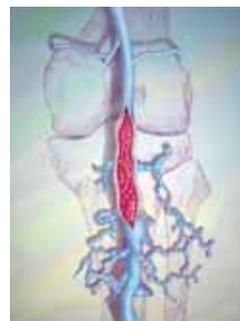


# Cost Implications of Using Unfractionated Heparin or Enoxaparin in Medical Patients at Risk for Venous Thromboembolic Events

Richard M. Weinberg, MD, CPE, Leo K. Lichtig, PhD, Joseph A. Caprini, MD, MS, Geno J. Merli, MD, and F. Randy Vogenberg, RPh, PhD



## ABSTRACT

**Background.** Previous economic studies have compared the cost effectiveness of different heparins used as prophylaxis against venous thromboembolism (VTE) in medical patients at risk. These pharmacoeconomic evaluations have revealed cost benefits of enoxaparin over unfractionated heparin (UFH). However, these modeling studies generally do not use “real-life” hospital data to calculate the actual cost difference from a hospital perspective.

**Objective.** We sought to compare the total cost of care, from a hospital perspective, of thromboprophylaxis with UFH and enoxaparin in patients at risk.

**Research Design and Methods.** Using modified, All-Payer, Severity-Adjusted Diagnosis-Related Groups (M-APS-DRGs), we performed a retrospective analysis of administrative data from 89,584 at-risk patients in 15 U.S. hospitals. Patients were considered for this study if they were in nonsurgical M-APS-DRGs in which at least 50% of patients stayed in the hospital for five or more days. Patients receiving UFH and enoxaparin were identified and compared, within the same M-APS-DRGs, based on the total cost of care associated with the various therapies. We also calculated costs at the cost-center level in order to elucidate where the use of inpatient hospital resources differed.

**Results.** Forty-seven M-APS-DRGs (with 10,953 discharged patients receiving UFH and 6,246 receiving enoxaparin) had used both drugs sufficiently for inclusion in the study. Lower costs were observed with enoxaparin than with UFH in 35 M-APS-DRGs (74%). Differences were statistically significant in 17 M-APS-DRGs (36.2%); 15 of those showed lower costs with enoxaparin. The severity-adjusted mean saving per discharge with enoxaparin was \$1,002. Overall, length of hospital stay was 0.6 days greater with enoxaparin than with UFH.

**Conclusion.** Enoxaparin was associated with lower total inpatient costs of care than UFH for preventing VTE in hospitalized at-risk patients.

**KEY WORDS** enoxaparin, low-molecular-weight heparin, unfractionated heparin, thrombosis, health care economics, drug utilization review, medical patients

## INTRODUCTION

In recent years, it has become clear that patients hospitalized for medical illnesses are at significant risk of venous thromboembolism (VTE). Numerous studies have demonstrated that thromboprophylaxis with heparin is a safe and effective therapy for preventing VTE in this patient population.<sup>1</sup> International guidelines recommend the use of either unfractionated heparin (UFH) or low-molecular-weight heparin (LMWH) for thromboprophylaxis in general medical patients with risk factors for VTE.<sup>2</sup> Large, randomized clinical trials have shown that LMWHs are safer and more effective than placebo for reducing the incidence of VTE in medical patients.<sup>3,4</sup> Furthermore, in medical patients with heart failure or respiratory disease, the LMWH enoxaparin (Lovenox, Sanofi-Aventis) has been at least as effective as UFH in preventing VTE—and it is safer.<sup>5</sup>

LMWHs have a more favorable pharmacokinetic profile than UFH and are easier to administer.<sup>6</sup> Although these advantages help make LMWHs the treatment of choice for preventing VTE in these patients, the use of heparin has implications for hospital budgets. Several economic evaluations of heparin have been published.<sup>7–13</sup> A number of these studies used either decision-tree models<sup>11,13</sup> or Markov models<sup>9,10,12</sup> to compare the cost-effectiveness of enoxaparin with placebo from the perspectives of individual countries, based on the Prophylaxis of Medical Patients with Enoxaparin (MEDENOX) trial.<sup>3</sup> However, because the acquisition cost of LMWH is substantially higher than that of UFH, it is important that hospitals base their choice of thromboprophylactic agent on specific cost studies.

In comparisons of the daily acquisition cost of subcutaneous UFH and enoxaparin, the cost differential for prophylaxis is nearly 10-fold at the average wholesale price (AWP), and the drug acquisition cost differential for the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) is more than 25-fold.<sup>14</sup> Earlier studies were based on models, assumptions, or hypothetical patient cohorts, or they have used general costing data from certain countries. In previous studies, the investigators did not consider “real-life” hospital data in calculating the actual cost difference from a hospital perspective.

