

CME/CPE Article

## Economics of Low-Molecular Weight Heparins

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### Abstract

Low-molecular weight heparins (LMWHs) have become attractive alternatives to standard unfractionated heparin (UFH) for the treatment and prophylaxis of deep vein thrombosis (DVT), and for the management of acute coronary syndrome (ACS). The economic impact of the use of LMWHs has been studied in randomized controlled studies, in demonstration projects in managed care institutions, and in decision models. These studies provide valuable insight into the ways LMWHs can be economically attractive despite higher per unit costs compared with UFH. For the treatment of DVT, the cost benefit of using LMWHs results primarily from the cost shifting from inpatient to outpatient care, and might be limited by the eligibility of patients for outpatient management. In contrast, the attractiveness of LMWHs for ACS and DVT prophylaxis hinges on the increased effectiveness of LMWHs compared with standard UFH.

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Low-molecular weight heparins (LMWH) have recently emerged as the treatment of choice for a variety of medical conditions. A recent review summarized the pharmacology of LMWH and their clinical efficacy for the treatment of venous thromboembolic disease and acute coronary syndrome (ACS).<sup>1</sup> We focus our review on the economics of LMWH for the treatment of deep vein thrombosis (DVT) because the literature on this subject is instructive of the range of approaches to economic evaluation and because the treatment of DVT illustrates the ways in which new treatments might impact the amount and types of resources used. These resource shifts are important to consider before making aggressive efforts to change clinical practice because the changes can reverberate throughout the medical community. We comment briefly on the economics of LMWH for the acute treatment of ACS and for the prophylaxis of DVT.

### Deep Vein Thrombosis

DVT is a relatively common disease affecting approximately 450,000 to 2 million Americans each year.<sup>2,3</sup> Since the 1960s, the administration of intravenous unfractionated heparin (UFH) followed by warfarin has been widely accepted as the standard of care.<sup>2,4</sup> More recently, however, LMWH have been compared to UFH for the initial treatment of DVT. Four recent meta-analyses of randomized controlled trials have shown that LMWHs are at least as safe as UFH with regard to major bleedings, and as

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effective in preventing thromboembolic recurrences, and in reducing mortality.<sup>5-8</sup> Therefore, LMWH is now widely accepted as an alternative to UFH for the initial treatment of DVT.<sup>9</sup> Although the unit cost of LMWH is greater than that of UFH, physicians and healthcare managers have focused their interest on increased patient convenience and potential hospital costs savings by increasing the number of patients treated at home.<sup>3, 10-17</sup>

Different approaches have been used to address the economics of LMWHs in the treatment of DVT. In turn we will consider cost analyses of randomized controlled trials, demonstration projects, and cost-effectiveness models.

### Studies Indicating Economic Impact of DVT Treatment

Several studies that have analyzed the economic impact of treating

patients with LMWH or UFH are described (Table 1).

Hull et al reported the economic analysis of the American-Canadian Thrombosis Study, a multicenter, double-blind, randomized placebo-controlled trial comparing the efficacy of in-hospital intravenous infusion of UFH with a once-daily in-hospital subcutaneous dose of tinzaparin sodium in 432 patients with proximal venous thrombosis.<sup>18</sup> The economic analysis included cost of administering the treatment (cost of treatment plus hospitalization costs) and the cost for the diagnosis and treatment of recurrent venous thromboembolism for 12 months and for major bleeding complications.<sup>19</sup> The number of events was obtained from the original study and cost data were based on the actual costs that were derived from patient care. The primary analysis showed that although all patients

