of mercury), among others	*Limitation:* Based on the premise that the authorized decision-makers can make the value judgement trade-offs necessary to integrate a disparate list of pros and cons (the costs and consequences) of the various alternatives and reach a final decision
Cost–benefit analysis	Cost–benefit ratio	Monetary	Monetary; valued by asking patients what they would be willing to pay for services that achieve these particular outcomes	Rarely used *Limitation:* Difficult to express clinical results in dollars; ethical concerns related to placing a pecuniary value on human life and health
Cost-effectiveness analysis	Used when a single dimension of effectiveness characterizes the relevant outcome for all therapies, and competing therapies do not have the same clinical effectiveness; describes the incremental gain in therapeutic benefits derived from the extra costs and aids in decision as to whether the extra benefits are worth the extra costs	Monetary	Physical units such as life years gained, cases successfully treated, blood pressure (as millimetres of mercury), among others	*Preferred strategy:* Option that shows the least cost per outcome measure gained *Limitation:* Treatment strategies cannot be compared across diseases or programs
Cost–utility analysis	Used when units for measuring the benefits of the therapies compared are different and a cost-effectiveness analysis cannot be performed; compares alternative approaches to a single health problem or treatment strategies across a variety of health problems	Monetary	Outcomes of different types are weighted by a person's preference for experiencing the outcome to produce a composite index (e.g., quality-adjusted life years [QALY] or healthy years equivalent)	*Preferred strategy:* Option with the lowest cost per QALY *Limitation:* Difficult to compare QALYs across people, since individuals' preferences over health states may vary
Cost-minimization analysis	Costs of each alternative are compared and the one with the lowest cost is selected	Monetary	Identical clinical effectiveness of different therapies is assumed	Simplest method

The results of economic studies should be expressed in terms of differences in the costs of various therapies in relation to differences in their benefits. This is known as "incremental analysis."[2] If one therapy demonstrates greater benefits at lower cost, it is said to dominate the comparator.

It must be remembered that most of these methods of economic evaluation ultimately lead to some type of social valuation indicating what we, as a society, are willing to pay to derive the benefits described. However, the design of economic studies depends very much on the medical patterns for treating the disease in question, which can vary greatly from one country to another. Thus, even if the clinical consequences or outcomes measured in a clinical trial performed in another country are considered applicable to a local population, care must be taken to ensure that the economic evaluation is equally applicable.

The following paragraphs describe the various aspects of evaluating a pharmacoeconomic study, as developed by the Evidence-Based Medicine Working Group.[4,5] These concepts are applied to the case of enoxaparin use in acute coronary syndromes, as presented in the Efficacy and Safety of Subcutaneous Enoxaparin in Non-Q-Wave Coronary Events Study (ESSENCE),[6,7] along with data from the Canadian cost-effectiveness analysis of ESSENCE.[8]

CASE EXAMPLE OF ENOXAPARIN

The ESSENCE study[6] was a multicentre, randomized, double-blind, controlled clinical trial that compared the effect of enoxaparin with that of unfractionated heparin on a composite endpoint of total mortality, myocardial infarction or recurrent angina in 3171 patients presenting with unstable angina or non-Q-wave myocardial infarction. It demonstrated a significant (15%) decrease in the composite endpoint at 14 and 30 days,[6] a benefit that was maintained for up to 1 year.[7] The risk of major bleeding associated with enoxaparin was similar to that associated with unfractionated heparin (6.5% and 7.0% respectively), although enoxaparin was associated with significantly more bleeding overall, primarily because of ecchymoses at the site of injection.[6]

In critically evaluating a pharmacoeconomic study, such as the ESSENCE trial, various approaches may be used. One of these methods, developed by the Evidence-Based Medicine Working Group,[4] is based on 3 questions: Are the study and its results valid? What were the results? and Can I expect the same results for my patients? Here, these questions are answered with regard to the use of enoxaparin in patients with acute coronary syndromes.

Are the Study and Its Results Valid?

