Cost-Effectiveness of Rosuvastatin for Primary Prevention of Cardiovascular Events According to Framingham Risk Score in Patients With Elevated C-Reactive Protein

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Context: The Food and Drug Administration (FDA) recently approved rosuvastatin calcium for prevention of cardiovascular events in patients who have elevated levels of highsensitivity C-reactive protein (hs-CRP) but not overt hyperlipidemia. The FDA’s decision was based primarily on research reported by the JUPITER (Justification for the Use of Statins in Prevention: An Intervention Trial Evaluating Rosuvastatin) Study Group. The cost-effectiveness of such treatment is unknown.

Objective: To compare the cost-effectiveness of treatment with rosuvastatin vs standard management, according to Framingham Risk Score (FRS), for the primary prevention of cardiovascular events in patients who have hs-CRP levels of 2.0 mg/L or higher and low-density lipoprotein cholesterol (LDL-C) levels of less than 130 mg/dL.

Methods: A Markov-type model was used to calculate the incremental cost-effectiveness ratio of rosuvastatin (20 mg daily) vs standard management for the primary prevention of cardiovascular events in patients over a 10-year period. Cost data were obtained from the Centers for Medicare & Medicaid Services and the Red Book drug reference. Health utility measures were obtained from the literature. Cardiovascular event data were obtained directly from the JUPITER Study Group. One-way sensitivity analysis and probabilistic sensitivity analysis were conducted.

Results: Treating patients with rosuvastatin to prevent cardiovascular events based on a hs-CRP level greater than 2.0 mg/L and an LDL-C level of 130 mg/dL or lower would result in estimated incremental cost-effectiveness ratios of $35,455 per quality-adjusted life year (QALY) in patients with an FRS greater than 10% and $90,714 per QALY in patients with an FRS less than or equal to 10%. Results of probabilistic sensitivity analysis suggested that in patients with an FRS greater than 10%, the probability that rosuvastatin is considered cost-effective at $50,000 per QALY is approximately 98%. In patients with an FRS less than or equal to 10%, the probability that rosuvastatin is considered cost-effective at $50,000 per QALY is 0%.

Conclusions: Compared with standard management, treatment with rosuvastatin is a cost-effective strategy over a 10-year period for preventing cardiovascular events in patients with FRS greater than 10%, elevated hs-CRP levels, and normal LDL-C levels.

Complications from cardiovascular disease (CVD) account for more than one-third of all deaths in the United States—more deaths than from any other single disease. Rates of first cardiovascular events (eg, myocardial infarction, ischemic stroke, unstable angina) range from 3 per 1000 men at ages 35 to 44 years to 74 per 1000 men at ages 85 to 94 years. Comparable rates occur for women 10 years later in life. The monetary impact of CVD in the United States in 2009 was an estimated $475.3 billion, including direct and indirect costs. These cost are almost certain to increase in the future.

Current guidelines for the primary prevention of cardiovascular events center on the reduction of risk factors. These risk factors, which form the basis for calculating the 10-year risk of a cardiovascular event, are derived from results of the Framingham Heart Study. Many of the risk factors, such as blood pressure, cholesterol level, and smoking status, are modifiable. However, age, sex, and family history are not modifiable. In most cases, drug therapy is instituted after an attempt to modify or reduce risk has failed. Treatment with HMG-CoA reductase inhibitors (ie, statins) is the mainstay of pharmacotherapy for lowering low-density lipoprotein cholesterol (LDL-C) levels and cardiovascular event risk.

In recent years, inflammation has been recognized as having a significant impact on the development and progression of atherosclerosis. In an effort to isolate a marker for inflammation, high-sensitivity C-reactive protein (hs-CRP) has become the biomarker of choice. The hs-CRP level is a precise indicator of an ongoing inflammatory process. How-
ever, this biomarker is nonspecific for CVD. Elevated hs-CRP levels are also associated with cancer, diabetes mellitus, high blood pressure, increased age, infection, metabolic syndrome, obesity, obstructive sleep apnea, rheumatologic disorders, and smoking.8-12