## OBJECTIVE

Our study sought to determine whether the use of LMWH, with its higher acquisition cost, was associated with higher or lower total inpatient hospital costs when compared with the use of UFH for matched patients. Our methodology provides P&T

---

*Dr. Weinberg is Chief Quality Officer at Stamford Hospital in Stamford, Connecticut. Dr. Lichtig is Vice President at Aon Consulting, Life Sciences Practice, in Somerset, New Jersey. Dr. Caprini is Louis W. Biegler Professor of Surgery and Bioengineering in the Department of Surgery at Evanston Northwestern Healthcare in Evanston, Illinois, and at Northwestern University Feinberg School of Medicine, in Chicago, Illinois; and at the Robert R. McCormick School of Engineering and Applied Sciences in Evanston. Dr. Merli is Director of the Division of Internal Medicine at Thomas Jefferson University Hospital and Jefferson Medical College in Philadelphia, Pennsylvania. Dr. Vogenberg is Senior Vice President of Aon Consulting, Life Sciences Practice, in Providence, Rhode Island.*

## Costs of UFH and Enoxaparin in VTE

committee members and other decision-makers in hospitals with a tool that can measure the actual costs of inpatient care associated with therapy choices and patterns in their own hospitals.

The Clinical Effectiveness Resource Management (CERM) methodology captured all costs associated with all relevant diagnosis-related groups (DRGs) in each hospital.<sup>15</sup> This allowed all prophylaxis-related costs for each inpatient to be considered without ignoring the costs associated with prophylaxis failure. Using All-Payer Severity-Adjusted (APS)-DRGs enables us to draw conclusions on cost differences between UFH and LMWH in comparable (risk-adjusted) patient groups. This method also reveals any differences between the two drugs with respect to all hospital cost centers and takes into account the length of hospital stay.

To our knowledge, this is the first study that provides a “real-life” cost-minimization analysis comparing enoxaparin with UFH prophylaxis in medical patients at risk for VTE. These data, taken from hospitals throughout the U.S., will aid hospital professionals in learning about the costs of caring for these patients, based on total in-hospital costs and the distribution of these costs among the various hospital cost centers, as reported in the Centers for Medicare & Medicaid Services (CMS) cost report (Form 2552).

### PATIENTS AND METHODS

We performed a retrospective analysis of administrative databases from a convenience sample of 15 hospitals to compare the costs of treating similar, severity-adjusted medical-inpatient cohorts receiving either UFH or enoxaparin for VTE prevention. Formal agreements were executed in compliance with the Health Insurance Portability and Accountability Act of 1996 (HIPAA) to address patient confidentiality, and institution review board (IRB) evaluations were conducted by each participating hospital.

Because of the nature of the study, which retrospectively analyzed large hospital data sets without identifying individual patients, patient consent was not required. The majority of LMWH patients received enoxaparin, and insufficient numbers of patients had been treated with other LMWHs to allow reliable analysis; therefore, we excluded LMWH patients not receiving enoxaparin from this analysis. All costs for inpatients receiving

UFH or enoxaparin were captured and analyzed.

The analysis included patients who received thromboprophylaxis and those whose thromboprophylactic treatment failed in the hospital; that is, the patients required subsequent treatment for DVT or PE; therefore, we considered the in-hospital effectiveness of both drugs.

We did not include patients who were admitted specifically for DVT or PE treatment, based on the principal discharge diagnosis. We included unstable angina patients, most of whom would be expected to receive therapeutic doses of UFH or LMWH, who met our criteria for at-risk medical patients. If a patient met the criteria for inclusion on more than one occasion, the data from each admission were recorded and considered for this analysis.

### Data Collection and Management

Fifteen hospitals in the U.S. volunteered to provide data for this study: five from the Northeast, five from the Midwest, three from the South, and two from the West. Six hospitals had fewer than 300 beds, five had 300 to 600 beds, and four had more than 600 beds. Seven were major teaching hospitals, and all were nonprofit institutions.

The participating hospitals provided data on 720,982 discharged patients for periods ranging from 16 to 35 months (mean, 25.5 months), from 1999 to 2003. Data were edited, and cost outliers were removed, as previously described.<sup>15</sup> In total, less than 2% of records were excluded because of inaccurate or inappropriate data. Data were obtained from standard, detailed billing data sets.<sup>16</sup>

Table 1 lists the data elements provided by each hospital.

### Definition of “at-Risk” Medical Patients

Our focus was on medical inpatients at risk for VTE. In the MEDENOX trial and in the Prospective Evaluation of Dalteparin Efficacy for Prevention of VTE in Immobilized Patients Trial (PREVENT), the investigators demonstrated the effectiveness of enoxaparin and dalteparin sodium injection (Fragmin, Pfizer) in preventing VTE in a carefully defined group of medical inpatients who were characterized by a predicted length of hospital stay. The investigators used comprehensive inclusion and exclusion criteria that required individual chart reviews—an approach not feasible for this large study.<sup>3,4</sup>

Table 1 Patient Data as Provided by Participating Hospitals

Uniform Billing System	Pharmacy or Billing System
Patient identifier	Admission identifier for linking to Uniform Billing data for the same admission
Admission identifier	Drug identifier
Admission and discharge dates	Drug quantity
Date of birth	Drug charges
Sex	Date of service
Discharge status	
Principal and 14 secondary diagnoses	
Principal and 14 secondary procedures	
Attending physician identifier and specialty	
Total charges	
Charges by Uniform Bill-92 revenue code	

*continued on page 327*

## Costs of UFH and Enoxaparin in VTE

continued from page 323

From interviews performed at each of the participating hospitals, it appeared that practicing physicians generalized the findings of MEDENOX to a larger group of inpatients characterized by a longer length of hospital stay and reduced mobility. Therefore, in this study, at-risk medical patients were defined as those in nonsurgical M-APS-DRGs in which at least 50% of patients were in the hospital for five days or more. Newborns, patients admitted for physical rehabilitation, and those with a principal diagnosis of DVT or PE were excluded. No patients with another risk factor, such as prior DVT or hypercoagulability, were identified or excluded. The patient group included in the analysis comprised 203 M-APS-DRGs.