**Table 1.** LMWH for the Management of DVT: Event Rates and Costs per 100 Patients in Randomized Controlled Trials

Study	Treatment Arms	Recurrent VTE (%)	Major Bleed (%)	Deaths (%)	Hospital Days (mean)	Cost (US\$ per Patient)	Cost Difference (US\$ per Patient)	Follow Up
Hull et al <sup>19</sup> (American-Canadian Thrombosis Study)	UFH versus tinzaparin	7 3	5 3	10 5	All inpatients	3578 3357	401	1 year
van den Belt et al <sup>20</sup> (TASMAN study)	UFH versus fraxiparin	8.6 6.9	2 0.5	8.1 6.9	9.7 4.0	4649* 1664*+	2985	6 months
O'Brien et al <sup>16</sup>	UFH versus enoxaparin	7.3 6.7	0.7 3.4	6.7 <sup>‡</sup> 4.5 <sup>‡</sup>	6.7 0.9	3857§ 1651§	2206	3 months
Belcaro et al <sup>11</sup>	UFH versus nadroparin versus SC heparin	6.2 6.1 7.1	0 0 0	NA	5.4 5.1 0	2760 773 221	1987	3 months
Boccalon et al <sup>17</sup>	LMWH in hospital versus at home	2 1	2 2	2 0	9.6 1.0	4025   1775	2250	6 months

\*Based on 1993 exchange rate (1 US\$ = 0.54 NGL); †Based on 51 patients treated in Amsterdam Medical Center; ‡Based on 500 patients included in the initial trial; §Based on 1997 exchange rate (1 US\$ = 1.38 Can\$); ||Based on 1993-1997 exchange rate (1 US\$ = 5.2 FF). DVT = deep vein thrombosis; LMWH = low-molecular weight heparin; SC = subcutaneous; UFH = unfractionated heparin; VTE = venous thromboembolic event.

were treated as inpatients, the use of LMWH was associated with cost savings of \$401 per patient. Because of the double-blind design of the study, the investigators were not able to evaluate the use of outpatient care directly. Therefore, they hypothesized that the 37% of patients without comorbidities could receive LMWH as outpatients after 2 days of hospitalization. Using this hypothesis, the authors estimated that LMWH would save \$2845 per patient compared to UFH.

In the TASMAN study, 400 patients were randomized in 9 centers (Europe, Australia, New Zealand) to either outpatient management with fraxiparine or inpatient intravenous UFH. Patients randomized to outpatient management were treated at home as soon as feasible.<sup>14</sup> On average 35% (range, zero to 87%) of the patients were never admitted to a hospital, but a wide variability in management strategies was observed between the centers.<sup>20</sup> Although a resource utilization analysis (including number of hospital days, outpatient visits, telephone calls, and domiciliary care) was performed on the entire population of the study patients, a cost-minimization analysis was limited to detailed data on a subset of 51 patients treated in the Amsterdam Academic Medical Center. Eighty-three percent of this group were treated as outpatients, which limits the generalizability of the cost analysis. In the entire population, hospital stays were reduced from 9.7 to 4.0 days. In the subgroup, cost savings were approximately \$3000 per patient.

O'Brien et al reported an economic evaluation of a randomized, unblinded study comparing the in-hospital administration of UFH with the at-home administration of enoxaparin in 500 Canadian patients.<sup>16</sup> The economic analysis was performed on the 300 patients presenting with proximal vein thrombosis as outpatients. Costs included healthcare costs, patient

travel costs, and productivity costs. In the LMWH group, 81% of the patients were treated entirely as outpatients. This resulted in cost savings of approximately \$2200 per patient. The authors observed that patients receiving standard heparin had a mean of 6.79 days of work absence compared with 3.14 days for patients receiving LMWH. In contrast, patient travel was higher for LMWH patients than for those patients receiving standard heparin (89.9 versus 0.7 km, respectively). Finally, there was no difference in quality of life assessed by the Short-Form-36 questionnaire, except for the domain of social functioning, where a greater improvement from baseline to day 7 was observed in the LMWH group.

Belcaro et al randomized 294 patients with acute proximal DVT to receive intravenous UFH in the hospital, nadroparin twice daily at home or at the hospital with an early discharge, or subcutaneous heparin at home.<sup>11</sup> Patients treated with intravenous UFH or LMWH were switched to oral anticoagulant that was maintained for 3 months. Patients receiving subcutaneous heparin were injected twice daily for 3 months without oral anticoagulants. In the cost analysis, the authors considered costs associated with hospital stay and with treatment and monitoring. The costs in the LMWH group were only 28% of the cost of UFH, and the mean duration of hospital stay was reduced from 5.4 to 5.1 days, with 33.7% of the patients being not hospitalized at all.