Statin therapy has been shown to lower hs-CRP levels and to reduce the risk of cardiovascular events in patients with elevated hs-CRP levels.13,14 Routine measurement of hs-CRP levels for the purpose of intervention is not currently recommended, though elevated levels are recognized to play an important role in the development of CVD.2

In February 2010, the US Food and Drug Administration (FDA) approved rosuvastatin calcium (Crestor; AstraZeneca, Wilmington, Delaware) for the prevention of cardiovascular events in women aged 60 years or older and in men aged 50 years or older who have hs-CRP levels greater than or equal to 2 mg/L and one additional CVD risk factor—without hyperlipidemia.15 Implementation of hs-CRP monitoring for means of risk stratification and treatment will lead to expansion of rosuvastatin treatment as millions of Americans will be prescribed a statin for the first time.16 Although previous studies have suggested that statin therapy is cost-effective in both primary and secondary prevention of cardiovascular events, there have been no previous statin cost-effectiveness studies examining a patient population with elevated levels of hs-CRP and normal levels of LDL-C over a period of 10 years.

Methods
For the present study, cardiovascular event data were obtained directly from JUPITER (Justification for the Use of Statins in Prevention: An Intervention Trail Evaluating Rosuvastatin) Study Group (Paul M. Ridker, MD, MPH, personal communication, September 2009), allowing for the separation of JUPITER patients into two categories—patients with an FRS greater than 10% and patients with an FRS less than or equal to 10%. The information received was in a similar format to that reported in table 3 of the JUPITER Study Group’s previous publication.14

Patients in JUPITER14 had a median age of 66 years. More than one-third of the patients were women. Initial LDL-C levels for patients were within normal ranges for their particular health states, and initial hs-CRP levels were greater than or equal to 2 mg/L. All patients were statin naive and without previous history of cardiovascular events.14

Design of the Markov Model
TreeAge Pro 2009 software (TreeAge Software, Inc, Williamstown, Massachusetts) was used to design a Markov-type model from a healthcare system perspective (Figure 1). A Markov model is a type of decision-analytic model that is dynamic over time. It allows for variation in disease states, costs, and health utility over a specified time frame. This model was applied to the group of patients with FRS greater than 10% and the group with FRS less than or equal to 10%, mirroring the design of JUPITER14 in terms of treatment arms and outcomes assessment. The treatment arms used in the model were rosuvastatin therapy and standard management, which was defined as no statin therapy, with annual monitoring of lipid profiles and hs-CRP levels.

The model applied the same exclusion criteria for patient eligibility and hs-CRP testing as established in JUPITER.14 The rationale for using these exclusion criteria was based on the lack of specificity of hs-CRP testing. Clinicians should recognize that patients who have disease states that would elicit an elevated hs-CRP level are unlikely to benefit from such testing or treatment. Whether there are outcome benefits in such patients remains to be seen.

The model was designed for primary prevention insofar that only those parameters up to and including a cardiovascular event were considered. A 10-year timeframe was used in an effort to coordinate the timeline of cost-effectiveness with that of disease risk models, such as the FRS model and the Reynolds Risk Score model.19-21

The outcome used for the design of the model was a primary endpoint event, defined as a patient having experienced a nonfatal myocardial infarction, nonfatal ischemic stroke, arterial revascularization, hospitalization for unstable angina, or death from a cardiovascular cause. The model was designed to move patients through 40 cycles of 3 months per cycle, for a total of 10 years, using constant probabilities for each cycle.

The patients in the statin group entered the model as being assigned to a “healthy/no event” state, an adverse event state, or a primary endpoint event state, based on the probability of such events (Table 1). An adverse event was defined as any event requiring discontinuation of treatment.22 Any discontinuation of therapy led the patient to cycle through the model without treatment, as if he or she were in the standard management group. Patients in the standard management group entered the model as being assigned to a “healthy/no event” state or a primary endpoint event state, based on the probability of such events (Table 1).

Patients who experienced a primary endpoint event would transition to the primary endpoint event state. This transition was a temporary state in the model, allowing for appropriate accumulation of costs and reduced quality-adjusted life year (QALY) measures before terminating into a secondary prevention state. Because the analysis evaluated primary prevention only, a secondary prevention state was built into the model as the final absorbing state. This secondary prevention state was used for accounting purposes only, and it was not populated with costs or utility data.

