

Economic Evaluation of Enoxaparin as Prophylaxis Against Venous Thromboembolism in Seriously Ill Medical Patients: A US Perspective

Gregory de Lissovoy, PhD; and Prasun Subedi, BS

Objective: To determine the cost and cost effectiveness of adding venous thromboembolism (VTE) prophylaxis with enoxaparin, a low-molecular-weight heparin, to standard care for acutely ill, hospitalized medical patients.

Methods: A pharmacoeconomic model was developed to simulate the 6- to 14-day course of enoxaparin prophylaxis evaluated in the MEDENOX trial in a US healthcare setting. Clinical results as reported for the trial were applied to resource use and treatment costs in a US healthcare environment. The model projects hospital length of stay and cost for an acute medical admission from a third-party payer perspective, as well as costs for the course of enoxaparin.

Results: VTE prophylaxis with enoxaparin would account for 1.2% to 2.4% of the cost of a hospital admission, with an additional \$23 ± \$28 to \$99 ± \$122 to complete the course of prophylaxis out of hospital. Incremental cost effectiveness of VTE prophylaxis relative to no prophylaxis ranges from \$1249 to \$3088 per VTE avoided. Venous thromboembolism prophylaxis appears to be a break-even intervention, with the cost recouped through avoided treatment, if the rate of treated VTE without prophylaxis is at least 3-4%.

Discussion and Conclusions: The MEDENOX trial demonstrated that prophylaxis with enoxaparin substantially decreases the risk of VTE among acutely ill, hospitalized medical patients. Economic analysis indicates that this protection represents a small increase in current treatment costs. Prophylaxis is cost effective in terms of incremental cost per VTE avoided. Furthermore, there is a reasonable likelihood that the cost of prophylaxis will be offset by avoided future VTE treatment.

(*Am J Manag Care* 2002;8:1082-1088)

VTE incidence among patients receiving enoxaparin 40 mg once daily was 5.5% versus 14.9% for a control group treated with placebo.⁴

With good evidence for the clinical benefit of VTE prophylaxis among acutely ill, hospitalized medical patients,⁵ many organizations are evaluating this procedure as a new standard of care.⁶ In today's cost-conscious healthcare environment, decisions about the adoption of new treatments are based on economic as well as clinical factors. Results of the MEDENOX trial provide a basis for addressing 3 issues important to decision makers:

1. What is the cost of making VTE prophylaxis with enoxaparin a standard of care for acutely ill, hospitalized medical patients?
2. Can VTE prophylaxis be considered a cost-effective intervention?
3. To what extent is the cost for VTE prophylaxis offset by the avoided cost of future VTE treatment?

We begin this paper with a brief summary of the MEDENOX trial and then describe the design of a pharmacoeconomic model that combines trial results with treatment cost data to address the 3 questions of interest.

Acutely ill, hospitalized medical patients are at high risk of venous thromboembolism (VTE).¹⁻³ A recent international multicenter clinical trial (MEDENOX) demonstrated that thromboprophylaxis with enoxaparin, a low-molecular weight heparin, substantially reduces that risk. The

From MEDTAP International, Inc, Bethesda, MD (GD); and the Pharmaceutical Health Services Research, School of Pharmacy University of Maryland, Baltimore, MD (PS).

Funding for this study was provided through an unrestricted grant from Aventis Pharmaceuticals US, Bridgewater, NJ.

Summary findings from this study were presented as a poster at a meeting of the International Society of Pharmaceutical Outcomes Research; November 12, 2001; Cannes, France.

Address correspondence to: Gregory de Lissovoy, PhD, MEDTAP International, Inc, 7101 Wisconsin Avenue, Suite 600, Bethesda, MD 20814. E-mail: delissovoy@medtap.com.