A small trial from Singapore analyzed the costs of LMWH and UFH in 16 patients.<sup>21</sup> Considering the costs of the drugs, materials, lab tests, and medical/nursing time, the authors found that LMWH was slightly more expensive (approximately \$7 per patient) than UFH. This study did not include the potential savings associated with early discharge from the hospital or other efficacy benefits of LMWH.

Finally, a study was conducted that randomized 201 patients to receive LMWH (nadroparin, enoxaparin, or dalteparin) either at home or in the hospital.<sup>17</sup> In the "at home" group, 48% of the patients were never admitted to the hospital, and 9.2% had a hospital stay longer than 48 hours. Because the clinical results for efficacy were similar, a cost-minimization analysis was performed for the initial 10-day period of treatment. The outpatient strategy was associated with cost savings of approximately \$2250 per patient.

**DVT: Demonstration Projects**

Following the results of randomized controlled trials showing the efficacy and potential cost savings of LMWH, different groups have implemented DVT management programs (Table 2).

One hundred twenty-five patients were included in a multidisciplinary outpatient DVT program in a 532-bed teaching hospital in North Carolina.<sup>13</sup> Sixty-seven percent of the patients were in the hospital for less than 24 hours and the average length of stay was 0.97 days, which represented a decrease of 4.5 days compared with before the program. Economic data were collected for

each patient, from the hospital's perspective. Net hospital profit was estimated to be \$2471 per patient, computed as the difference between the hospital reimbursement (\$3436) and hospitalization (\$601) plus drug (\$364) costs. No new staff members were hired for this program and the only additional cost of the program was for outpatient drug supplies.

Another program implemented in a multispecialty physician group in Boston belonged to a large health maintenance organization.<sup>22</sup> This program was anchored to a central coordinating group in the urgent care department of the health center, which was staffed by nurses and physicians. Utilization of resources and costs of the program were compared to data collected before the program was implemented. The program was associated with an increase in the number of outpatients (from 10% to 54%). This required on average 2.4 outpatient visits within 2 weeks of diagnosis and 2.4 visiting nurse home visits per patient. Despite an increase of \$469 per patient in the outpatient costs (including LMWH cost of \$194), a decrease in hospitalization costs (\$2215 per patient) resulted in a

**Table 2.** LMWH for the Management of DVT: Demonstration Projects

Study	Setting	Treated as Outpatients (≤ 24 hours in hospital)	Reduction in Hospital Days (mean)	Savings per Patient (US\$)
Pearson et al <sup>22</sup>	Multispecialty group practice, Boston	54%	1.4	1746 (healthcare system perspective, HMO)
Dedden et al <sup>23</sup>	Kaiser Permanente Medical Center, Fontana, California	NA	NA	547 (healthcare system perspective, HMO)
Groce <sup>13</sup>	532-bed teaching hospital, North Carolina,	67%	4.5	2471 (hospital perspective)
Lindmarker et al <sup>24</sup>	14 hospitals in Sweden	35%	NA	810* (payer perspective)

\*Based on 1994 exchange rate (1 US\$ = 7.7 Swedish crowns). DVT = deep vein thrombosis; HMO = health maintenance organization; LMWH = low-molecular weight heparin.