Patients without an event in each cycle were allowed to
continue cycling through the model as healthy patients with no event—either until an event occurred or until the end of the 10-year study period.

Clinical Parameters
Outcomes data associated with the primary endpoint event were obtained directly from the JUPITER Study Group (Dr Ridker, personal communication, September 2009). Constant event probabilities over the 10-year timeline were used in the model and were not adjusted for age-associated risk. Actual event data are not reported with any measure of certainty. The uncertainty in the event data was compensated in 1-way sensitivity analysis by setting the standard deviation at an arbitrary 20% to achieve robustness.

The 3-month probabilities of a primary endpoint are summarized in Table 1. An adverse event rate of 1.4% was applied within the first 3 months of statin therapy.

Cost Data
Costs analyzed in the present study included costs of the study drug (rosuvastatin, 20 mg daily), costs associated with outpatient management, and costs associated with cardiovascular events (Table 1). The average wholesale price of rosuvastatin 20 mg was obtained from the 2009 edition of the Red Book drug reference published by Thomson Reuters.23 Because this price does not accurately reflect costs that the typical patient or insurer might pay now or in the future, the price of the drug was arbitrarily adjusted in 1-way sensitivity analysis between $4.00 per month (the price of a generic statin at many retail pharmacies) and $150.00 per month (a price that exceeds the common retail price of rosuvastatin).

Costs associated with outpatient management were calculated at national levels for Current Procedural Terminology (CPT) codes for a typical office visit and laboratory tests associated with statin therapy.24,25 All outpatient management costs were adjusted by 20% for 1-way sensitivity analysis to account for uncertainty in the estimates, for variability of regional and institutional reimbursement rates, and for clinicians’ outpatient management practices.

Costs associated with cardiovascular events were calculated according to Diagnosis Related Groups (DRGs), which were available from the Centers for Medicare & Medicaid Services.26,27 A composite cost for the primary endpoint event was estimated by assigning weights to each of the events. These weights were estimated based on the event numbers published in JUPITER and were assumed to be constant over the 10-year period for the present analysis.14 All outcomes contained within the primary endpoint had multiple DRGs associated with them. To arrive at a point estimate for each event, the costs of all DRGs within a given event were averaged, and the range (lowest cost to highest cost) was used for 1-way sensitivity analysis (Table 1).
### Table 1