### Drug Categories

The hospital records documented every drug provided to each patient, and the records of patients who received LMWH, UFH, or other anticoagulants were identified.

### Severity Adjustments

To adjust for differences in patients' clinical conditions and management patterns, we used a severity-adjusted set of DRGs, the APS-DRGs.<sup>17</sup> These DRGs were assigned on the basis of the principal diagnosis, secondary diagnoses, significant procedures, age, sex, and hospital discharge status. The APS-DRGs comprised 378 "consolidated" DRGs, which were based on those used nationally in the Medicare Prospective Payment System. These 378 APS-DRGs were subdivided into three predefined severity levels:<sup>17</sup>

- without complications or comorbid conditions
- with complications or comorbidity
- with major complications or comorbidity

Severity levels were assigned according to the definition manual for APS-DRGs assignment<sup>18</sup> and were indicated by a single-digit modifier added to the DRG; this resulted in 1,130 different APS-DRGs. We added a second digit modifier to facilitate tracking subsets of patients who were important for the analysis of thromboprophylaxis. The resulting groups were referred to as "modified" APS-DRGs (M-APS-DRGs).

### Cost

Data from the CMS report (Form 2552) were used to provide costs, charges, and statistics needed to calculate patient-care expenses uniformly. This method supported cost comparisons between similar groups of patients receiving different drugs. We had to align patient-billing data with data from hospital cost reports to derive ratios of costs to charges<sup>15</sup> specific for each cost center, thus providing uniform cost data for participating hospitals and allowing the data to be pooled.

We adjusted costs to 2004 U.S. dollars using the annual Medicare hospital "market basket" cost trend.<sup>19</sup> We standardized data for regional cost differences by applying the Medicare Wage Index to the hospital costs related to compensation.<sup>20</sup>

### Statistical Analysis

We calculated the mean costs per discharge for patients receiving UFH or enoxaparin in M-APS-DRGs that contained at least 30 UFH patients and 30 LMWH patients. If fewer than 30

patients in an M-APS-DRG were treated with either drug, we could not make financial comparisons because of a lack of statistical power. From a practical perspective, this means that the comparison was limited to patients who were perceived by their physicians as appropriate for PE or VTE prophylaxis or treatment with either UFH or LMWH.

Preliminary severity-adjusted "savings" per discharge with enoxaparin in an M-APS-DRG were calculated as the difference in mean cost for patients treated with each drug (UFH cost minus enoxaparin cost). Cost differences between the two groups of patients were calculated on a total cost basis and for each cost center.

The preliminary savings were then reduced by 50% to reflect an estimate of "fixed" costs (i.e., those that could not be eliminated by the selection of a drug—for example, equipment depreciation or utilities). Although we used 50% as a mid-range value acceptable for financial decision-making, individual hospitals in the future might modify this value by using this method when analyzing potential cost savings. Multiplying the saving or loss per discharge by the number of enoxaparin patients and summing this across all M-APS-DRGs provided severity-adjusted total savings or loss.

The statistical significance of a cost difference within an M-APS-DRG was based on a two-tailed *t*-test using log-transformed total cost, with a *P* value of .05 or less considered statistically significant. Log transformation was used to accommodate the skewed distribution of cost and was performed in Microsoft Access, with the two-tailed *t*-tests performed in Microsoft Excel (Microsoft Office, 2003 version).

### Potential Savings

In a different scenario, we projected potential savings per M-APS-DRG by multiplying the savings per discharge by half the number of patients treated with UFH as an estimate of the number of patients who could be switched to enoxaparin. A value of 50% was selected solely to demonstrate the magnitude of additional savings that might be realized if this percentage of additional patients were switched to enoxaparin instead of UFH. For this scenario, it was also assumed that utilization would be shifted in those M-APS-DRGs showing an achievement of savings. Averaging this amount for all M-APS-DRGs provided an estimate of severity-adjusted potential savings per switched patient.

## RESULTS

The 15 hospitals provided data on 720,982 patients in 1,176 M-APS-DRGs. A total of 203 M-APS-DRGs, containing 89,548 patients, met the criteria for inclusion in the analyses before drug utilization was taken into account. After incomplete data sets and cost outliers were removed, 88,626 patients remained for the analysis.

Fifteen percent of patients (13,529 of 88,626; range, 3% to 37% in all of the hospitals) in the 203 M-APS-DRGs who met the inclusion criteria received only UFH; 10% of patients (8,568 of 88,626; ranging from 4% to 17%) received a single LMWH; and 4% of patients (3,428 of 88,626) received multiple heparins. Among the participating patients receiving a single LMWH, 93% (7,938 of 8,568) received enoxaparin and 7% (627 of 8,568) received dalteparin.

