Cost-effectiveness of Gemfibrozil for Coronary Heart Disease Patients With Low Levels of High-Density Lipoprotein Cholesterol

The Department of Veterans Affairs High-Density Lipoprotein Cholesterol Intervention Trial

John A. Nyman, PhD; Melissa S. Martinson, PhD; David Nelson, PhD; Sean Nugent, BA; Dorothea Collins, ScD; Janet Wittes, PhD; Carol L. Fye, RPh; Timothy J. Wilt, MD, MPH; Sander J. Robins, MD; Hanna Bloomfield Rubins, MD, MPH; for the VA-HIT Study Group

Background: Although numerous clinical trials and economic analyses have established the efficacy and cost-effectiveness of lowering cholesterol for the prevention of coronary heart disease, there are few data on the role of raising high-density lipoprotein cholesterol (HDL-C) levels and lowering triglyceride levels. The US Department of Veterans Affairs (VA) Cooperative Studies Program HDL-C Intervention Trial (VA-HIT) was a multicenter, randomized trial of gemfibrozil, an agent that raised HDL-C levels and lowered triglyceride levels, yet had no effect on low-density lipoprotein cholesterol (LDL-C) levels. The study showed that gemfibrozil therapy significantly reduced major cardiovascular events (cardiovascular death, myocardial infarction, and stroke) in patients with coronary heart disease, low HDL-C levels, and low LDL-C levels.

Objective: To report the results of a cost-effectiveness study based on the results of the VA-HIT.

Methods: The cost per year of life gained with gemfibrozil therapy was calculated. Hazard functions were estimated, and the resulting probabilities were used in a Markov model simulation to estimate the effect of gemfibrozil on life expectancy and costs over a simulated lifetime. Sensitivity analyses were used to account for uncertainty.

Results: Using the prices of gemfibrozil that were negotiated by the VA, gemfibrozil was cost saving. Using drug prices found outside the VA, a quality-adjusted life-year saved by gemfibrozil therapy cost between $6300 and $17100.

Conclusions: Gemfibrozil reduces major cardiovascular events in male coronary heart disease patients with low levels of HDL-C and low levels of LDL-C and would result in cost saving at annual drug costs of $100 or less in 1998 dollars. Even at the higher drug prices represented by the average wholesale price in the United States, the cost of a life-year saved is well below the threshold that would be deemed cost-effective. To our knowledge, this is the first economic analysis based on clinical trial data to assess the cost-effectiveness of raising HDL-C levels and lowering triglyceride levels in a setting in which LDL-C levels were not lowered.

Arch Intern Med. 2002;162:177-182

Low-density lipoprotein cholesterol (LDL-C) is a risk factor for coronary heart disease (CHD), and numerous trials have shown that drugs that lower elevated LDL-C levels reduce major cardiovascular events, such as CHD death, myocardial infarction, and stroke. Approximately 40% of patients with CHD, however, do not have elevated LDL-C levels. Many of these patients instead exhibit low levels of high-density lipoprotein cholesterol (HDL-C). Because no clinical trials had determined the efficacy of lipid therapy in these patients, the US Department of Veterans Affairs (VA) conducted a multicenter randomized controlled clinical trial (the VA Cooperative Studies Program HDL-C Intervention Trial [VA-HIT]) to determine whether therapy aimed at increasing HDL-C levels and decreasing triglyceride levels would reduce major cardiovascular end points in CHD patients whose primary lipid abnormality is low HDL-C levels. The VA-HIT study compared gemfibrozil (1200 mg/d) with placebo in 2531 men (average±SD age, 64±7 years) who had CHD, low HDL-C levels (mean, 32 mg/dL [0.83 mmol/L]), and low LDL-C levels (mean, 111 mg/dL [2.87 mmol/L]). The median follow-up period was 5.1 years. At 1 year, participants who underwent gemfibrozil therapy had mean HDL-C levels 6% higher, mean triglyceride levels 31% lower, and mean total cholesterol lev-
METHODS

DATA

The data for this cost-effectiveness study come from the VA-HIT study. Participants in that study were men younger than 74 years at enrollment, with a history of CHD, an HDL-C level of 40 mg/dL (1.03 mmol/L) or less, and an LDL-C level of 140 mg/dL (3.6 mmol/L) or less. Patients with clinically evident chronic heart failure or other major medical problems likely to result in mortality within 5 years were excluded. Patients with long-term stable conditions, such as diabetes and hypertension, were included. The details of the study and data can be found elsewhere.5

PERSPECTIVE

Costs in this analysis were defined as the direct costs of gemfibrozil therapy minus any cost savings due to the reduction in downstream medical treatment costs attributable to the therapy. Effects were defined as the number of life-years gained with gemfibrozil therapy.