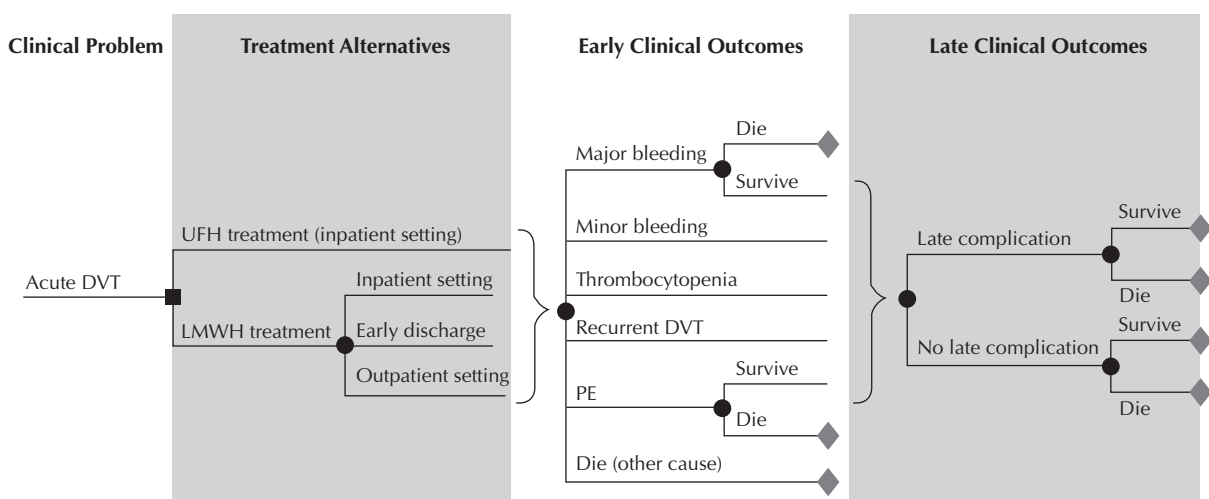
mean savings of \$1746 per patient. Considering only patients treated as outpatients, the average cost per patient was \$1402. Interestingly, patients who required hospitalization after the implementation of the program had longer hospital stays (1.6 extra days) and higher hospital costs (extra \$1481) than did patients hospitalized before the program.

In another managed care setting—Kaiser Permanente Medical Center in Fontana, California—a program for home enoxaparin treatment of DVT was developed.<sup>23</sup> After eligibility criteria were verified (uncomplicated proximal DVT without pulmonary embolism, pregnancy, obesity, or unstable morbidity) and it was established that the patient met assessed criteria of having the ability to inject LMWH subcutaneously in the home, the patient was admitted to a holding unit where he or she received the first doses of treatment and was instructed on how to inject enoxa-

parin. At the patient's discharge, a team consisting of inpatient and outpatient pharmacists, a physician, and a nurse from the home health agency was responsible for the follow up of the anticoagulation treatment after consulting the patient's family. The total cost of the program was estimated at \$738 per patient for 5 days, compared to \$1285 for a 5-day hospitalization for treatment with UFH (resulting in \$547 savings per patient).

An open, nonrandomized trial in 14 Swedish hospitals evaluated 434 patients who were treated with dalteparin.<sup>24</sup> Complete outpatient treatment was possible for 35% of the patients, and 80.2% received at least a part of their treatment as outpatients. Cost data were analyzed for 2 hospitals and were compared with costs of traditional hospitalization. A cost reduction of approximately \$810 per patient was observed with the administration of LMWH.

**Figure.** The Cost-Effectiveness Decision Model



DVT = deep vein thrombosis ; LMWH = low-molecular weight heparin ; UFH = unfractionated heparin.

Source: Gould MK, Dembitzer AD, Doyle RL, Hastie TJ, Garber AM. Low-molecular-weight heparins compared with unfractionated heparin for treatment of acute deep venous thrombosis. A meta-analysis of randomized, controlled trials. *Ann Intern Med* 1999;130:800-809.

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### DVT: Decision Models

The third approach to evaluate the cost effectiveness of LMWH for the treatment of DVT is the use of decision models.