**Model Parameters and Base Case Values Used in 1-Way Sensitivity Analysis**

<table>
<thead>
<tr>
<th>Model Parameters</th>
<th>Weight*</th>
<th>Base Case Value (Range)†</th>
<th>Value Reference (Range Reference)</th>
</tr>
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<tbody>
<tr>
<td><strong>Probabilities of Primary Endpoint Event‡</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- FRS &gt; 10%</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>- Probability of primary endpoint event</td>
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<td></td>
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<tr>
<td>Statin group</td>
<td>...</td>
<td>0.0031 (0.0024-0.0037)</td>
<td>Ridker§ (Author assumption)</td>
</tr>
<tr>
<td>Standard manage-</td>
<td></td>
<td>0.0054 (0.0043-0.0065)</td>
<td>Ridker§ (Author assumption)</td>
</tr>
<tr>
<td>ment group</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>- FRS &lt; 10%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Probability of primary endpoint event</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Statin group</td>
<td>...</td>
<td>0.0011 (0.0009-0.0013)</td>
<td>Ridker§ (Author assumption)</td>
</tr>
<tr>
<td>Standard manage-</td>
<td></td>
<td>0.0020 (0.0016-0.0024)</td>
<td>Ridker§ (Author assumption)</td>
</tr>
<tr>
<td>ment group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Probability of adverse event§</td>
<td></td>
<td>0.014 (0.008-0.02)</td>
<td>AstraZeneca²³ (Author assumption)</td>
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<td><strong>Costs, mean</strong></td>
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<tr>
<td>- Outpatient costs, statin group</td>
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<td></td>
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<tr>
<td>- Office visit (CPT 99213)</td>
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<td>$61.31</td>
<td>CMS²⁴</td>
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<tr>
<td>- Lipid panel</td>
<td>...</td>
<td>$19.01</td>
<td>CMS²⁵</td>
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<td>- Alanine aminotransferase</td>
<td>...</td>
<td>$10.44</td>
<td>CMS²⁵</td>
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<td>- Aspartate aminotransferase</td>
<td>...</td>
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<td>- hs-CRP</td>
<td>...</td>
<td>$25.55</td>
<td>CMS²⁵</td>
</tr>
<tr>
<td>- Venipuncture</td>
<td>...</td>
<td>$3.00</td>
<td>CMS²⁵</td>
</tr>
<tr>
<td>- Total initial outpatient cost§</td>
<td>...</td>
<td>$129.51 ($103.61-$155.41)</td>
<td>☐ (Author assumption)</td>
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<td>- Total incremen-</td>
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<td>tal outpatient cost#</td>
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<tr>
<td>- Outpatient costs, standard management group</td>
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<tr>
<td>- Office visit (CPT 99213)</td>
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<td>$61.31</td>
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<td>tal outpatient cost#</td>
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<tr>
<td><strong>Other costs</strong></td>
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<tr>
<td>- Rosuvastatin, 20 mg/tablet</td>
<td>...</td>
<td>$4.11 ($0.13-$5.00)</td>
<td>Red Book²³ (Author assumption)</td>
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<td>- Nonfatal myocar- dial infarction</td>
<td>0.14</td>
<td>$6891.39 ($4459.66-$9951.16)</td>
<td>CMS²⁶,²⁷ (Author estimate)</td>
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<tr>
<td>- Nonfatal stroke</td>
<td>0.19</td>
<td>$7973.14 ($4327.86-$14,727.25)</td>
<td>CMS²⁶,²⁷ (Author estimate)</td>
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<tr>
<td>- Arterial revascularization</td>
<td>0.45</td>
<td>$20,581.76 ($9809.11-$39,200.54)</td>
<td>CMS²⁶,²⁷ (Author estimate)</td>
</tr>
<tr>
<td>- Hospitalization for unstable angina</td>
<td>0.10</td>
<td>$2549.85 ($2039.88-$3059.82)</td>
<td>CMS²⁶,²⁷ (Author estimate)</td>
</tr>
<tr>
<td>- Death from cardiovas- cular causes</td>
<td>0.12</td>
<td>$7599.23 ($0.00-$39,200.54)</td>
<td>☠ (Author estimates)</td>
</tr>
<tr>
<td><strong>Health Utilities‡‡</strong></td>
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<td></td>
</tr>
<tr>
<td>- Primary endpoint event</td>
<td>...</td>
<td>0.606 (0-1)</td>
<td>**</td>
</tr>
<tr>
<td>- Nonfatal myocar- dial infarction</td>
<td>0.14</td>
<td>0.704</td>
<td>Sullivan and Ghushchyan²⁸</td>
</tr>
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<td>0.650</td>
<td>Sullivan and Ghushchyan²⁸</td>
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<tr>
<td>- Arterial revascularization</td>
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<td>0.695</td>
<td>Author estimate</td>
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<td>- Hospitalization for unstable angina</td>
<td>0.10</td>
<td>0.695</td>
<td>Sullivan and Ghushchyan²⁸</td>
</tr>
<tr>
<td>- Death from cardiovascular causes</td>
<td>0.12</td>
<td>0</td>
<td>Author assumption</td>
</tr>
<tr>
<td>- Healthy/no event</td>
<td>...</td>
<td>1.00 (0.90-1.00)</td>
<td>Author assumption</td>
</tr>
</tbody>
</table>

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* Weight estimates based on event numbers in JUPITER study. † Weighted averages are calculated only for parameters used to calculate weighted averages.

* Ranges specified only where appropriate for data analysis.

‡ Probabilities—on a 0-1 scale—calculated for 3-month period. The primary endpoint event was defined as a nonfatal myocardial infarction, nonfatal stroke, arterial revascularization, hospitalization for unstable angina, or death from cardiovascular causes.