The VA-HIT study was performed from the perspective of a health care organization such as the VA; thus, it omitted indirect costs (eg, travel costs and productivity costs stemming from absence from work). Omitting indirect costs would produce conservative cost-effectiveness results, if the study were performed from the perspective of society. This is because it is unlikely that indirect costs would be a substantial portion of the cost of a pharmacologic intervention such as gemfibrozil. Moreover, because gemfibrozil is associated with fewer cardiovascular events, the omission of indirect costs in the downstream costs leads to an underestimate of the cost savings associated with gemfibrozil. Therefore, the cost-effectiveness ratios from the perspective of the health plan would represent conservative estimates of the cost-effectiveness of gemfibrozil from the perspective of society.

ESTIMATES OF EFFECTS

To promote standardization and facilitate comparisons across similar studies, the analysis was modeled after the cost-effectiveness analysis from the Scandinavian Simvastatin Survival Study.6 Accordingly, a Markov model was developed to estimate the effects of gemfibrozil on future years of life.

In the Markov model, a cohort of individuals with age characteristics of the study participants was followed from their current age to age 110 years, which was deemed to be the longest possible survival time. In each year, the men could experience a cardiovascular event or die of a noncardiovascular cause. Cardiovascular events were either fatal or nonfatal, as described in detail elsewhere.7 Nonfatal events included myocardial infarction or stroke. If the person experienced a nonfatal event, it was assumed that he would remain in a temporary state of disease during the subsequent year, during which time he was assumed to have an increased risk of death. If the patient survived this year, he would enter a period of chronic disease, during which time the risk of death was higher than normal but lower than during the first year following an event. At the end of every period in the chronic disease state, patients had a probability of dying or surviving for another year in that state.

Hazard functions were estimated from the VA-HIT data and used to determine the probabilities of transitioning from one state to another in the Markov model. Four probabilities were estimated separately from the VA-HIT data: (1) the annual risk of a CHD patient dying from a non–CHD-related cause, (2) the annual risk of a CHD patient experiencing a cardiovascular event, (3) the annual risk of a patient dying in the first year after a nonfatal event, and (4) the annual risk of a patient dying in the chronic state, that is, in a year subsequent to the first year after a nonfatal event. The hazard functions were estimated from exponential survival models, and each included a variable that represented whether the patient was in the gemfibrozil group or not. This variable was only significant in the function estimating the annual risk of a CHD patient experiencing a cardiovascular event. Thus, the differential treatment and control probabilities used to generate the life expectancy effects due to gemfibrozil therapy in the discrete Markov model were based on this factor alone.

The hazard functions included age as a risk factor but not sex because all the participants were male. The age variable allowed for the estimation of effectiveness and costs of gemfibrozil in treating patients of varied ages. The proportion of cardiovascular events that were fatal, however, affects 4% lower than the placebo group. (The levels of LDL-C during the trial did not differ significantly between treatment arms.) At the end of the trial, those in the treatment group had a 22% reduction in relative risk (a 4.4% absolute risk reduction) for the primary end point of nonfatal myocardial infarction and CHD death. For the expanded end points of nonfatal myocardial infarction, CHD death, and stroke, the relative risk reduction with drug therapy was 24% (a 5.6% absolute reduction).4

Although the VA-HIT study showed that gemfibrozil was associated with a reduction in major cardiovascular events in CHD patients whose primary lipid abnormality was a low level of HDL-C, in an era of concern over rapidly growing health care expenditures, it is also necessary to investigate the economic consequences of this therapeutic approach. In the present study, we analyze the cost-effectiveness of gemfibrozil for the treatment of CHD patients with this lipid profile. To our knowledge, this is the first economic analysis based on clinical trial data to assess the cost-effectiveness of raising HDL-C levels and lowering triglyceride levels in a setting in which LDL-C levels were not lowered.