SUMMARY OF THE MEDENOX
CLINICAL TRIAL

MEDENOX was an international, randomized, double-blind, controlled clinical trial that evaluated prophylaxis with enoxaparin, a low-molecular-weight heparin, in hospitalized patients with acute medical illness. One study treatment group received enoxaparin 40 mg once daily for 6-14 days ($n = 291$), while a comparison group received placebo ($n = 371$). The primary study end point was the incidence of VTE events occurring between days 1 and 14 postrandomization.⁴

The VTE incidence by day 14 was 5.5% among patients receiving enoxaparin 40 mg versus 14.9% in the placebo group ($P < .001$). Treatment-related adverse events were rare and not different between treatment groups. For example, there were 2 cases of symptomatic deep vein thrombosis (DVT) in the placebo arm (0.7%) versus 1 in the enoxaparin group (0.3%). Major hemorrhage occurred among 4 patients (1.1%) in the placebo group versus 6 (1.7%) in the enoxaparin group. Severe thrombocytopenia also was rare, with 3 cases in the placebo group and none in the enoxaparin group.⁴

DESIGN OF THE
PHARMACOECONOMIC MODEL

The model simulates the 6- to 14-day episode of enoxaparin prophylaxis evaluated in the MEDENOX trial in a US healthcare setting. Clinical results as reported for the trial were applied to resource use and treatment costs in a US healthcare environment. The model projects hospital length of stay and cost, as well as the cost for enoxaparin prophylaxis, from a third-party payer perspective.

Hospital admission costs were derived from a national database summarizing discharges from US acute care hospitals during 1998.⁷ Each record in the database listed patient age and sex, length of stay, *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9-CM) codes for primary and secondary diagnoses, codes for primary and secondary procedures, and billed charge. Records were selected according to inclusion-exclusion criteria designed to obtain a cohort similar to patients enrolled in the MEDENOX trial. Inclusion criteria were a primary diagnosis of acute respiratory failure (ICD-9-CM code 518.81), heart failure (ICD-9-CM code 428.x), or infectious disease (ICD-9-CM code 038.x); these were the 3 most common reasons

for admission in the MEDENOX trial. ("Acute infectious disease" is a very general diagnosis that could potentially encompass a wide range of conditions. Therefore, we utilized the diagnostic code for septicemia [ICD-9-CM 038.x] to select discharge records for the study. Septicemia is a common type of acute generalized infection due to a broad range of pathogens.) Exclusion criteria were age less than 40 years and length of stay (LOS) less than 2 days or more than 30 days. The billed charge was converted to cost via the hospital-specific ratio of costs to charges.

We used the resulting file ($n = 374\,855$ discharge abstracts) to perform multiple regression analyses to determine parameters of equations to predict (1) LOS as a function of age, sex, and diagnosis; and (2) cost of admission as a function of age, sex, diagnosis, and predicted LOS. These equations were coded in an Excel spreadsheet (Microsoft Corporation, Redmond, Wash) that performed Monte Carlo simulation of 2 cohorts of 3000 patients each (prophylaxis, no prophylaxis). For each simulated patient, the model first predicted patient age and sex as a random function of the age distribution (mean \pm standard deviation) and sex (proportion male) in the MEDENOX study. Next, the model predicted hospital LOS as a random function based on a diagnosis-specific LOS distribution derived from the hospital discharge dataset previously described. This set of stochastic variables was multiplied by the set of parameters from the regression equation predicting cost of the admission; regression parameters were held constant for each iteration. This operation resulted in a predicted cost for the admission. Finally, the model calculated an additional cost for enoxaparin as a function of LOS and—when the predicted LOS was less than 6 days—a cost for out-of-hospital administration to achieve at least 6 days of prophylaxis.

Acquisition cost for enoxaparin was set at \$19.57 per 40-mg subcutaneous dose.⁸ Hospitals may add a mark-up or dispensing fee to the acquisition price of a drug to account for costs of storage, handling, and delivery to the floor. As a form of sensitivity analysis, the model included 4 alternative dispensing costs: \$0, \$5, \$10, and \$20 per dose. In addition, the model included 3 different scenarios for out-of-hospital enoxaparin administration. In the first scenario, patients would be taught to self-administer enoxaparin via subcutaneous injection; the cost includes only the drug. The second scenario assumed that enoxaparin would be administered by a physician or nurse during, a "brief office visit with an established patient" (CPT code 99211) at a fee of \$27 plus the

Table 1. Cost of Venous Thrombosis Prophylaxis With Enoxaparin: Inpatient Hospital Component