## Costs of UFH and Enoxaparin in VTE

Sixteen percent of the patients received other anticoagulants and antiplatelet drugs, alone or in combination, including aspirin (if they took only one tablet per day), warfarin (Coumadin, Bristol-Myers Squibb), abciximab (ReoPro, Centocor/Eli Lilly), anagrelide (Agrylin, Shire), bivalirudin (Angiomax, The Medicines Company), cilostazol (Pletal, Otsuka), clopidogrel (Plavix, Bristol-Myers Squibb/Sanofi), dipyridamole (Persantine, Boehringer Ingelheim), eptifibatid (Integrilin, Cor Therapeutics), fondaparinux (Arixtra, GlaxoSmithKline), ticlopidine (Ticlid, Roche), and tirofiban (Aggrastat, Merck, not sold in U.S.). These patients were not included in the calculations.

In total, 55% of patients (48,901 of 88,626; ranging from 42% to 79%) received no pharmaceutical thromboprophylaxis.

Of the 203 M-APS-DRGs, 47 contained at least 30 discharged patients receiving UFH and 30 receiving enoxaparin. These 47 M-APS-DRGs contained a total of 58,406 discharged patients, including 17,199 patients who received either UFH (10,953 patients) or enoxaparin alone (6,246 patients); these 17,199 patients were included in the cost comparisons (Figure 1). The mean length of hospital stay in this group was 8.3 days for patients receiving UFH and 8.9 days for patients receiving enoxaparin.

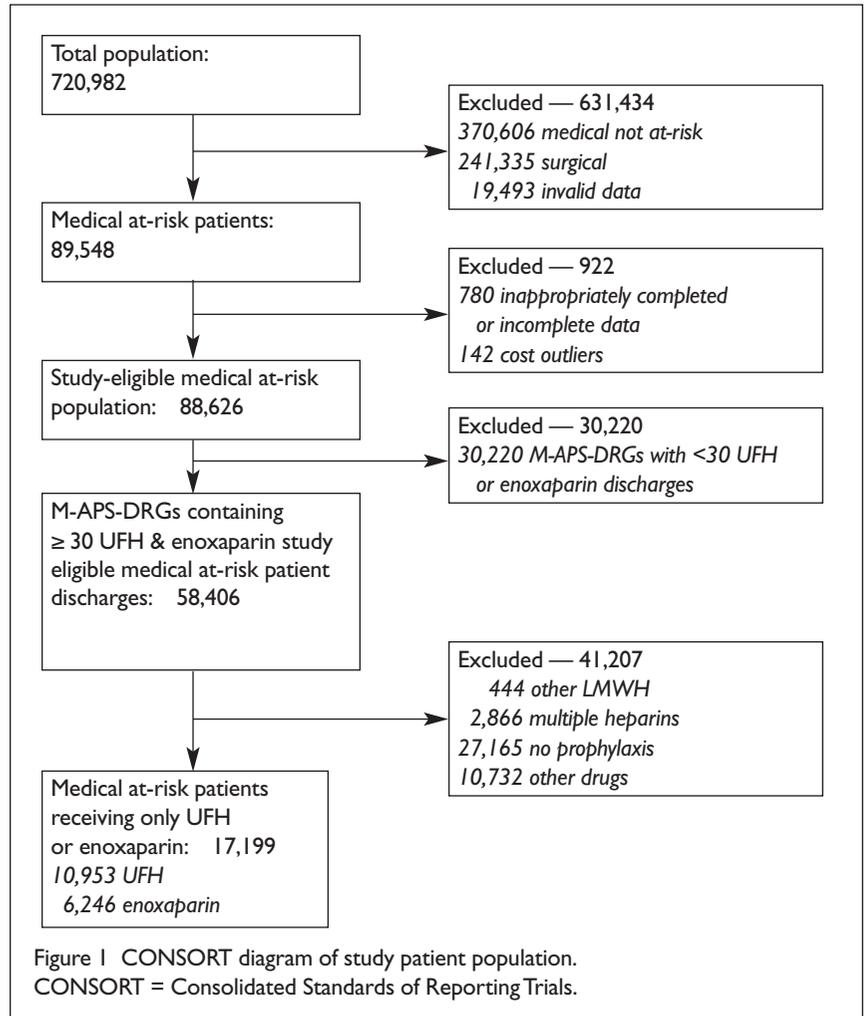
Baseline characteristics of patients in the two groups are shown in Table 2.

The severity-adjusted total savings, summed for all 47 M-APS-DRGs, showed that thromboprophylaxis with enoxaparin was less costly by \$1,002 per discharge compared with UFH. When individual M-APS-DRGs were evaluated, enoxa-

parin thromboprophylaxis was less costly than UFH in 35 of the 47 M-APS-DRGs; the differences were statistically significant ( $P < .05$ ) in 15 M-APS-DRGs. Thromboprophylaxis with UFH was less costly than enoxaparin in 12 M-APS-DRGs, and the differences were statistically significant ( $P < .05$ ) in two M-APS-DRGs. Table 3 shows the savings in the 17 statistically significant groups.