RESULTS

For the 65-year-old reference case, the life expectancy is estimated at 17.45 years without gemfibrozil therapy and 18.07 years with the therapy, for an increase in survival of 0.62 years. The estimated costs using VA prices are $10462 without gemfibrozil and $10352 with gemfibrozil, for a net lifetime cost savings with gemfibrozil of $110 per patient. The estimated cost with gemfibrozil...
using national wholesale drug prices is $14,431, for a net cost with gemfibrozil of $3969. Therefore, for drug therapy applied in settings in which gemfibrozil is purchased at prices that reflect the average national wholesale price, the incremental cost-effectiveness ratio (ICER) is $6403 in costs per life-year saved. For comparison, the corresponding estimates for all 3 age levels (ages 55, 65, and 75 years) are presented in Table 3.

Sensitivity analyses were performed for the 3 age levels, using the 3 discount rates (0%, 3%, and 5%) and with effectiveness measured by 2 quality-adjusted life-year (QALY) weights (1.00 and 0.88). The results (Table 4) indicate a robustness of the cost-saving result using the low drug prices negotiated by large health plans such as the VA and a range in ICERS from $6305 to $17,075 using national average drug prices. In general, ICERS were found to decrease with age and increase with the discount rate.

In addition, break-even annual drug costs were calculated for the 3 age levels (Table 5). These results suggest that, as a general rule, if the annual cost of gemfibrozil therapy is $100 or less, the use of the drug would result in a lifetime cost saving. The average age at first event was also calculated for the 3 age levels. Gemfibrozil therapy resulted in the greatest delay in the occurrence of the first event for those in the 65-year-old group (Table 5).

Finally, the analysis was replicated using lognormal and Weibull hazard functions. The ICERS calculated using probabilities from these hazards showed a larger range in results; that is, the costs per QALY were greater for the positive ICERS and the savings per QALY

was remarkably similar across age groups. Although there were more events for patients aged 65 to 74 years, the percentage of events that were fatal in both the 65- to 74-year and 55- to 64-year age groups was 28%, using data from both arms of the trial (Table 1).

The differential risks of a cardiovascular event attributable to gemfibrozil therapy were applied to the Markov model using a Monte Carlo simulation. After 5 years of gemfibrozil treatment, it was assumed that the treatment would stop and the risk of cardiovascular events for those in the treatment group would revert to the level found in the control group. Although the effectiveness of continued gemfibrozil treatment would likely extend beyond 5 years, the Markov model did not extrapolate effectiveness beyond the period observed and documented by the VA-HIT. Also, the reduction in risk was assumed to apply only to the first event and not to any subsequent event. This assumption is also conservative because the occurrence of an event increases the absolute risk of further events, and thus any reduction of events would have downstream effects on risk rates not captured in the analysis.

ESTIMATES OF COSTS

The annual cost of gemfibrozil at two 600-mg tablets per day (Lopid, Parke-Davis, New York, NY) using the price negotiated by the VA is $46.75. The annual cost of gemfibrozil based on the 1998 average wholesale price in the United States (Medi-Span Inc, San Bruno, Calif) is $956.96. The VA vs wholesale prices were used in an alternative analyses.

The cost of one additional fasting lipid profile per year was also included as part of the direct treatment costs. Although the number of lipid profiles ordered is largely a matter of physician practice style, it was thought that patients undergoing gemfibrozil therapy may receive one additional lipid test each year, compared with those not receiving a lipid medication. The 1998 price of a lipid panel (Current Procedural Terminology code 80061) was assumed to be $10.16, based on a sample of this procedure's cost at 5 VA medical centers. It was assumed that the therapy would cease with the cardiovascular event, so the drug and monitoring costs were incurred by patients only until the period in which they transitioned to a cardiovascular event or death.

The direct medical care costs are represented by hospital costs attributable to treatment of fatal and nonfatal cardiovascular events. A list of diagnosis related groups (DRGs) that are associated with the treatment of cardiovascular events was identified (Table 2). For any participant experiencing an event in the VA-HIT study, the DRG treatment costs incurred by the participant during the subsequent year were summed to determine the annual cost of an event. The annual cost per participant with an event was averaged, based on the experience of participants in both arms of the study. In the Markov model, for any subject who was simulated to have experienced an event, this average cost was applied. Separate average cost figures were calculated for the year following a nonfatal event, for a year subsequent to that year, and for fatal events. Thus, for any person who was simulated to have experienced a nonfatal coronary event, their annual hospital costs were estimated to be $10,152 during the first year after an event and $1600 during a subsequent year. For any person who was simulated to experience a fatal event, their cost was estimated to be $3430 for the year of the event. All drug and medical care use was evaluated at 1998 prices.