Pharmacy Dispensing Cost (\$)	Mean \pm SD Cost (\$)		Cost of Enoxaparin as % of Total
	For Enoxaparin Prophylaxis Only	Total for Admission*	
0	94.42 \pm 28.17	7908 \pm 4732	1.2
5	118.55 \pm 35.37	7932 \pm 4737	1.5
10	142.67 \pm 42.57	7956 \pm 4742	1.8
20	190.92 \pm 56.97	8005 \pm 4751	2.4

*The mean \pm SD length of hospital stay was 6.96 \pm 4.61 days.

drug cost.⁹ In the third scenario, enoxaparin would be administered at the patient's residence by a home health nurse, at a \$65 per visit charge as well as the drug cost.¹⁰

RESULTS

Projections from the model were used to sequentially address each of the 3 study issues: the cost for VTE prophylaxis with enoxaparin, cost effectiveness of VTE prophylaxis versus no prophylaxis, and the cost for prophylaxis versus avoided future costs of VTE treatment (break-even analysis).

Cost of Venous Thromboembolism Prophylaxis

The cost for VTE prophylaxis with enoxaparin has 2 components: the cost for inpatient hospital prophylaxis and the out-of-hospital cost to complete a 6-day prophylaxis regimen when the LOS is less than 6 days.

Table 2. Cost of Venous Thrombosis Prophylaxis With Enoxaparin: Out-of-Hospital Component

Method of Enoxaparin Administration	Mean \pm SD Cost for Enoxaparin (\$)*
Patient self-administration	23.00 \pm 28.17
Office visit or outpatient clinic	54.73 \pm 67.04
Home health nurse visit	99.38 \pm 121.75

*The mean \pm SD number of out-of-hospital doses was 1.18 \pm 1.44.

Enoxaparin prophylaxis would add from \$94 \pm \$28 to \$191 \pm \$57 to the cost of inpatient hospital care, depending on a dispensing cost ranging from \$0 to \$20 per dose. The predicted mean total cost for a hospital admission that included VTE prophylaxis ranged from \$7908 \pm \$4732 to \$8005 \pm \$4751. Prophylaxis would represent from 1.2% to 2.4% of the total cost of admission (see **Table 1**).

For the out-of-hospital component, the model predicted that a mean of 1.2 \pm 1.4 doses of enoxaparin would be required to complete the course of prophylaxis after discharge. Cost would range from a low of \$23 \pm \$28 for self-administration to a high of \$99 \pm \$122 for administration by a home healthcare provider (**Table 2**).

Figure 1 shows the total cost for enoxaparin prophylaxis with 4 different costs for inpatient hospital dispensing (\$0, \$5, \$10, \$20) and 3 different settings for out-of-hospital administration (patient self-administration, outpatient clinic, home healthcare). When both inpatient and outpatient costs are considered, enoxaparin prophylaxis would add between \$117 \pm \$40 to \$290 \pm \$65 to the total cost of treatment.

Cost Effectiveness of Venous Thromboembolism Prophylaxis

The results described in the previous section were used to construct a cost-effectiveness measure by calculating the incremental cost per VTE avoided with enoxaparin prophylaxis. As the primary end point of the MEDENOX trial, VTE was documented among 5.5% of patients treated with enoxaparin versus 14.9% in the placebo group. Another way to state this result is that 9.4 VTE events were avoided per 100 patients receiving enoxaparin prophylaxis. This incremental-effect value combined with the incremental cost of VTE prophylaxis (**Figure 1**) yields the incremental cost-effectiveness ratio.

Table 3 shows the result of calculating the incremental cost-effectiveness ratio for all combinations of the 4 inpatient hospital enoxaparin dispensing costs (\$0, \$5, \$10, \$20) and the 3 modalities for administering out-of-hospital enoxaparin (self-administration, office visit or outpatient clinic, home healthcare). The cost for enoxaparin prophylaxis ranges from a low of \$1249 (zero dispensing cost, patient self-administration) to a high of \$3088 (\$20 dispensing cost, home care administration).