These data suggest that in this model and in these hospitals, the largest cost savings achieved by substituting enoxaparin for UFH were seen in the M-APS-DRG of respiratory diseases with major complications or comorbidity and unstable angina. The choice of UFH or LMWH for patients with unstable angina might have been driven primarily by their coronary artery disease, but these patients were retained in this study because they also met our definition of at-risk medical patients. High cost savings with enoxaparin use were also observed in the M-APS-DRG with renal failure and a major complication or comorbidity.

In applying the at-risk medical criteria



**Table 2 Baseline Characteristics of Medical Patients at Risk for Venous Thromboembolic Events Who Are Receiving Enoxaparin and Unfractionated Heparin (UFH) (N = 17,199)**

Demographic	UFH (n = 10,953)	Enoxaparin (n = 6,246)	PValue*
Age in years (mean ± SE)	67.5 ± 0.2	71.9 ± 0.2	< .001
Men (%)	47%	43.5%	—
Length of hospital stay, days (mean ± SE)	8.3 ± 0.1	8.9 ± 0.1	< .001
Inpatient deaths	11.1%	11.0%	—
ICU admissions	40.8%	40.2%	—
Total costs (mean ± SE)	\$14,867 ± 135	\$12,625 ± 143	< .001
• Drug costs (mean ± SE)	\$1,887 ± 31	\$1,844 ± 36	NS
• ICU costs (mean ± SE)	\$3,032 ± 60	\$2,496 ± 63	< .001

\* Two-tail t-test comparing enoxaparin with UFH groups.  
ICU = intensive-care unit; NS = not significant; SE = standard error.

## Costs of UFH and Enoxaparin in VTE

to the individual hospitals in this study, one hospital had no M-APS-DRGs that qualified, one hospital showed a per-discharge loss (\$269), and all others showed cost savings: five hospitals saved under \$500; four hospitals saved \$501 to \$1,000; three hospitals saved \$1,001 to \$2,000; and one hospital saved more than \$2,000 per discharge.

We calculated potential savings by assuming that an identical group of patients was to be treated again and that 50% of the patients who were formerly treated with UFH would receive enoxaparin. In this scenario, the net potential savings with enoxaparin in those M-APS-DRGs showing savings would be \$1,451 per case shifted. This calculation is a financial-modeling exercise and does not suggest that clinicians base their decisions

on these figures.

Figure 2 shows cost savings with enoxaparin over UFH at all cost centers. The largest savings were seen for the intensive-care unit (ICU), laboratory, and medical-surgical supplies.

### DISCUSSION

With enoxaparin being among the top five drugs included in most hospital pharmacy budgets,<sup>21</sup> accurate data on the total costs of thromboprophylaxis with this anticoagulant and UFH—and the savings or loss that can be achieved—are especially relevant for hospital decision-makers. Previous economic analyses comparing enoxaparin and UFH in non-severity-adjusted medical patients have shown that enoxaparin may be more cost-

**Table 3 M-APS-DRGs with Statistically Significant\* Savings or Losses with Enoxaparin versus Unfractionated Heparin (UFH) for Thromboprophylaxis in Patients at Risk for Venous Thromboembolism**

M-APS-DRG Name	M-APS-DRG Code	Mean Cost per Discharge (\$) ± SE				Variable Cost Savings† per Discharge (\$)
		Discharges	UFH	Discharges	Enoxaparin	
Respiratory system diagnoses with ventilator support with MCC with UA	475.21	54	30,204 ± 2,410	36	22,125 ± 2,812	4,040
Renal failure with MCC	316.20	306	22,304 ± 1,113	48	14,825 ± 2,223	3,740
Pulmonary edema or respiratory failure with MCC	87.20	71	18,574 ± 2,055	63	11,612 ± 1,012	3,481
Circulatory disorder with AMI, expired with MCC with UA	123.21	77	18,564 ± 1,647	40	12,129 ± 1,753	3,217
Respiratory system diagnoses with ventilator support with MCC without UA or DVT/PE	475.29	686	30,489 ± 879	430	24,757 ± 902	2,866
Circulatory disorder with AMI discharged alive with MCC with UA	121.21	234	18,847 ± 842	211	13,266 ± 575	2,791
Cardiac arrhythmia or conduction disorder with MCC without UA	138.29	136	15,256 ± 1,095	108	10,868 ± 793	2,194
Circulatory disorder with AMI discharged alive with MCC without UA	121.29	175	17,793 ± 866	88	13,718 ± 941	2,038
Septicemia, aged >17 years with MCC	416.20	492	21,656 ± 865	279	17,881 ± 860	1,888
Intracranial hemorrhage or stroke with infarct with MCC	14.20	319	20,896 ± 901	98	17,149 ± 1,421	1,874
Heart failure or shock with MCC without UA	127.29	636	16,223 ± 509	475	13,732 ± 517	1,246
Bone diseases or arthropathies with CC without DVT/PE	246.19	62	7,538 ± 687	173	5,395 ± 207	1,072
Circulatory disorder with AMI, discharged alive with CC without UA	121.19	335	10,021 ± 364	199	8,093 ± 292	964
Circulatory disorder with AMI discharged alive with CC with UA	121.11	511	9,651 ± 262	431	7,873 ± 244	890
Intracranial hemorrhage plus stroke with infarct with CC	14.10	715	11,061 ± 308	220	9,393 ± 395	834
Simple pneumonia, pleurisy or interstitial lung disease aged >17 years with CC	89.10	1003	8,239 ± 212	675	8,491 ± 200	-127
Circulatory disease without AMI with catheterization with complex cardiac diagnosis with CC without UA	124.19	601	10,405 ± 299	66	10,721 ± 584	-158