Gould et al designed a decision model to evaluate LMWH versus UFH for the treatment of acute DVT (Figure).<sup>25</sup> Probabilities for clinical outcomes were obtained from a meta-analysis of randomized trials,<sup>7</sup> and cost estimates derived from Medicare reimbursement and other sources.<sup>25</sup> First a base-case analysis was performed for representative 75 kg males 60 years of age, from a societal perspective, assuming that all patients were treated in a hospital for a duration of 6 days. Including costs of initial treatment, early and late complications, and future healthcare utilization, the cost-base analysis showed that total cost for UFH was \$26,361 compared to \$26,516 for LMWH. (Note that costs were high relative to other studies because of the inclusion of lifetime health costs.) Treatment with LMWH resulted in a net gain of 0.02 quality-adjusted life years (QALYs), corresponding to an increase in life expectancy of approximately 8 days. The incremental cost effectiveness was \$7820 per QALY gained. In a secondary analysis, the authors hypothesized that 30% of LMWH patients could be completely treated as outpatients, and that an additional 25% could be discharged after 3 days. Using this strategy, initial treatment costs were \$701 less for LMWH than for UFH, and total costs were reduced by \$762 per patient. The authors concluded that LMWH is cost effective compared to UFH for inpatient management of acute DVT and is dominant (more efficacious and cost effective) when complete outpatient management is permitted for more than 8% of patients with DVT or when more than 13% of patients with DVT are discharged after 3 days.

Rodger et al performed an incremental cost-effectiveness analysis for 4 treatment strategies (inpatient UFH, inpatient LMWH, outpatient LMWH for patients eligible for outpatient care and inpatient LMWH for patients not eligible, outpatient LMWH for patients eligible for outpatient care and inpatient UFH for patients not eligible).<sup>26</sup> Probabilities of clinical endpoints at 3 months were estimated from a meta-analysis. Costs for UFH treatment were prospectively collected for 105 patients and costs for LMWH were modeled. The cost for inpatient care was \$3048 per patient for UFH and \$2993 for LMWH. When using LMWH in an outpatient setting, the cost was \$1641 per patient. The cost-effectiveness analysis showed that LMWH was more cost effective than UFH in any treatment setting, except for the extreme scenario in which care was provided entirely as an inpatient and all the model inputs were placed at values that favored UFH.

A third cost-effectiveness analysis was performed by Estrada et al.<sup>27</sup> A decision model was used to compare UFH, LMWH, or UFH for patients who required hospitalization and LMWH for patients treated at home (UFH/LMWH). Costs and benefits were specified from the healthcare system (payer) perspective. Probabilities for clinical events were obtained from meta-analyses and other reports. In a case-base analysis, total cost was \$2775 per patient for LMWH, \$3040 for UFH, and \$2662 for the UFH/LMWH strategy. Both treatments using LMWH were dominant over the UFH treatment, unless the proportion of eligible patients for home treatment was less than 14%, or patients who received LMWH were hospitalized for more than 6.5 days.

### Acute Coronary Syndrome

Four large, randomized trials<sup>28-31</sup> and a smaller one<sup>32</sup> have compared the administration of LMWH with

UFH. Mark et al and O'Brien et al have analyzed the economics of the Efficacy and Safety of Subcutaneous Enoxaparin in Non-Q-wave Coronary Events (ESSENCE) trial in the United States and in Canada.<sup>33,34</sup> This randomized controlled trial compared enoxaparin with UFH for the treatment of unstable coronary disease in 3171 patients.<sup>29</sup> In the United States, the mean cost of enoxaparin was \$155 per patient, compared to \$80 for UFH. Despite this initial extra cost, enoxaparin saved \$763 per patient during the initial hospitalization compared to UFH ( $P = 0.18$ ), and these savings reached \$1172 at 30 days ( $P = 0.04$ ).<sup>33</sup> This was mainly attributable to a reduction in the use of coronary angioplasty, diagnostic catheterization, and length of stay in the intensive care unit. In Canada, the total cost of initial hospital stay was reduced by \$743 (Canadian dollars) using LMWH ( $P = 0.14$ ), and by \$1485 (Canadian dollars) at 1 year ( $P = 0.06$ ).<sup>34</sup> An important point is that in the case of ACS, the economic value of enoxaparin hinges on the medication's effectiveness in reducing expensive medical events.

### Thrombosis Prophylaxis

*Prophylaxis After Hip or Knee Replacement.* In a retrospective study of 56 patients, Saunders et al compared the cost of DVT prophylaxis with either enoxaparin or warfarin after hip replacement surgery.<sup>35</sup> Despite an increased cost of medication, costs associated with laboratory monitoring or bleeding events were reduced, resulting in a cost savings of \$1253 per patient.