SENSITIVITY ANALYSIS AND THE REFERENCE CASE

Separate cost-effectiveness ratios were calculated for men aged 35, 65, and 75 years, consistent with the range of ages of the men in the VA-HIT study. In a sensitivity analysis, costs and life-years were calculated with discount rates of 0%, 3%, and 5%, consistent with recommendations from the Panel on Cost-effectiveness in Health and Medicine. The expected life-years of CHD patients were also adjusted for quality of life. Because quality of life data were not collected in the VA-HIT study, a measure was obtained from the literature. Accordingly, it was assumed that a life-year with CHD could either take on a weight of 1.00 or 0.88, the latter reflecting the concept that the quality of a year of life with CHD was worth 0.88 times a year of life in perfect health. Finally, we replicated the entire analysis, replacing our original exponential hazard function with log normal and Weibull functions.

Although the sensitivity analysis calculated cost-effectiveness ratios for all these potential cases, the case of the 65-year-old man, undiscounted and unadjusted for quality of life, was considered the reference case.
market power to command similarly low drug prices.

The VA estimated that roughly 20% to 25%, or 2 million to 3 million people, have CHD and low HDL-C levels in the absence of high LDL-C levels.15 Among the 3 million patients cared for in the VA Health Care System and possibly by other large health care organizations place gemfibrozil therapy in this price range. This is an important finding because only a handful of health care interventions have shown to be cost saving (ie, improve clinical outcomes and save money). Even allowing for higher gemfibrozil prices, this intervention would still be considered cost-effective (ie, improve outcomes and cost money), with a range of cost-effectiveness ratios from $6300 to $17 100 per year of life saved.9-12 Indeed, cost-effectiveness ratios of $100 000 or more per life saved have been deemed to be cost-effective, based on estimates of the value of year of life from consumers’ revealed preferences for work-related risk.13,14 To our knowledge, this is the first economic analysis based on clinical trial data to assess the cost-effectiveness of raising HDL-C levels and lowering triglyceride levels in a setting in which LDL-C levels were not lowered.

These findings have potentially widespread implications. It is estimated that among the approximately 13 million patients with established CHD in the United States roughly 20% to 25%, or 2 million to 3 million people, have low HDL-C levels in the absence of high LDL-C levels.15 Among the 3 million patients cared for in the VA Health Care System, it is estimated that approximately 25% have CHD.16,17 Therefore, approximately 175 000 veterans have CHD and low HDL-C levels in the absence of high LDL-C levels. At an undiscouned lifetime cost saving of $110 per patient treated, about $19 million could be saved by the VA from treatment of the existing cohort of CHD patients. Large savings could also be realized in other health care system settings with sufficient market power to command similarly low drug prices.

These results, however, should not be extrapolated to patients without established CHD in whom the efficacy and the cost-effectiveness of gemfibrozil have not been evaluated.

We chose to compare gemfibrozil to the alternative strategy of no lipid therapy because gemfibrozil is the only lipid intervention that reduces clinical events in a large-scale randomized trial in CHD patients whose primary lipid abnormality is low HDL-C levels. Other medications, such as statins, have never been tested in a similar population. The cost-effectiveness, however, of statins for patients without established CHD in whom the efficacy and the cost-effectiveness of gemfibrozil have not been evaluated.

This analysis suggests that gemfibrozil therapy will result in a lifetime cost savings for CHD patients with low HDL-C levels as their primary lipid abnormality if the drug can be purchased for less than $100 per year (in 1998 prices). Drug prices negotiated by the VA Health Care System and possibly by other large health care organizations place gemfibrozil therapy in this price range. This is an important finding because only a handful of health care interventions have shown to be cost saving (ie, improve clinical outcomes and save money). Even allowing for higher gemfibrozil prices, this intervention would still be considered cost-effective (ie, improve outcomes and cost money), with a range of cost-effectiveness ratios from $6300 to $17 100 per year of life saved.9-12 Indeed, cost-effectiveness ratios of $100 000 or more per life saved have been deemed to be cost-effective, based on estimates of the value of year of life from consumers’ revealed preferences for work-related risk.13,14 To our knowledge, this is the first economic analysis based on clinical trial data to assess the cost-effectiveness of raising HDL-C levels and lowering triglyceride levels in a setting in which LDL-C levels were not lowered.