In determining whether a study and its results are valid, it must be established that the economic analysis actually determines which of the clinical strategies would provide the most benefits for the available resources. Several factors must be taken into account, as follows.

Did the Analysis Provide a Full Economic Comparison of Effective Health Care Strategies?

An economic analysis compares 2 or more treatment strategies, and it is crucial that all relevant clinical strategies be included. In addition, both costs and outcomes (efficacy and risk, as determined in a randomized clinical trial) must be analyzed for each treatment strategy, with a broad enough viewpoint to be clinically useful.

Were all of the relevant clinical strategies compared? The first assessment evaluates the scope of each of the treatment strategies being compared. One of the therapies evaluated should be the current, approved, standard treatment, so that the new therapy can be compared with the current standard of care. The new (alternative) therapy must not be viewed as an all-or-nothing option that would necessarily replace the standard therapy for all patients. Some strategies are best applied selectively to the specific populations that would benefit most from them. In the ESSENCE trial, all patients received the current standard of care for the management of acute coronary syndromes.[6] Everyone received acetylsalicylic acid (ASA), and the need for any other medications and the decision to proceed with coronary angiography and revascularization were left to the discretion of the treating physician. In addition, patients were randomly assigned to receive either unfractionated heparin or enoxaparin at the standard dose for patients presenting with unstable angina or non-Q-wave myocardial infarction.[9] The standard dose of heparin was an IV bolus (usually 5000 units) followed by a continuous infusion at a dose adjusted according to the activated partial thromboplastin time. The standard dose of enoxaparin was 1 mg/kg SC bid. Both therapies were administered for 2 to 8 days. The question of whether any subpopulations would benefit more from enoxaparin therapy will be addressed in a later section.

Was the viewpoint broad enough? Cost and outcomes may be examined from different points of

view, for example, those of the patient, the pharmacy department, the hospital, and society as a whole. Although pharmacists tend to focus mainly on the relative costs of drugs that are covered by the pharmacy budget, this may be too narrow a viewpoint, especially in cases where drug use affects the use of other hospital resources.

O'Brien and others[8] hypothesized that, from the perspective of a Canadian health care payer, the 1-year cumulative mean cost of health care for patients treated initially with enoxaparin would be less than for patients who received unfractionated heparin. Therefore, they conducted a pharmacoeconomic study based on resources consumed by all Canadian participants in the ESSENCE trial during the initial hospital stay and a 1-year follow-up period, including all readmissions to hospital. Because this study was conducted from the perspective of a Canadian health care payer, the costs include physicians' fees in addition to hospital costs.

Were the Costs and Outcomes Properly Measured and Valued?

To determine whether costs and outcomes were properly measured and valued, 3 main questions must be addressed.

Was clinical effectiveness established? If a pharmacoeconomic evaluation is to be considered valid, the clinical efficacy of the therapeutic strategy must first be established. Although randomized clinical trials are considered the best way to evaluate the clinical efficacy of a drug, it is preferable to base pharmacoeconomic evaluations on effectiveness data that reflect clinical practice as closely as possible. For example, some randomized clinical trials use very specific populations, as determined by the inclusion and exclusion criteria, and it becomes difficult to extrapolate the results obtained to the population at large. Therefore, the "generalizability" of economic data based on such trials must be carefully reviewed. Nonetheless, a pharmacoeconomic evaluation based on prospective economic data collected during a well-designed clinical trial has high internal validity.

If the rules of evidence-based medicine are applied in a critical appraisal of the ESSENCE trial, strong support emerges for the clinical effectiveness of enoxaparin in the management of acute coronary syndromes. The ESSENCE trial meets the criteria for a valid study. It was a multicentre, double-blind, placebo-controlled, randomized study. Both groups, which were similar at the start of the trial, were treated equally, except in terms of the administration of unfractionated or low-molecular-weight heparin. However, the authors did not specify whether all patients who entered the trial were accounted for at its conclusion.