\*  $P < .05$  for the cost difference within an M-APS-DRG based on a two-tailed t-test using log-transformed total cost.

† Savings are reduced by 50% to reflect an estimate of fixed costs.

AMI = acute myocardial infarction; CC = comorbid conditions or complications (as defined by HSS, Inc.<sup>18</sup>); DVT = deep vein thrombosis; M-APS-DRG = modified All-Payer, Severity-Adjusted Diagnosis-Related Groups (see Leary et al.<sup>17</sup>); MCC = major comorbid conditions or complications (as defined by HSS, Inc.<sup>18</sup>); PE = pulmonary embolism; SE = standard error; UA = unstable angina.

## Costs of UFH and Enoxaparin in VTE

effective, with the main savings appearing to be related to differences in bleeding and length of hospital stay.<sup>7,8</sup>

This retrospective analysis of actual hospital costs associated with thromboprophylaxis with these two agents in at-risk medical patients, using “real-life” data from 15 U.S. hospitals, demonstrated a severity-adjusted average savings in cost per discharge of \$1,002 with enoxaparin.

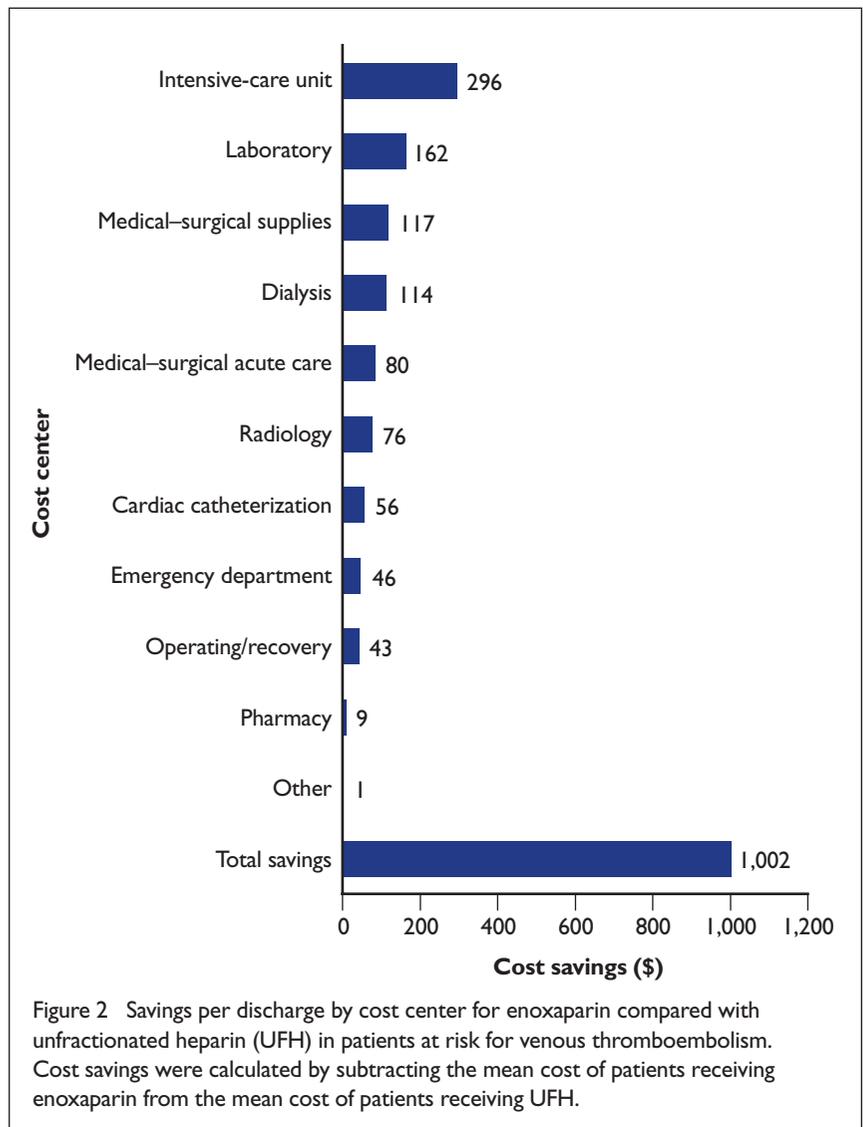
A breakdown of costs by cost center revealed that the savings for ICU, laboratory, and medical-surgical supplies made up a large part of the total savings. Further analysis in the 17 M-APS-DRGs with statistically significant differences by drug provided insight into savings that can be expected in specific groups of medical patients. The data also revealed that enoxaparin patients stayed in the hospital 0.6 day longer than patients taking UFH.

