

The Cost-Effectiveness of C-Reactive Protein Testing and Rosuvastatin Treatment for Patients With Normal Cholesterol Levels

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- Objectives** We sought to evaluate the cost-effectiveness of applying the JUPITER (Justification for the Use of statins in Prevention: an Intervention Trial Evaluating Rosuvastatin) trial results into clinical practice.
- Background** The JUPITER trial found that rosuvastatin reduces vascular events in apparently healthy subjects with elevated high-sensitivity C-reactive protein (hs-CRP) but normal low-density lipoprotein (LDL) cholesterol levels. The implications of expanding treatment recommendations based on these results have not been evaluated.
- Methods** We constructed a cost-effectiveness model of men ≥ 50 years and women ≥ 60 years with LDL cholesterol levels of < 130 mg/dl and no known cardiovascular disease. We compared: 1) hs-CRP testing followed by rosuvastatin treatment for patients with hs-CRP levels ≥ 2.0 mg/l; and 2) usual care (i.e., no testing and no treatment). Estimates of treatment effectiveness were based on the JUPITER trial and were varied in sensitivity analyses.
- Results** Among patients with LDL < 130 mg/dl and hs-CRP levels ≥ 2.0 mg/l, rosuvastatin had an incremental cost-effectiveness of \$25,198 per quality-adjusted life year (QALY) gained compared to usual care. If the effectiveness of rosuvastatin were 50% of that observed in JUPITER, the incremental cost-effectiveness ratio would increase to \$50,871 per QALY. Implementing this strategy only in patients with a Framingham risk score $\geq 10\%$ yielded an incremental cost-effectiveness of \$14,205 per QALY. Among such intermediate-risk patients, a JUPITER-based strategy becomes cost-saving at a rosuvastatin price of $< \$0.86$ per day.
- Conclusions** Rosuvastatin treatment for JUPITER-eligible patients appears to be cost-effective, particularly among those with a Framingham risk score $\geq 10\%$. (J Am Coll Cardiol 2011;57:784–91) © 2011 by the American College of Cardiology Foundation

High-sensitivity C-reactive protein (hs-CRP) levels are associated with cardiovascular risk and have been proposed as a target for therapeutic intervention (1). The JUPITER (Justification for the Use of statins in Prevention: an Intervention Trial Evaluating Rosuvastatin) study tested this association in apparently healthy subjects with elevated hs-CRP levels (≥ 2.0 mg/l) and

low-density lipoprotein (LDL) cholesterol below treatment thresholds (< 130 mg/dl) (2). Patients randomized to receive rosuvastatin had substantial reductions in their risk of vascular events compared with those treated with placebo (2,3).

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The implications of applying the JUPITER trial results into routine practice are unclear. Although JUPITER found impressive relative reductions in vascular events from rosuvastatin, the corresponding absolute benefits were modest (4). Some have questioned whether the trial overestimated treatment effects because it was terminated early for efficacy (5). In addition, hs-CRP screening costs almost \$20 per test, rosuvastatin is available only as a brand-name agent, and treatment for eligible patients would likely be continued indefinitely. Accordingly, we evaluated the balance between

potential benefits and health care expenditures that would result from adopting a strategy of hs-CRP testing followed by rosuvastatin treatment, if indicated, for patients with below-target LDL levels.

Methods

We constructed a model to evaluate 2 management strategies in men ≥ 50 years and women ≥ 60 years with LDL cholesterol levels of < 130 mg/dl and no known cardiovascular disease. The first strategy consisted of testing hs-CRP followed by rosuvastatin for patients with hs-CRP levels ≥ 2.0 mg/l; the second strategy was usual care (no testing and no treatment). The model (Fig. 1) simulates a cohort of patients with an age, sex, and Framingham risk score distribution based on the characteristics of the JUPITER trial participants as they move, in annual cycles, through health states that represent the occurrence of cardiovascular, thrombotic, and statin-related adverse events as well as death. Movement between these states is based on transition probabilities observed in JUPITER, supplemented by an extensive review of the clinical literature.

The model was run separately for patients who undergo a test-and-treat strategy and those who do not. Incremental cost-effectiveness ratios were calculated as the difference in costs for these 2 strategies divided by their difference in quality-adjusted life-years (QALYs) produced. We did not explicitly model health effects or costs for patients with low hs-CRP levels because we assumed that in both treatment

arms, these patients would not receive a statin and thus their outcomes and costs (other than for initial hs-CRP screening in the test-and-treat arm) would be the same in both cases (i.e., were nondifferential).