In the ESSENCE trial, enoxaparin had statistically significant benefits in patients with unstable angina or non-Q-wave myocardial infarction. The primary outcome (composite endpoint of death, myocardial infarction or recurrent angina at 14 days) was 16.2% lower with this drug (odds ratio [OR] 0.80, 95% confidence interval [CI] 0.67–0.96, $p = 0.02$).[6] Furthermore, the composite endpoint was 15% lower at 30 days (OR 0.81, 95% CI 0.68–0.96, $p = 0.02$) and 10% lower at 1 year (hazard ratio 0.87, 95% CI 0.77–0.98, $p = 0.022$) among patients who received enoxaparin.[7]

From a safety standpoint, there was no significant difference between the 2 groups with regard to serious hemorrhagic complications (which occurred in 6.5% of patients who received enoxaparin and 7.0% of those who received unfractionated heparin; $p = 0.57$).[6] There was, however, a higher frequency of minor hemorrhagic complications among patients treated with enoxaparin than among those treated with unfractionated heparin (11.9% and 7.2% respectively; $p < 0.001$). The most frequent minor hemorrhagic event was injection-site ecchymosis.

Were the costs measured accurately? To answer this question, it is helpful to have information about the physical quantities of resources consumed or released by the therapies, in addition to their costs. This type of information allows detailed interpretation of the data, such as a determination of how monetary values were assigned to resources, and helps in comparing the results of a study done in one setting with those of a study done elsewhere, given that costs may differ between locations. In addition, costs may change over time; for example, some agents might be less expensive today than when the study was performed. Finally, some authors may report charges (to the patient or the third-party payer) rather than costs.

Among the Canadian participants in the ESSENCE trial, enoxaparin use resulted in a decrease in the use of some other health care resources, especially the number of coronary angioplasty procedures for revascularization (Table 2). For the Canadian pharmacoeconomic study of ESSENCE,[8] cost weights for hospital stays and procedures were obtained from 2 hospitals participating in the Ontario Case-Costing Project, and the Canadian market prices for enoxaparin and unfractionated heparin were used. All costs were reported in 1997 Canadian dollars. In addition, the length of hospital stay

Table 2. Health Care Resource Utilization for Canadian Patients in the ESSENCE Trial

Aspect of costs	Treatment; % of patients*		*p* value
	Heparin	Enoxaparin	
Initial hospital stay			
Diagnostic cardiac catheterization	39.1	35.0	0.15
Percutaneous transluminal coronary angioplasty	15.0	10.6	0.03
Coronary artery bypass grafting	9.1	7.9	0.52
Mean length of stay (days ± SD)	10.7 ± 8.9	10.0 ± 8.5	0.16
Follow-up costs			
Diagnostic cardiac catheterization	51.9	48.9	0.24
Percutaneous transluminal coronary angioplasty	19.7	16.0	0.08
Coronary artery bypass grafting	19.6	16.3	0.16
Mean length of stay (days ± SD)	16.7 ± 17.4	15.4 ± 14.8	0.15

*Except where indicated otherwise.

and the use of procedures during the initial hospital stay and for 1 year afterward were presented by treatment group.

Were data on costs and outcomes appropriately integrated? As previously mentioned, an incremental analysis should be performed. Furthermore, adjustments should be made for any differences in timing of the measurement and valuation of costs and outcomes. Usually, lower weight is allocated to costs and benefits occurring in the future; an annual discount rate of 5% is commonly used.

In the ESSENCE study, enoxaparin had greater efficacy than unfractionated heparin in terms of the composite endpoint of death, myocardial infarction and recurrent angina, a difference that was observed for up to 1 year.[6,7] From an economic point of view (Table 3) enoxaparin use resulted in an overall initial mean hospital cost saving of $743 (95% CI of –$1,809 to $244) per patient, even though the mean cost of enoxaparin was higher by $62.[8] After discharge, lower risks and costs were maintained. When initial hospital and follow-up costs (to 1 year) were combined, the 1-year cost saving was $1,485 (95% bootstrap CI[10] –$93 to $3,167, $p = 0.06$) per patient receiving enoxaparin. Although they did not reach statistical significance at the conventional 5% level, these results demonstrated a strong trend in favour of enoxaparin. The confidence interval indicates a 95% chance that the real difference in cost associated with enoxaparin use was between an additional cost of $93 and a saving of $3,167 over a 1-year period. Statistically, then, enoxaparin use would probably result in a cost saving, even though the exact amount might be more or less than $1,485. In this case, because cost savings are likely and the therapy is more effective than the control, there is no incremental cost, and calculation of the incremental cost-effectiveness ratio is unnecessary. However, an incremental cost-effectiveness ratio could be calculated for the cost associated with the lower limit of the confidence interval (additional cost of $93).