These findings have potentially widespread implications. It is estimated that among the approximately 13 million patients with established CHD in the United States roughly 20% to 25%, or 2 million to 3 million people, have low HDL-C levels in the absence of high LDL-C levels.15 Among the 3 million patients cared for in the VA Health Care System, it is estimated that approximately 25% have CHD.16,17 Therefore, approximately 175 000 veterans have CHD and low HDL-C levels in the absence of high LDL-C levels. At an undiscouned lifetime cost saving of $110 per patient treated, about $19 million could be saved by the VA from treatment of the existing cohort of CHD patients. Large savings could also be realized in other health care system settings with sufficient market power to command similarly low drug prices.
spectively in a randomized clinical trial, thus allowing the analysis to rely on fewer assumptions than if the analysis were based on epidemiologic data. Analyses based on epidemiologic data must make assumptions about the treatment efficacy based on presumed benefits that would accrue from a given change in a risk factor. In contrast, analyses based on clinical trial data are more robust because the estimates of effectiveness are based on data from a population that was actually treated with the intervention.

Even economic analyses that are based on clinical trial data, however, must resort to some assumptions. Still, another strength of our study is that conservative assumptions were chosen where possible. For example, in the Markov analysis, it was assumed that the treatment would be discontinued after 5 years, the period of follow-up in the actual study. However, based on the evidence of the effectiveness of treatment in 75-year-old patients, it is likely that if treatment were continued beyond 5 years in the 55- and 65-year-old cohorts, it would be similarly cost-effective or cost saving. Also, the reduction in the probability of initial events was assumed not to have any effect on the probability of subsequent events, when in fact the probability of subsequent events would be expected to increase following an initial event. Thus, the analysis underestimates the reduction of future events caused by the treatment.

The results of the study held up well in the sensitivity analysis. Adjusting for higher drug prices than were paid by the VA, discounting future cost savings at discount rates greater than 0, and adjusting the value of a life saved for the quality of life all increased the cost-effectiveness ratios, but these increases resulted in ICERs that were still within acceptable ranges.

One limitation of our study may have been the lack of data on indirect costs. Indirect costs would include the

<table>
<thead>
<tr>
<th>Variable</th>
<th>Age 55 y</th>
<th>Age 65 y</th>
<th>Age 75 y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Life expectancy, y</td>
<td>22.55</td>
<td>23.15</td>
<td>0.60</td>
</tr>
<tr>
<td>Lifetime costs, $</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drugs at $46.75 per year</td>
<td>13 464</td>
<td>13 259</td>
<td>–205</td>
</tr>
<tr>
<td>Drugs at $956.00 per year</td>
<td>13 259</td>
<td>10 352</td>
<td>8232</td>
</tr>
<tr>
<td>Costs per year of life saved, $</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drugs at $46.75 per year</td>
<td>...</td>
<td>...</td>
<td>Savings</td>
</tr>
<tr>
<td>Drugs at $956.00 per year</td>
<td>...</td>
<td>6607</td>
<td>...</td>
</tr>
</tbody>
</table>

*Ellipses indicate data not applicable.*

Table 4. Sensitivity Analysis*

<table>
<thead>
<tr>
<th>Costs, $</th>
<th>Age Discount 0%</th>
<th>Age Discount 3%</th>
<th>Age Discount 5%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>13 464</td>
<td>10 462</td>
<td>8284</td>
</tr>
<tr>
<td>Treatment (drug cost = $46.75)</td>
<td>13 259</td>
<td>10 352</td>
<td>8232</td>
</tr>
<tr>
<td>Treatment (drug cost = $956.00)</td>
<td>17 429</td>
<td>14 431</td>
<td>12 193</td>
</tr>
<tr>
<td>Effectiveness, y</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control (QALY = 0.88)</td>
<td>19.84</td>
<td>15.35</td>
<td>11.76</td>
</tr>
<tr>
<td>Treatment (QALY = 0.88)</td>
<td>20.37</td>
<td>15.90</td>
<td>12.30</td>
</tr>
<tr>
<td>Control (QALY = 1.00)</td>
<td>22.55</td>
<td>17.45</td>
<td>13.36</td>
</tr>
<tr>
<td>Treatment (QALY = 1.00)</td>
<td>23.15</td>
<td>18.07</td>
<td>13.98</td>
</tr>
<tr>
<td>ICERs, $/y</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>QALY (0.88)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug cost ($46.75)</td>
<td>–387</td>
<td>–198</td>
<td>–96</td>
</tr>
<tr>
<td>Drug cost ($956.00)</td>
<td>7480</td>
<td>7217</td>
<td>7239</td>
</tr>
<tr>
<td>QALY (1.00)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug cost ($46.75)</td>
<td>–342</td>
<td>–176</td>
<td>–83</td>
</tr>
<tr>
<td>Drug cost ($956.00)</td>
<td>6607</td>
<td>6403</td>
<td>6305</td>
</tr>
</tbody>
</table>