Of note, 55% of at-risk medical patients received no thromboprophylaxis, which may indicate an underuse of, or an inadequate use of, prophylaxis; however, this is speculative, because data enabling an assessment of the appropriateness of therapy were not collected. Furthermore, a national consensus on which at-risk medical patients should receive thromboprophylaxis is being sought only now.

Our study provides important information for P&T committees and other hospital decision-makers; choosing a therapy cannot be based on the acquisition cost of a drug alone, and it is often difficult to balance costs against the effectiveness of a drug. When prescribed for VTE prophylaxis, UFH is approximately 10-fold less expensive than enoxaparin.

Several health economic studies have shown that compared with placebo, enoxaparin is a cost-effective approach to preventing VTE in medical patients.<sup>9-13</sup> Methodological differences between the studies, however, make it more complicated to compare the different approaches to thromboprophylaxis. Hospital decision-makers must be able to calculate the average cost of care from a hospital perspective while considering their specific patient-management approaches, the clinical effectiveness of drugs, and all other factors in the hospital that contribute to the final cost of patient care. The CERM technique used in our study is one such approach to estimating these costs.

Besides the actual cost savings based on discharge data, other possible savings from shifting patients to another clinically appropriate alternative drug are also of interest to hospital decision-makers. Based on the current model and M-APS-DRGs and assuming that 50% of the patients were switched from UFH to enoxaparin in the patient groups for whom enoxaparin provided cost savings, the net potential savings using enoxaparin would be \$1,451 per switched patient. This estimate should be



considered cautiously, however, because it does not take into account costs such as altered management patterns when medication is switched.

As previously discussed, the CERM technique for estimating costs has some advantages.<sup>15</sup> This integrated approach provides hospitals with the appropriate cost analysis of therapies used by patients. In contrast to other systems currently used by hospital administrators, this method accounts for all costs throughout a hospital stay and the cost of adverse events that occur during this period. This method is designed to deliver estimates for potential savings if a hospital decides to investigate alternatives for patient management.

### STUDY LIMITATIONS

As with all methods used to estimate and compare costs in health care, our study has some limitations. For instance, regression analysis of the data might be used to examine more thoroughly some factors that could contribute to the difference between UFH and LMWH (e.g., age, sex). We chose a severity-adjusted DRG-based analysis because it is more familiar to

*continued on page 333*

## Costs of UFH and Enoxaparin in VTE

continued from page 330

the physicians, pharmacists, hospital quality-management personnel, and hospital managers, all of whom, we hope, will find this study useful. We also thought that the large numbers of patients studied and the surprisingly uniform savings identified made regression analysis unnecessary.

We did not determine the duration of thromboprophylaxis for each group according to the drug; considering the potential implications for differences in outcomes (and costs), that determination would be of interest, particularly for patients not responding to prophylaxis. On the other hand, the impact of any differences in duration of thromboprophylaxis is included in these measurements. We hope to measure duration in a later study.

This retrospective analysis of administrative databases was not designed to assess drug effectiveness, because effectiveness measures were not included as outcomes.

### CONCLUSION

Our retrospective study shows that in a large sample of more than 17,000 medical patients at risk for VTE, enoxaparin was associated with lower *total* costs of inpatient care than UFH for most patient subgroups studied despite its higher acquisition cost. The lower cost was attributable not to a shorter hospital stay but to savings in several cost centers within the hospital.

Additional studies in the near future are needed to compare these costs with the alternatives of either mechanical prophylaxis or no prophylaxis. These health economic data contribute to the currently available literature on thromboprophylaxis in medical patients and should help P&T committees and other hospital decision-makers in selecting thromboprophylactic therapy. In light of the beneficial safety and efficacy profile of enoxaparin that has already been established in the clinical literature, the data suggest that enoxaparin may be the drug of choice for thromboprophylaxis in at-risk medical patients.

**Acknowledgments.** We thank Paul J. O'Connor, RPh, MBA; Nimisha Vyas Bhatt, MPH; and Christe S. Bruderlin, MS, for their research, editorial assistance, and preparation of this manuscript. Some text in this article was based on information from posters and abstracts of data presented at the 2004 annual meeting of the American College of Chest Physicians and the 2005 annual meeting of the American Public Health Association.