Was Appropriate Allowance Made for Uncertainties in the Analysis?

Imprecise estimation or methodological controversy may lead to uncertainties in economic evaluations. Typically, such uncertainties are taken into consideration through a sensitivity analysis, whereby estimates of key variables are modified to evaluate their impact on the study results.

In the pharmacoeconomic study of Canadian participants in the ESSENCE trial, such sensitivity analyses were appropriately conducted on the costs of various resources, in 3 different ways: using the upper 95% confidence limits from the regression model for the cost of all revascularization procedures, using the lower 95% confidence limits from the regression model for the cost of all revascularization procedures, and using the estimated cost for a community hospital.[8]

Are Estimates of Costs and Outcomes Related to the Baseline Risk in the Treatment Population?

Categorization of patients according to risk is common in clinical practice. It is important to realize that the baseline risk of participating patients will influence the costs and outcomes of treatments. Such information is valuable in evaluating which of a group of patients should receive the alternative therapy.

In the case of ESSENCE, neither the parent trial nor the pharmacoeconomic analysis divided patients into risk categories. It would have been interesting to confirm that all patients benefited equally or to learn that some patients in fact benefited more than others.

Table 3. Mean Cost of Resources per Patient*

Aspect of Cost	Treatment; mean cost per patient ($)		Difference (E – H)	*p* value (bootstrapping[10])
	Heparin (H)	Enoxaparin (E)		
Initial hospital stay	10,663	9,920	–743	0.14
Drugs	39	101	62	
Health care	10,624	9,819	–805	
Follow-up	5,833	5,092	–741	0.26
Total	16,497	15,012	–1,485	0.06

*Some of the values do not sum to totals given because of rounding.

What Were the Results?

Once it has been established that the results of the study under consideration are valid, then it is worth examining these results further. If it is determined that the study was not valid, the results should be discarded, regardless of the apparent effect size. In the case of the pharmacoeconomic study of Canadian participants in ESSENCE, the results were valid. The next step is to evaluate the effect size. Again, a number of questions can be asked in making this evaluation.[5]

What Were the Incremental Costs and Effects of Each Strategy?

In the pharmacoeconomic study of Canadian participants in ESSENCE, resources used were quantified by treatment group for 2 time periods: initial hospital stay and 1-year post-discharge follow-up (Table 2).[8] The enoxaparin group had a slightly shorter length of stay than the unfractionated heparin group (although the difference was nonsignificant), and the use of cardiac procedures was also lower. The costs of the initial hospital stay, including the cost of the study drug, were $10,663 per patient treated with unfractionated heparin and $9,920 per patient treated with enoxaparin. The main difference in cost resulted from the cost of revascularization procedures and other health care resources (such as hospital stay) (Table 3). The overall difference in cost over the first year between enoxaparin and unfractionated heparin treatment was therefore a saving of $1,485 with enoxaparin.

The measure of effectiveness in this case was the composite endpoint of mortality, myocardial infarction or recurrent angina. The follow-up data available to 1 year demonstrated a lower event rate (by 10%).[7] Therefore, enoxaparin appears to be more effective than unfractionated heparin, and it costs less.

Do Incremental Costs and Effects Differ between Subgroups?

As mentioned earlier, subgroup analysis was not performed in the pharmacoeconomic study of Canadian ESSENCE participants. However, it would have been interesting to confirm that all subgroups benefited equally or to determine which patients were more likely to benefit from such therapy.

How Much Does Allowance for Uncertainty Change the Results?