The analysis was conducted over a lifetime time horizon from a societal perspective, such that all costs were included regardless of payer. Future costs and life years were discounted at an annual rate of 3%. We describe additional details about our analytic strategy, including the sensitivity analyses we performed, in the Online Appendix.

Data inputs for the model were published and unpublished trial data obtained from the JUPITER investigators and supplemented with other data from the published literature (Table 1, Online Table 1).

HS-CRP SCREENING AND ROSUVASTATIN TREATMENT. Using data from JUPITER, we estimated that 50.3% of patients with normal LDL levels have elevated hs-CRP levels (6). This is consistent with other published estimates (7). For patients with hs-CRP levels ≥ 2.0 mg/l, treatment was assumed to consist of rosuvastatin 20 mg daily. Patients in the usual care arm were assumed to initiate rosuvastatin treatment only if they had myocardial infarction, unstable angina hospitalization, stroke, or diabetes onset.

Abbreviations and Acronyms

hs-CRP = high-sensitivity C-reactive protein
LDL = low-density lipoprotein
MI = myocardial infarction
QALY = quality-adjusted life year

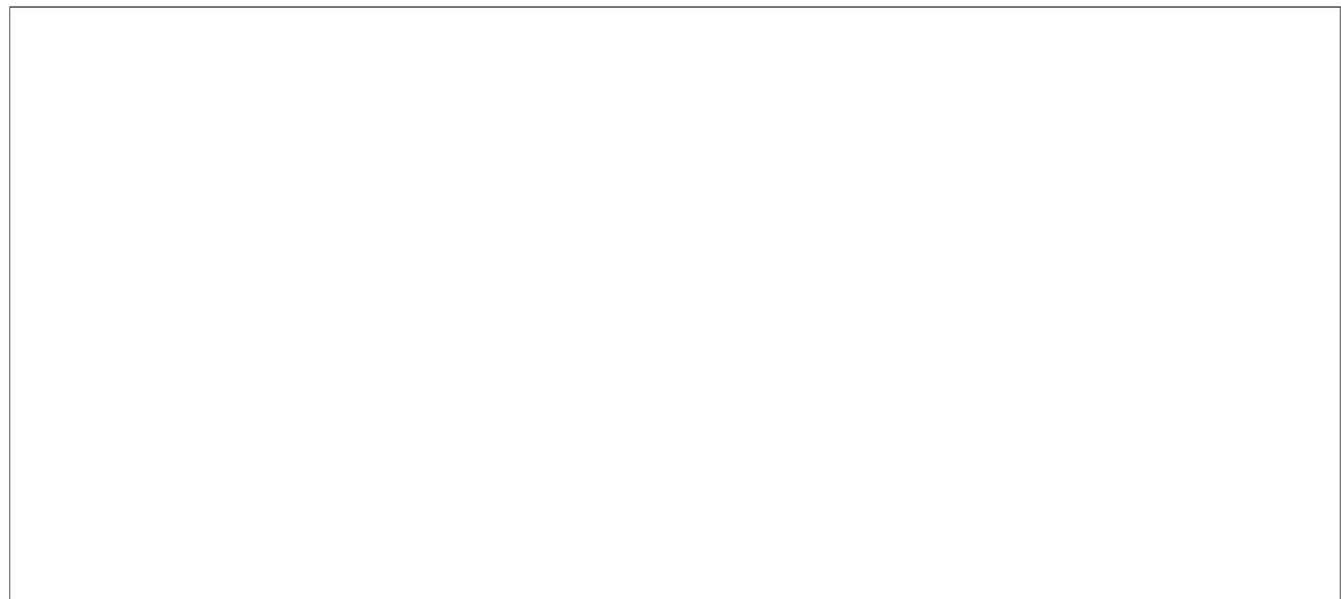


Figure 1 Cost-Effectiveness Model Structure Comparing the Test-and-Treat Strategy and Usual Care

In each 1-year cycle, patients may experience 8 possible clinical events, resulting in survival or death, and 1 or more complications. Based on their status at the end of the cycle, patients begin the next 1-year cycle in one of 33 possible health states. *Clinical event and complication rates are modeled as a function of treatment status. †There are a total of 33 health states depicting disease history and treatments. Dimensions are: ACS/no prior ACS, prior stroke/no prior stroke, prior VTE/no prior VTE, diabetes/no diabetes, and statin/no statin. ACS = acute coronary syndrome(s); CV = cardiovascular; DVT = deep venous thrombosis; hs-CRP = high sensitivity C-reactive protein; LDL = low-density lipoprotein; LFT = liver function test; MI = myocardial infarction; PE = pulmonary embolism; VTE = venous thromboembolism.