§ According to the JUPITER Study Group (Paul M. Ridker, MD, MPH, personal communication, September 2009).

// Adverse event modelled as a one-time event during the initial 3 months of statin therapy. Probability is on a 0-1 scale.

† Costs calculated for initial 3-month period as sum of all outpatient costs.

# Costs calculated for incremental 3-month period as sum of all outpatient costs divided by 2. One office visit per year was assumed (ie, one-quarter of costs of initial office visit for each incremental 3-month period).

** Weighted average of primary endpoint events. Range explained in “Utility Data” section of text.

†† Estimated cost calculated as average of the other events. Low range of $0 was assumed because a patient could expire without being admitted to a hospital.

‡‡ Utility is defined on a 0-1 scale, in which 0 represents death and 1 represents perfect health.

Abbreviations: CMS, Centers for Medicare & Medicaid Services; CPT, Current Procedural Terminology; FRS, Framingham Risk Score; hs-CRP, high-sensitivity C-reactive protein; NA, not applicable.
Costs associated with adverse reactions were omitted under the assumption that the majority of these reactions would subside upon discontinuation of therapy.

**Utility Data**

Utilities of the various events in the model were obtained from the literature. Event utilities—more appropriately termed health utilities—are quantitative assessments of a particular health state. Health utility is commonly defined on a 0-to-1 scale, in which 0 represents death and 1 represents perfect health. A composite health utility was calculated using event weights.

The utility of arterial revascularization was estimated as the average utility of nonfatal myocardial infarction and unstable angina. The reasoning for using this method was that patients who receive a revascularization procedure typically experience a myocardial infarction or unstable angina before the procedure is performed. A state of healthy/no event was included in the model to represent all individuals within a cycle who did not have a primary endpoint event. The utility for this health state was assumed to have a range of 0.9 to 1 to account for uncertainty in the health state of each patient as he or she cycled through the model.

**Analyses**

An incremental cost-effectiveness ratio (ICER) was calculated as a cost per QALY, which was obtained after the model was populated with the cost and utility estimates and event probabilities. Costs and utilities were discounted at 3% per year (0.75% per cycle) and were adjusted between 0% and 7% for sensitivity analysis.

All parameters in the model, except for those associated with the probability of no event, were analyzed using 1-way sensitivity analysis and were allowed to vary between the high and low values shown in Table 1. The utility (ie, QALY) associated with a primary endpoint event was allowed to vary between 0 and 1. The rationale behind this decision was to allow the range in which the utility varied to act as a proxy for the amount of time that a patient remained in a primary endpoint event state.

A probabilistic sensitivity analysis was conducted with a sample size of 10,000 and a sampling rate of once per Markov stage. The results were plotted on a cost-effectiveness acceptability curve. All model inputs were assigned a distribution, and distribution parameters (ie, alpha, beta) were estimated using the point estimate and a 20% standard deviation. A gamma distribution was assigned to all cost estimates, and a beta distribution was assigned to all probabilities and health utility estimates.

The distribution parameters for the probability of a primary endpoint event were calculated from the event data obtained from the JUPITER Study Group (Dr Ridker, personal communication, September 2009) by using the TreeAge Pro 2009 software.

**Results**

**Base Case Analysis**

Based on the data obtained from the JUPITER Study Group (Dr Ridker, personal communication, September 2009) and other sources, it was estimated that using rosuvastatin to prevent a cardiovascular event in patients with FRS greater than 10% would cost $11,700 more per patient than would standard management over a 10-year period. Using rosuvastatin to treat patients with FRS less than or equal to 10% would cost an estimated $12,700 more than standard management. These estimates include the cost of the statin, the costs of outpatient medical management, and the cost associated with a cardiovascular event.

Over the 10-year study period, patients treated with rosuvastatin accrued an estimated 0.33 more QALYs compared to their standard management counterpart if they had an FRS greater than 10%, and an estimated 0.14 more QALYs compared to their standard management counterpart if they had an FRS less than or equal to 10%. The resulting ICER was estimated at $35,455 per QALY gained in those patients with an FRS greater than 10%—but $90,714 per QALY gained in patients with an FRS less than or equal to 10% (Table 2).