The authors looked at 3 scenarios with alternative cost assumptions.[8] With the upper 95% confidence limit of the cost of all revascularization procedures, the 1-year cost saving associated with enoxaparin was $1,523 per patient, and with the lower 95% confidence limit of these costs, the saving was $1,447. Finally, with the costs observed in a community hospital, the 1-year cost saving associated with enoxaparin use was $1,075 per patient. Therefore, allowing for some uncertainty in costs did not substantially change the results. Regardless of the scenario, use of enoxaparin in the management of acute coronary syndromes cost less than using unfractionated heparin.

Hence, on the basis of the evaluation presented above, it is cost-effective to use enoxaparin in the setting of acute coronary syndromes.

Can the Results Be Applied to My Patients?

If the economic analysis yields valid and important results, each pharmacist must then examine whether these results can be applied in his or her own clinical setting,[5] according to the following questions.

Are the Treatment Benefits Worth the Harms and Costs?

Table 4 presents a simple way of categorizing economic results based on incremental costs and effects.

It consists of a 3 x 3 matrix defining the new treatment as being more, the same, or less costly than the control therapy and as being more, the same, or less effective. The numbers in the matrix represent the 9 possible combinations of these 2 factors.

When a treatment falls into category 1 or 2, the decision to be taken is evident: for category 1, the treatment is more effective and less costly than the control and therefore should be used without question, whereas for category 2, the treatment is less effective and more costly and thus should be rejected. Categories 3 and 6 represent treatments that are more effective and as expensive and those that are as effective and less expensive than the control, respectively. Again, use of the new treatments should be recommended, as the patient or the payer may benefit from better effectiveness or lower cost. If the new treatment is as effective but more expensive (category 4) or as expensive but less effective (category 5), it should be rejected. Therefore, for the shaded cells of Table 4, cost-effectiveness ratios need not be calculated. However, further analysis is required if the results fall into one of the unshaded cells, 7, 8, or 9. Category 7, where the new therapy is more effective and also more expensive, occurs most frequently. At times, the new therapy may be just as effective and just as costly as the standard therapy (category 9), or it may be less effective but also less expensive (category 8). In such cases, it is useful to calculate the incremental cost-effectiveness ratio of the new therapy.

The ESSENCE trial[6] demonstrated that enoxaparin had greater effectiveness than standard therapy with unfractionated heparin, and the pharmacoeconomic study[8] reported lower health care costs. Thus, it appears that enoxaparin falls into category 1 and hence it "dominates" unfractionated heparin. Therefore, the treatment benefits associated with enoxaparin can be considered worth the additional costs.

Can My Patients Expect Similar Health Outcomes?

Once a potential benefit for patients has been established, individual pharmacists must determine whether this benefit can be expected in his or her practice setting. Two factors must be taken into account in determining whether the economic data are applicable to the local setting: first, whether the estimated treatment effect observed in the clinical trial can be expected in the local clinical setting and second, whether or not the costs are applicable in the local setting. In summary, if the economic analysis is to be applicable, the cost-effectiveness evaluation should show little variation in terms of clinical practice patterns and amount and cost of health care resources consumed.

Two other factors must be evaluated to determine whether patients in the local practice setting can expect the same health outcomes: the similarity between the study patients and those in the local setting, and the similarity in clinical management between the 2 patient groups. If the local patients meet the inclusion and exclusion criteria of the clinical study, there is little doubt that the patients are similar. However, the local patients often do not perfectly replicate the study patients, in which case the pharmacist should try to determine how the local population differs, and if and how these patients might respond differently to the new therapy.