In a decision model, Hawkins et al<sup>36</sup> compared enoxaparin with warfarin for the prevention of DVT events after knee replacement, using probabilities of clinical events derived from a randomized, controlled trial.<sup>37</sup> Although cost per patient was \$104 higher with enoxaparin than with warfarin, the

expected cost per DVT avoided was \$2525 less with enoxaparin than with warfarin.<sup>36</sup> As with ACS, the savings were driven by the estimated reduction in event rates.

Hawkins et al applied a similar model to compare the administration of enoxaparin with the subcutaneous administration of heparin for DVT prophylaxis after total hip replacement,<sup>38</sup> using clinical probabilities from 3 previously published studies. Using this model, the total mean cost of enoxaparin prophylaxis exceeded the cost of heparin, but LMWH was more cost effective in avoiding DVT than heparin.

Hull et al conducted a randomized trial comparing warfarin with tinzaparin (for a standard time of 9 days) for prophylaxis of DVT after knee or hip replacement surgery in 1436 patients.<sup>39</sup> DVT occurred in 37.4% of the patients treated with warfarin compared to 31.4% of patients treated with LMWH. In 1992 Canadian dollars, the use of LMWH was associated with cost savings of \$24 per patient in the provision of prophylaxis for DVT compared with the use of warfarin. The researchers concluded that the decision to use LMWH or warfarin prophylaxis in patients undergoing major joint replacement surgery is a "finely tuned trade-off" and that the most significant parameters that influence the cost effectiveness are the cost of the drug, the cost of international normalized ratio monitoring, and the costs associated with major bleeding.

This observation was confirmed by a meta-analysis and cost-effectiveness model that showed that the use of LMWH was the dominant strategy compared to UFH as long as the price ratio between LMWH and standard heparin did not exceed 3.7:1.<sup>40</sup>

In another study, Menzin et al used a decision-analytic model to compare enoxaparin with low-dose warfarin to prevent DVT after total hip replacement surgery.<sup>41</sup> Data for this analysis were drawn primarily from the pub-

lished literature. Although enoxaparin resulted in increased costs of care by approximately \$50 per patient, the cost effectiveness of this treatment compared to low-dose warfarin was estimated at \$12,000 per death averted.

O'Brien et al compared enoxaparin versus warfarin using a decision model.<sup>42</sup> A meta-analysis of published data was used to determine the probabilities of clinical events. For 10,000 patients treated with enoxaparin, 47 additional DVT, 3 pulmonary embolisms, and 4 deaths were prevented when compared to warfarin treatment with an incremental cost effectiveness of \$29,120 (in 1992 Canadian dollars) per life-year gained.

Finally, Wade compared 2 LMWHs (danaparoid and 2 different dosages of enoxaparin) for the prophylaxis of DVT after hip replacement surgery.<sup>43</sup> Wade found the higher dosage of enoxaparin (40 mg/day) was more cost effective than the lower dosage (30 mg/day), and that both dosages of enoxaparin were more cost effective than danaparoid, with \$15,000 savings per thromboembolic event prevented.

*Prophylaxis in Other Medical and Surgical Settings.* The use of LMWH compared to standard UFH for the prophylaxis of DVT has also been tested for other medical conditions, including colorectal surgery<sup>44</sup> and internal medicine patients.<sup>45</sup> In both analyses, the authors concluded that because of the similarity in efficacy and the lack of cost saving for patients who otherwise require hospitalization, low-dose standard heparin was judged to be preferred over LMWH.

**Discussion**

The literature suggests that the use of LMWHs is more effective and less expensive (economically dominant), equally effective and less expensive (cost saving), or more effective and more costly, yet those additional costs are judged to be beneficial (cost effective). We must temper our enthusiasm

with an understanding that translating resource use literature is not entirely straightforward and several issues merit consideration before the decision is made to change clinical practice.