**1-Way Sensitivity Analysis**

In the 1-way sensitivity analysis of patients with an FRS greater than 10%, the ICER was most sensitive to the following variables: the probability of a primary endpoint event in the standard management group, the cost of the statin, the probability of a primary endpoint event in the statin group, and the utility of a primary endpoint event (Figure 2). In the 1-way sensitivity analysis of patients with an FRS less than or equal to 10%, the ICER was most sensitive to the following variables: the cost of the statin, the probability of a primary endpoint event in the standard management group, the probability of a primary endpoint event in the statin group, the utility of a primary endpoint event, the discount rate, and the utility of no event (Figure 3).

The maximum incremental cost-effectiveness ratio observed during 1-way sensitivity analysis was $69,000 per QALY for patients with an FRS greater than 10% and $165,000 per QALY for patients with an FRS less than or equal to 10% (Table 3). These ratios indicate that if all other parameter estimates are unbiased, and if the true value of the probability of a primary endpoint event in the standard management group is 20% less than that reported in JUPITER, then the resulting ICER in both Framingham cohorts would be as stated.

When the cost of rosuvastatin was set at a retail price of $4.00 per month, the ICER was -$1000 per QALY for patients with an FRS greater than 10% and $2,000 per QALY for patients with an FRS less than or equal to 10% (Table 3).

**Probabilistic Sensitivity Analysis**

When event probabilities, costs, and utilities were simultaneously varied according to their respective probability distri-
manage ment in the number of patients who had diabetes mellitus. In addition, a recent meta-analysis reported a 9% increased risk of incident diabetes mellitus among patients on statin therapy for a period of 4 years (odds ratio, 1.09; 95% confidence interval, 1.02-1.17). Costs associated with the possible development of diabetes mellitus were not considered in the present analysis.

The present analysis was also limited in that it took into account only the outcomes data from the single existing study—JUPITER14—examining the outcomes benefit of statins in patients who have elevated hs-CRP levels. This limitation subjected the current analysis to many of the same biases that are present in JUPITER. Further research is needed to evaluate whether patients will have comparable outcomes from using other statins besides rosuvastatin. If results of such studies are similar to that of JUPITER, a generic statin could be substituted, leading to a large cost savings and a much lower ICER.

**Cost Questions**

The price of statins has decreased in recent years as a result of a proliferative generic market and fierce competition in the branded market. Reduced price, combined with the relative safety of statins, has led to the question of whether expansion of statin treatment as a whole is cost-effective. A recent study by Pletcher et al30 suggests that when the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) guidelines are fully implemented for the primary prevention of cardiovascular events, statin therapy will be cost-effective, with an estimated ICER of $42,000 per QALY given a statin price of $2.11 or less per tablet.

AstraZeneca’s patent for rosuvastatin will expire in 2016, allowing generic drug manufacturers to seek profits from rosuvastatin’s indication for hyperlipidemia and elevated hs-CRP levels. As the price for rosuvastatin decreases, its ICER will decrease. When the price of rosuvastatin equals $8 for a 30-day supply, the ICER will be $0 per QALY in patients with an FRS greater than or equal to 10%. That will represent the breakeven point at which there is no net cost for treatment.

An estimated 17.9 million people in the United States older than 35 years would require testing for hs-CRP levels if results of JUPITER14,16 were applied broadly. Patients in JUPITER had a median age of 66 years. When stratifying patients based on FRS and considering only those patients with an FRS greater than 10% based on the favorable cost-effectiveness established in the present analysis, approximately 10.2 million Americans would require hs-CRP testing. If after hs-CRP testing, treatment was restricted to patients with a hs-CRP level greater than 3.0 mg/L, 2.1 million Americans would require treatment with a statin. This restriction could result in a lower ICER than was established in this analysis.