In the ESSENCE trial, patients were older than 18 years and had recent onset of angina at rest lasting at least 10 min and occurring within 24 h before randomization.[6] In addition, the patients had evidence of underlying ischemic heart disease without a left bundle branch block or pacemaker, angina with an established precipitating cause, or creatinine clearance of less than 30 mL/min. Most of the patients were men with hypertension (54%) or hypercholesterolemia (44%). As for clinical management, little information was

Table 4. Possible Outcomes* in Comparison of Study and Control Treatments in Terms of Incremental Cost and Effectiveness[5]

Incremental Cost of Treatment Compared with Control	Incremental Effectiveness of Treatment Compared with Control		
	More	Same	Less
More	7	4	2
Same	3	9	5
Less	1	6	8

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*The numbers in the cells represent 9 combinations of effectiveness and cost in the comparison between treatment and control. Shading indicates combinations for which the decision is evident and cost-effectivenenss ratios need not be calculated.

provided about other aspects of treatment, except that all patients received ASA. On the basis of these criteria, it can be expected that any patient presenting with similar characteristics can expect significant benefits from treatment with enoxaparin.

Can I Expect Similar Costs?

Two factors must be taken into consideration in determining whether cost data can be applied to a specific practice setting: the similarity in clinical practice patterns and local costs for health care resources. In some cases, clinical practice patterns differ to the extent that resource consumption associated with the treatment differs from that reported in the study. Thus, in an economic evaluation, resources used and unit prices must be examined separately to establish that practice patterns and costs will apply in a different practice setting.

In the case presented here, the pharmacoeconomic evaluation was undertaken for a large Canadian subgroup of patients from the ESSENCE trial (more than 40% of patients recruited for the trial were from Canadian centres). Thus, it can be safely assumed that clinical practice patterns measured in the clinical trial would be similar to those seen in other centres. To adjust for potential variations among centres, the authors performed a sensitivity analysis using costs from a community hospital.[8] Even with the lower per diem rate from a community hospital, the cost saving was $1,075 per patient treated over 1 year. Thus, treating patients with enoxaparin in this setting is still less costly and more effective than using unfractionated heparin.

DISCUSSION

The present article used a method developed by the Evidence-Based Medicine Working Group to evaluate the published pharmacoeconomic data about the use of enoxaparin in the setting of non-ST-elevation acute coronary syndromes.

A good understanding of applied pharmacoeconomics is needed to ensure that any decisions will be in the best interest of patients, the health care system, and society. Various authors have found wide variations in the quality and rigour of previously published pharmacoeconomic evaluations.[11-13] In an attempt to compensate for these problems, several methods have been developed to help health care professionals make better (and better-informed) decisions. In Canada, the Canadian Coordinating Office for Health Technology Assessment (CCOHTA) has published guidelines for the economic evaluation of pharmaceuticals.[1] This document presents 25 guidelines encompassing research methods and the reporting of analysis and results. In addition, the guidelines list 19 questions that should be answered to assess the validity of pharmacoeconomic evaluations. Similarly, Sanchez[14] developed a series of 34 questions, grouped according to 11 elements, that could be asked in evaluating a pharmacoeconomic study. The method used in the current article involved 13 questions, very similar in nature to the ones proposed by Sanchez and CCOHTA, although perhaps addressed less exhaustively.

In many instances, pharmacoeconomic data are unavailable when a decision must be made on including a drug in the formulary. In such cases, one possibility is to conduct an institution-specific pharmacoeconomic research trial. However, such research can be time consuming and challenging, because of lack of resources, small sample sizes, and other limitations. Nonetheless, guidelines for the design, conduct, and reporting of such investigations are available.[1,15]

In conclusion, to critically evaluate a pharmacoeconomic study, 3 main questions must be answered. First, the validity of the study and its results must be established. If the study is valid, the results should be scrutinized. If an efficacy or cost advantage is found, then it must be determined whether the results can be applied to a specific clinical practice.

For managing patients with unstable angina or non-Q-wave myocardial infarction who present with angina at rest, the ESSENCE trial showed that treating patients with enoxaparin is more effective and less costly than treating them with unfractionated heparin. The pharmacoeconomic evaluation of Canadian participants in the ESSENCE trial clearly demonstrated significant cost savings and clinical benefits of enoxaparin over unfractionated heparin, regardless of the clinical treatment setting. This saving should translate into better efficiency for individual treatment centres by allowing more patients to gain access to limited care resources, thus shortening waiting lists and increasing productivity.

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