First, the patient population included in the economic analysis may not be generalizable. Because of the restrictive exclusion criteria, 30% to 88% of the screened patients were excluded from randomized trials testing LMWH for the treatment of DVT.<sup>14,15,17</sup> Thus, economic conclusions resulting from analyses of these data may not apply to the decision maker's circumstances.

Second, it is important to understand the dynamics underlying a claim that a new treatment is economically attractive. As illustrated by the DVT example, LMWH may be cost saving if it can reduce the high costs of hospitalization by shifting costs to a less expensive outpatient environment. This does not require that the treatment be any more effective. However, it does depend on the proportion of patients who can be treated in the outpatient setting. Outpatient treatment is

**Table 3.** LMWH for the Management of DVT: Relative Contraindications to Outpatient Management with LMWH

<ul style="list-style-type: none"> <li>■ Symptomatic pulmonary embolism</li> <li>■ Active bleeding/recent surgery/active peptic ulcer disease</li> <li>■ History of familial bleeding disorder</li> <li>■ Marked renal insufficiency</li> <li>■ Severe liver disease</li> <li>■ Marked obesity</li> <li>■ Nonsteroidal anti-inflammatory drug use</li> <li>■ Pregnancy</li> <li>■ Comorbidities requiring hospitalization</li> <li>■ Uncertain follow up or compliance</li> </ul>
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DVT = deep vein thrombosis; LMWH = low-molecular weight heparin.



acceptable to most patients,<sup>46</sup> but because of contraindications to LMWH in the outpatient setting (Table 3),<sup>47-49</sup> only 40% of patients presenting as outpatients and 10% diagnosed during a hospital stay will be eligible for outpatient LMWH. This is the primary limitation to cost savings.<sup>49</sup> In addition, the use of an outpatient LMWH strategy may have undesirable economic consequences. For example, as shown by Pearson et al, hospital stays (and thus hospital costs) may increase for patients with DVT, which has a negative effect on hospitals with capitated reimbursement.<sup>22</sup>

In contrast to the DVT example, the attractiveness of LMWHs for ACS and DVT prophylaxis hinges on the judgment that these treatments decrease costs by decreasing expensive events. To rely on these analyses as policy guides, it is crucial that the decision maker accepts the medical effectiveness of the new treatment. Further study is clearly needed in this area.

Third, results obtained with one form of LMWH might not be carried over to all forms of LMWH. Although comparable results have been obtained with different forms of LMWHs for prophylaxis or treatment of DVT, there is some evidence of efficacy differences between forms of LMWH. In a meta-analysis of LMWH for ACS, Eikelboom et al found that LMWH was associated with a moderate but not significant reduction in the risk of death or myocardial infarction compared with UFH (OR: 0.88 [0.69-1.12],  $P = 0.34$ ).<sup>50</sup> The 2 studies using enoxaparin (ESSENCE and TIMI 11B) included in this meta-analysis showed a significant risk reduction for the composite endpoint of death, myocardial infarction, or recurrent angina requiring revascularization for patients treated with enoxaparin compared to UFH.<sup>30,31</sup> In contrast, studies using nadroparin<sup>31,32</sup> or dalteparin<sup>28</sup> failed to show any significant difference between LMWH and UFH. Again, as most of the eco-

nomie benefit of LMWH in ACS hinges on reduced event rates, the question of generalizability of efficacy estimates to all LMWHs requires further study.

Finally, some fears have been raised that the availability of a simpler treatment, such as outpatient treatment with LMWH, might lead to lower diagnostic and treatment thresholds resulting in potentially increased drug and human costs.<sup>51</sup> In one demonstration project, an outpatient DVT management program was associated with an approximately 70% greater rate of DVT treatment.<sup>22</sup>

LMWH is illustrative of a treatment that can lead to significant cost shifts, for example, increased pharmacy costs, decreased hospitalization costs, and increased home care costs. In addition to considering the evidence, and taking into account the special characteristics of the local population and healthcare environment, a complete analysis of LMWH strategies requires accounting for the impact on the stakeholders. Integrating all these components may be laborious, and decision making may require difficult negotiations to achieve a treatment program that is optimal from the larger perspective.

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