Breakeven Analysis: Cost for Venous Thromboembolism Prophylaxis Versus Avoided Future Cost

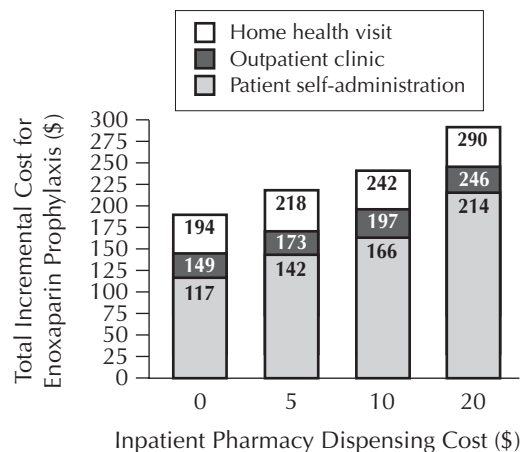
Breakeven occurs when the reduction in future treatment expenditure equals the current investment in prophylaxis. The break-even point is achieved when the expected cost of treatment without prophylaxis equals the expected cost of treatment with prophylaxis plus the cost of prophylaxis. For a specified cost of prophylaxis, the break-even point is determined by the likelihood of need for treatment in patients not receiving prophylaxis relative to the likelihood in patients who do receive prophylaxis, plus the cost of that treatment. If the likelihood of need for treatment is very small, then the average cost of treatment must be relatively high to break even. On the other hand, as likelihood of the eventual need for treatment increases, the break-even point occurs at progressively lower costs.

Figure 2 is a graphical representation of this relationship. The horizontal (X) axis represents the cost of treating a VTE event such as DVT or pulmonary embolism over a range from \$2500 to \$25 000. The vertical (Y) axis shows the percentages of seriously ill, hospitalized medical patients not receiving prophylaxis who will eventually require treatment for VTE-related events, a range of 0% to 20%. Curved lines define the break-even point with 3 different scenarios for the cost of VTE prophylaxis.

The low-cost scenario assumes a \$94 hospital cost (zero dispensing cost) and \$23 out-of-hospital cost (patient self-administration) for a total prophylaxis cost of \$117. At an intermediate level, total prophylaxis cost is set at \$198, based on a hospital cost of \$143 (\$10 dispensing fee) and out-of-hospital cost of \$55 (office visit administration). In the high-cost scenario, hospital cost is \$191 (\$20 dispensing) and out-of-hospital cost is \$99 (home health administration) for a total prophylaxis cost of \$290. Each break-even curve reflects the risk of VTE for a “no prophylaxis” cohort relative to patients receiving enoxaparin prophylaxis as documented in the MEDENOX trial.

One way to interpret the graph is to examine the lower and upper ends of the treatment cost range and determine the break-even point based on the rate of treated VTE events. If the average cost of treatment is as low as \$2500 per case,

Figure 1. Projected Total Inpatient and Outpatient Costs for Venous Thromboembolism Prophylaxis With Enoxaparin



breakeven occurs when the VTE event rate falls in a range of about 7.5% to 18.5%, depending on the VTE prophylaxis cost scenario. When average treatment cost is as high as \$25 000 per event, breakeven occurs when the event rate is in a range of less than 1% to 2%.

DISCUSSION

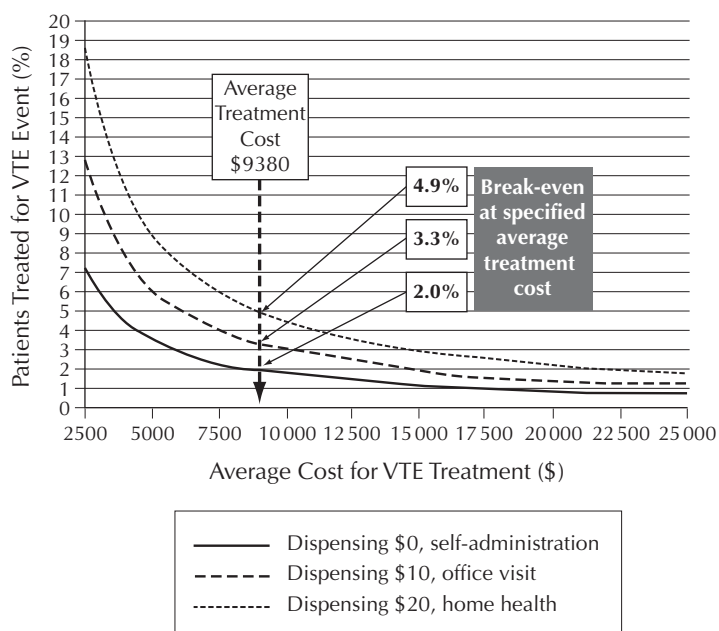
The MEDENOX trial demonstrated that seriously ill medical patients are at relatively high risk for VTE and that prophylactic administration of enoxaparin substantially reduces that risk. When evaluating prophylaxis as a new standard of care for acutely ill, hospitalized medical patients, managed care organi-