A large number of myocardial infarctions and cardiovascular events occur in individuals who have normal cholesterol levels and no history of atherosclerotic disease. The most
Model Parameters With Base Case Value Ranges

- Probability of Primary Endpoint in Standard Management Group: 0.0043-0.0065
- Cost of Rosuvastatin per Tablet: $0.13-$5.00
- Probability of Primary Endpoint in Statin Group: 0.0024-0.0037
- Utility of Aggregated Primary Event: 0-1
- Discount Rate: 0%-7%
- Cost of Aggregated Primary Event: $5397-$26,770
- Utility of No Event: 0.90-1.00
- Incremental Outpatient Costs of Statin Group: $25.90-$38.85
- Incremental Outpatient Costs of Standard Management Group: $21.77-$32.66
- Initial Outpatient Costs of Statin Group: $103.61-$155.41
- Initial Outpatient Costs of Standard Management Group: $97.98-$130.64
- Probability of an Adverse Event: 0.8%-2%

Figure 2. One-way sensitivity analysis, displayed as tornado diagram, for patients with a Framingham Risk Score greater than 10%, rosuvastatin group vs standard management group. Wider bars represent greater sensitivity. Ranges of base case values for various model parameters are shown to the right of the diagram (see also Table 1). The diagram shows that the incremental cost-effectiveness ratio was most sensitive to the probability of a primary endpoint event in the standard management group, the cost of rosuvastatin, the probability of a primary endpoint event in the statin group, and the utility of an aggregated primary endpoint event.

Figure 3. One-way sensitivity analysis, displayed as tornado diagram, for patients with a Framingham Risk Score less than or equal to 10%, rosuvastatin group vs standard management group. Wider bars represent greater sensitivity. Ranges of base case values for various model parameters are shown to the right of the diagram (see also Table 1). The diagram shows that the incremental cost-effectiveness ratio was most sensitive to the cost of rosuvastatin, the probability of a primary endpoint event in the standard management group, the probability of a primary endpoint event in the statin group, the utility of a primary endpoint event, the discount rate, and the utility of no event.
The results of this analysis indicate that rosuvastatin is cost-effective for patients with normal LDL-C levels, elevated hs-CRP levels, and an FRS greater than 10%, given a threshold of $50,000 per QALY. The ICER was favorable across the entire range of costs and health utilities in this cohort and exceeded the $50,000 per QALY threshold only when event probabilities were set at extreme values. In patients with an FRS less than or equal to 10%, the cost-effectiveness of rosuvastatin is considered favorable only when this drug’s price is less than $2.35 per tablet.

Although the present study does not address the much broader question of whether hs-CRP monitoring is cost-effective, it does answer the more limited question of whether rosuvastatin is cost-effective in patients with elevated hs-CRP levels. It is the opinion of this author that the present study represents one of many necessary steps needed to answer that broader question. Thus, further research is essential to assess whether hs-CRP monitoring for the purposes of primary prevention is cost-effective.

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**References**


7. Koenig W, Sund M, Frohlich M, et al. C-reactive protein, a sensitive marker commonly used CVD risk model—the Framingham Risk Score model—does not account for hs-CRP levels in risk stratification, whereas the Reynolds Risk Score model does. If we assume that the Reynolds Risk Score is a validated and acceptable method for calculating the risk of a cardiovascular event, the following two questions appear obvious: (1) are statins a cost-effective way of lowering cardiovascular event risk in patients with elevated hs-CRP levels?, and (2) is measurement of hs-CRP levels for the purposes of preventing disease cost-effective?

**Conclusion**

In the present study, a Markov-type model was designed to examine the cost-effectiveness of rosuvastatin therapy vs standard management for the primary prevention of cardiovascular events in patients with elevated hs-CRP levels according to FRS. The results of this analysis indicate that rosuvastatin is cost-effective for patients with normal LDL-C levels, elevated hs-CRP levels, and an FRS greater than 10%, given a threshold of $50,000 per QALY. The ICER was favorable across the entire range of costs and health utilities in this cohort and exceeded...


**Figure 4.** Cost-effectiveness acceptability curve, comparing both Framingham Risk Score (FRS) groups (FRS >10%, FRS ≤10%). The graph shows the probability that rosuvastatin is cost-effective given different willingness-to-pay thresholds. Such thresholds vary according to payer (ie, third-party or government).