*QALY indicates quality-adjusted life-year; ICERs, incremental cost-effectiveness ratios.*

Table 5. Break-even Costs and Average Age at First Event

<table>
<thead>
<tr>
<th>Variable</th>
<th>Age 55 y</th>
<th>Age 65 y</th>
<th>Age 75 y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Break-even drug costs, $</td>
<td>77</td>
<td>87</td>
<td>100</td>
</tr>
<tr>
<td>Break-even expected health care costs, $</td>
<td>6289</td>
<td>7407</td>
<td>8759</td>
</tr>
<tr>
<td>Average age at first event, y</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gemfibrozil group</td>
<td>70.11</td>
<td>78.75</td>
<td>85.53</td>
</tr>
<tr>
<td>Control group</td>
<td>69.68</td>
<td>77.48</td>
<td>85.02</td>
</tr>
</tbody>
</table>

*Ellipses indicate data not applicable.*
costs of traveling to a health care facility for care following an event and the wages lost in time spent traveling to and receiving the care. The omission of indirect costs, however, results in an underestimate of the cost savings from downstream procedures avoided, so including these costs would result in even lower cost-effectiveness ratios. This limitation, therefore, also creates a likely conservative bias, if the study is interpreted as reflecting a societal perspective, and is even more supportive of the conclusion that gemfibrozil therapy is cost-effective in this population. Another limitation is that our estimates of efficacy were based on the results of a clinical trial that, because of the selection of patients and the intensive follow-up, may overestimate the efficacy that would be observed in a routine clinical setting. Finally, it should be recognized that, although there are numerous trials that show efficacy and cost-effectiveness of statins for patients with elevated LDL-C levels, to date there is just a single trial that demonstrates efficacy and cost-effectiveness for gemfibrozil in CHD patients with low HDL-C levels.1,3,6

In conclusion, the VA-HIT demonstrated that gemfibrozil is a safe and well-tolerated therapy that significantly reduces major cardiovascular events, including myocardial infarction, cardiovascular death, and stroke, in patients with established CHD who have low levels of HDL-C and low-risk LDL-C levels.4 This study presents evidence that gemfibrozil therapy is also highly cost-effective, if not cost saving, thus providing a strong rationale for incorporating the therapy into practice. These results also suggest that raising HDL-C levels and lowering triglyceride levels, independent of changes in LDL-C levels, represent efficacious and cost-effective approaches for the secondary prevention of CHD.

Accepted for publication May 8, 2001.

From the School of Public Health, Division of Health Services Research and Policy, University of Minnesota (Drs Nyman and Martinson), and Center for Chronic Disease Outcomes Research, Department of Veterans Affairs Medical Center, Minneapolis, Minn (Drs Nelson, Wilt, and Rubins and Mr Nugent); Department of Veterans Affairs Cooperative Studies Program Coordinating Center, West Haven, Conn (Dr Collins); Statistics Collaborative, Washington, DC (Dr Wittes); Department of Veterans Affairs Clinical Research Pharmacy Coordinating Center, Albuquerque, NM (Ms Fye); and Department of Medicine, Boston University School of Medicine, Boston, Mass (Dr Robins). A list of the members of the VA-HIT study group was published previously (N Engl J Med. 1999;341:410-418).

The VA-HIT was supported by the Cooperative Studies Program of the Department of Veterans Affairs Office of Research and Development, Washington, DC, and by a supplemental grant from Parke-Davis.

The views expressed in this article do not necessarily represent the views of the Department of Veterans Affairs.

Corresponding author and reprints: John A. Nyman, PhD, Division of Health Services Research and Policy, University of Minnesota, 420 Delaware St SE, Mail Route 729, Minneapolis, MN 55455-0392 (e-mail: nyman001@tc.umn.edu).

REFERENCES