Table 3. Cost Effectiveness of Enoxaparin as Venous Thromboembolism Prophylaxis

Inpatient Hospital Pharmacy Dispensing Cost (\$)	Incremental Cost Per VTE Event Avoided (\$)		
	Patient Self-Administration	Office Visit or Outpatient Clinic	Home Health Nurse Visit
0	1249	1587	2062
5	1506	1843	2318
10	1762	2100	2575
20	2276	2613	3088

VTE indicates venous thromboembolism.

Figure 2. Break-even Analysis for Venous Thromboembolism Prophylaxis With Enoxaparin



VTE indicates venous thromboembolism.

zations will likely consider the potential economic impact, as well as the clinical benefit, of this intervention. In this analysis we addressed 3 issues that may figure in the decision-making process: (1) the cost of adding enoxaparin prophylaxis to current treatment regimens; (2) the cost effectiveness of VTE prophylaxis; and (3) the likelihood that the prophylaxis cost would break even with respect to avoided cost of future VTE treatment.

Cost of Enoxaparin Prophylaxis

In projecting the cost for prophylaxis, we included a cost for enoxaparin dispensing, ranging from \$0 to \$20 per dose. We also considered costs for out-of-hospital administration to continue a course of prophylaxis for patients whose LOS was shorter than 6 days. Modes for administration spanned patient self-administration (least costly) to administration by a home care nurse (highest cost).

Results of this cost-finding analysis indicated that a course of VTE prophylaxis with enoxaparin would represent from 1.2% to 2.4% of the projected cost for the hospital admission. The projected total cost, including the out-of-hospital component, ranged from a low of \$117 (hospital dispensing cost \$0,

patient self-administration of any out-of-hospital enoxaparin) to a high of \$290 (\$20 per dose hospital dispensing cost, administration of out-of-hospital enoxaparin by a home health nurse).

In a trial of home versus inpatient treatment for venous thrombosis, Levine et al reported that most patients or family caregivers readily learned how to perform the subcutaneous injection, and fully complied with their medication regimen.¹¹ However, some patients may be unable or unwilling to self-administer their out-of-hospital enoxaparin for a multitude of reasons, and may require assistance from a healthcare professional in either an outpatient clinic or home care setting. Because patients are likely to receive their out-of-hospital prophylaxis in a variety of settings, the middle range depicted in Figure 2 (\$150-\$246) appears to be a reasonable estimate for the total cost of VTE prophylaxis with enoxaparin.

Cost-effectiveness Analysis

Cost-effectiveness analysis offers a metric for assessing “value for money.” In the case of VTE prophylaxis, society should find intrinsic value in an intervention that reduces the risk of a condition that may be painful, may lead to reduced mobility, and could result in sudden death. Combining the MEDENOX clinical results with the cost of prophylaxis developed in this analysis yielded a range of \$1021 to \$2856 as the incremental cost per VTE event avoided. Another recent study derived from the MEDENOX results, conducted independently and using a different methodology, reported a somewhat lower figure of £796 (\$1155) per VTE avoided.¹² Because this analysis was based on healthcare costs in Great Britain, resource use and treatment costs may not be directly comparable.

Cost-effectiveness analysis is more interpretable when the “effect” is defined in more universal terms such as incremental cost per life-year saved. That was the case in a recent study that extrapolated MEDENOX trial findings to project lifetime costs and effects in the setting of France.¹³ Results were given in Euros, which are roughly equivalent to US dollars. The authors estimated the incremental cost per life-year saved as 2701 Euros (95% confidence interval 70-17 757), with an extremely conservative assumption of a 3-year life expectancy. With life expectancy of 6 years, the incremental cost per life-year saved

decreased to 1350 Euros (95% confidence interval 35-8878). In a secondary analysis, costs were included for treatment of postphlebotic syndrome subsequent to acute proximal DVT. With the addition of these costs, VTE prophylaxis yielded a net cost savings (95% confidence interval net savings to +374 Euros, assuming a 3-year life expectancy).