### REFERENCES

1. Mismetti P, Laporte-Simitsidis S, Tardy B, et al. Prevention of venous thromboembolism in internal medicine with unfractionated or low-molecular-weight heparins: A meta-analysis of randomized clinical trials. *Thromb Haemost* 2000;83:14-19.
2. Geerts WH, Pineo GF, Heit JA, et al. Prevention of venous thromboembolism: The Seventh American College of Chest Surgeons Conference on Antithrombotic and Thrombolytic Therapy. *Chest* 2004;126(3 Suppl):338S-400S.
3. Samama MM, Cohen AT, Darmon JY, et al. A comparison of enoxaparin with placebo for the prevention of venous thromboembolism in acutely ill medical patients: Prophylaxis in Medical Patients with Enoxaparin Study Group. *N Engl J Med* 1999;341:793-800.
4. Leizorovicz A, Cohen AT, Turpie AG, et al. Randomized, placebo-controlled trial of dalteparin for the prevention of venous thromboembolism in acutely ill medical patients. *Circulation* 2004;110:874-879.
5. Kleber FX, Witt C, Vogel G, et al. Randomized comparison of enoxaparin with unfractionated heparin for the prevention of venous thromboembolism in medical patients with heart failure or severe

- respiratory disease. *Am Heart J* 2003;145:614-621.
6. Hirsh J, Raschke R. Heparin and low-molecular-weight heparin: The Seventh American College of Chest Surgeons Conference on Antithrombotic and Thrombolytic Therapy. *Chest* 2004;126(3 Suppl):188S-203S.
7. McGarry LJ, Thompson D, Weinstein MC, et al. Cost effectiveness of thromboprophylaxis with a low-molecular-weight heparin versus unfractionated heparin in acutely ill medical inpatients. *Am J Manag Care* 2004;10:632-642.
8. Offord R, Lloyd AC, Anderson P, et al. Economic evaluation of enoxaparin for the prevention of venous thromboembolism in acutely ill medical patients. *Pharm World Sci* 2004;26:214-220.
9. Nuijten MJ, Villar FA, Kosa J, et al. Cost-effectiveness of enoxaparin as thromboprophylaxis in acutely ill medical patients in Spain. *Value Health* 2003;6:126-136.
10. de Lissovoy G, Subedi P. Economic evaluation of enoxaparin as prophylaxis against venous thromboembolism in seriously ill medical patients: A U.S. perspective. *Am J Manag Care* 2002;8:1082-1088.
11. Lamy A, Wang X, Kent R, et al. Economic evaluation of the MEDENOX trial: A Canadian perspective. Medical Patients with Enoxaparin. *Can Respir J* 2002;9:169-177.
12. Nuijten MJ, Berto P, Kosa J, et al. Cost-effectiveness of enoxaparin as thromboprophylaxis in acutely ill medical patients from the Italian NHS perspective. *Recenti Prog Med* 2002;93:80-91.
13. Lloyd AC, Anderson PM, Quinlan DJ, et al. Economic evaluation of the use of enoxaparin for thromboprophylaxis in acutely ill medical patients. *J Med Econ* 2004;4:99-113.
14. Unfractionated heparin (UFH) and Lovenox average wholesale price (AWP) comparison based on an average of 3 UFH suppliers' and Lovenox AWP. *2003 Drug Topics Red Book*. Montvale, NJ: Medical Economics, Thomson Healthcare; 2003:362-410.
15. Lichtig LK, Weinberg RM, Knauf RA, et al. Measuring clinical effectiveness with common hospital data. *P&T* 2004;29:304-313.
16. National Uniform Billing Committee (NUBC). UB-92: National Uniform Billing data element specifications as developed by the National Uniform Billing Committee as of September 17, 2003. Chicago: American Hospital Association; 2003.
17. Leary RS, Johantgen ME, Farley D, et al. All-Payer Severity-Adjusted Diagnosis-Related Groups: A uniform method to severity-adjust discharge data. *Top Health Inf Manage* 1997;17:60-71.
18. Definitions manual for All-Payer Severity-Adjusted DRG (APSDRGs) assignment (version 21.0). Hamden, CT: HSS, Inc.; 2004.
19. Medicare Program: Changes to the Hospital Inpatient Prospective Payment Systems and Fiscal Year 2004 Rates, Final Rule. Centers for Medicare & Medicaid Services, U.S. Department of Health and Human Services. *Fed Register* 2003;68:45461; and Fiscal Year 2003 Rates, Final Rule. *Fed Register* 2002;67:50040.
20. Medicare Program: Changes to the Hospital Inpatient Prospective Payment Systems and Fiscal Year 2003 Rates, Final Rule. Centers for Medicare & Medicaid Services, U.S. Department of Health and Human Services. *Fed Register*. 2002;67:502141-50221.
21. Chi J. Leading movers and shakers: Top 200 drugs for hospitals in 2003. *Drug Topics* June 21, 2004;148:HSE23. ■

### Disclosures

This study was developed and conducted by Aon Consulting, Life Sciences Practice, and was supported by an unrestricted grant from Sanofi-Aventis in Bridgewater, New Jersey. Dr. Weinberg has received grants from Aon Consulting and is the medical advisor to the Clinical Effectiveness Initiative. Dr. Lichtig has received a research grant from Sanofi-Aventis. Dr. Caprini has been a consultant for and has served on the speaker's bureau for Sanofi-Aventis. Dr. Merli has no relationships to disclose in regard to this article. Dr. Vogenberg has received grants from, and has done consulting and general research for, Sanofi-Aventis, Amgen, Pfizer, Abbott, and the National Pharmacy Purchasing Coalition.