Break-even Analysis

A rationale for VTE prophylaxis in the acutely ill medical patient is that this investment of resources not only reduces the risk of potentially life-threatening events, but also may reduce future treatment expenditures. A decision maker focusing only on economic impact would prefer VTE prophylaxis relative to no prophylaxis at any points above the break-even curves, as depicted in Figure 2. Is there evidence to indicate the likelihood of this occurring?

We can begin to answer that question by examining treatment costs for VTE events. Reported direct medical costs for treatment of VTE vary widely depending on the perspective of the analysis and the time horizon. In a clinical trial comparing inpatient treatment with enoxaparin versus unfractionated heparin (UFH) from a third-party payer perspective, average costs over a 3-month period ranged from \$11 558 for the enoxaparin group to \$12 146 for the UFH group.¹⁴ A study using decision-analytic modeling to project lifetime costs of acute DVT reported short-term costs of \$6526 and future DVT-related costs of \$19 990 for a lifetime total of \$26 516.¹⁵ A recent study in a managed care setting reported a total cost of \$9380 for a 90-day episode of care among patients treated with enoxaparin who received most of their care as outpatients.¹⁶

Figure 2 illustrates calculation of the break-even point with an average VTE treatment cost of \$9380, designated by a dashed vertical line. Intersection of this line with the break-even curves defines the VTE treatment event rate where the cost of prophylaxis equals the expected cost of treatment. As shown in the figure, the range is from 2.0% for the low-cost prophylaxis scenario (\$0 dispensing cost, patient self-administration) to a high of 4.9% in the high-cost prophylaxis scenario (\$20 dispensing cost, administration by a home health nurse). If the average short-term cost were as low as \$6506, as reported in the study by Gould et al,¹⁵ breakeven would be achieved with VTE events in the range of 2.9% to 7.1%. The low-cost and high-cost scenarios may be unlikely: not every patient will choose to self-administer out-of-hospital enoxaparin (low-cost scenario), nor will every patient require administration by a

home health nurse (high-cost scenario). Therefore, the intermediate-cost scenario is perhaps the best estimate for the cost of prophylaxis and suggests that a 3% to 4% VTE event rate would achieve breakeven.

Is an event rate of at least 3% to 4% likely? In the MEDENOX study, all patients with radiographically detected DVT at study day 14 (the primary end point) received VTE prophylaxis with enoxaparin. Nearly 14% of patients in the placebo group fell into this category, and in typical community practice, all would have been discharged at risk of subsequent events.

Virtually all published data on DVT incidence are based on clinical trials where the end point was determined by venography or ultrasonography rather than manifest DVT. For example, the American College of Chest Physicians consensus statement places medical patients at "moderate risk" for DVT, with a 16% incidence based on pooled analysis of trials with end points similar to the MEDENOX study.¹⁷ Evidence that a 3% rate is a reasonable lower limit may come from a prospective follow-up study of 200 medical patients without prophylaxis, 2.5% of whom suffered an autopsy-validated fatal pulmonary embolism.¹⁸

In a prospective follow-up study of 528 patients treated for a first episode of radiographically documented acute DVT, more than 17% developed recurrent VTE within 2 years.¹⁹ One third of patients with untreated DVT of the lower extremities will develop postthrombotic syndrome within 1 year. Symptoms range from minor discomfort to severe chronic pain, intractable edema, and leg ulceration.²⁰ Patients with the more severe symptoms require ongoing care, while the decrease in quality of life can be substantial.²¹

CONCLUSION

Acutely ill, hospitalized medical patients are at high risk of VTE. The MEDENOX trial demonstrated that prophylaxis with enoxaparin substantially decreases this risk. Our economic analysis indicated that this protection results in only a small increase in current treatment costs. Prophylaxis is cost effective in terms of incremental cost per VTE avoided, and there is a reasonable likelihood that the cost of prophylaxis will be offset by avoided future VTE treatment.

Managed care organizations are continually faced with decisions about new therapies, procedures, and treatment strategies. Clinical benefit must be balanced against the short- and long-term economic consequences of an adoption decision.

These economic results, combined with clinical findings from the MEDENOX trial, may be useful in establishing guidelines for VTE prophylaxis among patients who are at significant risk.

.....
REFERENCES

1. **Linblad B, Sternby NH, Bergqvist D, et al.** Incidence of venous thromboembolism verified by necropsy over 30 years. *BMJ*. 1991;302:709-711.
2. **Sandler DA, Martin JF, et al.** Autopsy proven pulmonary embolism in hospital patients: Are we detecting enough deep vein thrombosis? *J R Soc Med*. 1989;82:203-205.
3. **Clagett GP, Anderson FA, Heit JA, et al.** Prevention of venous thromboembolism. *Chest*. 1998;114(suppl):531S-560S.
4. **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. *N Engl J Med*. 1999;341:793-800.
5. **Geerts W, Heit J, Clagett G, et al.** Prevention of venous thromboembolism. *Chest*. 2001;119:132S-175S.
6. **Cohen AT, Zaw HM, Alikhan R.** Benefits of deep-vein thrombosis prophylaxis in the nonsurgical patients: The MEDENOX trial. *Semin Hematol*. 2001;38(2 suppl 5):31-38.
7. **InpatientView™ National Hospital Discharge Database.** Baltimore, MD: HCIA Sachs; 1998.
8. **Redbook ReadyPrice® System.** Greenwood, CO: MicroMedex Division, Thomson Health Care; 2002.
9. **Healthcare Consultants of America.** *Physicians' Fee and Coding Guide*. Augusta, GA: MAG Mutual Group; 1999.
10. **Health Care Financing Administration.** Home health agency cost limits data set. 1999. Available at: <http://www.hcfa.gov/stats/pufiles.htm>. Public Use File hhacyc16.exe. Accessed January 30, 2001.
11. **Levine M, Gent M, Hirsh J, et al.** A comparison of low-molecular-weight heparin administered primarily at home with unfractionated heparin administered in the hospital for proximal deep vein thrombosis. *N Engl J Med*. 1996;334:682-687.
12. **Lloyd AC, Anderson PM, Quinlan DJ, Bearne A.** Economic evaluation of the use of enoxaparin for thromboprophylaxis in acutely ill medical patients. *J Med Econ*. 2001;4:99-113.
13. **Pechivis M, Detournay B, Pribil C, Fagnani F, Chalanson C.** Economic evaluation of enoxaparin vs placebo for the prevention of venous thrombosis in acutely ill medical patients. *Value in Health*. 2001;3(6):389-396.
14. **de Lissovoy G, Yusen RD, Spiro TE, et al.** Cost for inpatient care of venous thrombosis. *Arch Intern Med*. 2000;160:3161-3164.
15. **Gould MK, Dembitzer AD, Doyle RL, Sanders GD, Garber AM.** Low-molecular-weight heparins compared with unfractionated heparin for treatment of acute deep venous thrombosis. *Ann Intern Med*. 1992;130(10):789-799.
16. **Spyropoulos A, Hurley JS, Ciesla GN, de Lissovoy G.** Management of acute proximal deep vein thrombosis: Pharmacoeconomic evaluation of outpatient treatment with enoxaparin versus unfractionated heparin. *Chest*. 2002;122:108-114.
17. **Geerts W, Heit J, Clagett GP, et al.** Prevention of venous thromboembolism. Sixth ACCP Consensus Conference on Antithrombotic Therapy. *Chest*. 2001;119(1 suppl):132S-175S.
18. **Baglin TP, White K, Charles A.** Fatal pulmonary embolism in hospitalized medical patients. *J Clin Pathol*. 1997;50:609-610.
19. **Prandoni P, Villalta S, Bagatella P, et al.** The clinical course of deep-vein thrombosis. Prospective long-term follow-up of 528 symptomatic patients. *Haematologica*. 1997;82:423-428.
20. **Bernardi E, Prandoni P.** The post-thrombotic syndrome. *Curr Opin Pulm Med*. 2000;6(4):335-342.
21. **Kahn S, Solymoss S, Lamping D, et al.** Long-term outcomes after deep vein thrombosis: Postphlebotic syndrome and quality of life. *J Gen Intern Med*. 2000;15(6):425-429.