Table 1	Model Variables	
Parameter	Base Case Estimate	Sensitivity Range Tested
Prevalence of elevated hs-CRP	50%	25%–75%
Event rates with usual care (per 100 person-yrs)*		
Myocardial infarction	0.37	0.29–0.46
Hospitalization for unstable angina	0.14	0.10–0.21
Revascularization	0.71	0.60–0.84
Stroke	0.34	0.27–0.44
Venous thromboembolism	0.32	0.25–0.42
Physician-confirmed diabetes onset	1.04	0.90–1.10
Elevated liver enzymes	0.09	0.06–0.14
Myopathy	0.05	0.02–0.09
Effect of rosuvastatin on event rates (hazard ratios)		
Myocardial infarction	0.46	0.30–0.70
Hospitalization for unstable angina	0.59	0.32–1.1
Revascularization	0.54	0.41–0.72
Stroke	0.52	0.34–0.79
Venous thromboembolism	0.57	0.37–0.86
Diabetes	1.26	1.04–1.53
Elevated liver enzymes	1.24	0.65–2.34
Myopathy	1.11	0.45–2.74
Event-related mortality (in the year an event occurs)†		
Myocardial infarction	12.5%	6%–19%
Unstable angina	0.4%	0.2%–0.6%
Stroke	13.2%	7%–20%
Venous thromboembolism	4.5%	2%–7%
Utilities		
Healthy	0.85	0.8–1
Vascular and adverse events‡		
Myocardial infarction, unstable angina	0.88	0.80–0.93
Stroke	0.73	0.50–0.90
Diabetes	0.88	0.80–1.00
End-stage renal disease	0.61	0.45–0.75
Daily statin consumption	1.00	0.98–1.00
Treatment and monitoring costs		
hs-CRP test	\$19	\$0–\$100
Liver function test	\$34	\$17–\$64
Rosuvastatin, 20 mg/day, daily cost		
Brand name	\$3.63	\$0.50–\$4
Generic	\$1	\$0.13–\$1

EVENT RATES WITH USUAL CARE. Rates of acute ischemic events with usual care were obtained by applying the observed age, sex, and Framingham risk score-specific event rates in the placebo arm of the JUPITER trial to the first 5 years of follow-up. Mortality from other causes was estimated by calibrating our model to annual survival estimates from JUPITER. Event rates beyond the trial period were estimated by multiplying the observed trial event rates by age- and sex-specific multipliers obtained from longitudinal cohort studies (8–10) to adjust for the aging of the study population. Mortality from nonischemic causes was estimated based on the age and sex distribution of surviving patients and age- and sex-specific U.S. life table data (11).

Table 1	Continued	
Parameter	Base Case Estimate	Sensitivity Range Tested
Costs (in the year an event occurs)		
Myocardial infarction	\$25,567	\$13,000–\$28,000
Unstable angina	\$8,510	\$4,300–\$13,000
Revascularization	\$30,209	\$15,000–\$45,000
Stroke	\$16,502	\$8,300–\$25,000
Pulmonary embolism	\$15,382	\$7,500–\$23,000
Deep vein thrombosis	\$1,058	\$500–\$1,600
Myopathy (including % resulting in rhabdomyolysis)	\$509	\$200–\$800
Elevated liver enzymes (including 0.5% resulting in liver failure)	\$325	\$100–\$500
Initial diagnosis of diabetes	\$117	\$50–\$200
Ongoing event costs (annual after first year)		
Myocardial infarction, unstable angina	\$430	\$200–\$700
Stroke	\$17,158	\$8,500–\$26,000
Diabetes, including end stage renal disease	\$6,240	\$3,000–\$9,300
Discount rate, per year	3%	0–5%

Data sources for the model inputs are presented online in Online Table 1. *The rates are increased after year 5 to reflect the aging of the study population. †Event-related mortality rates vary by age; the presented values are average values for the initial JUPITER trial population. ‡Utilities for patients with vascular and adverse events were calculated by multiplying utilities for the specific event with age-specific utilities for healthy individuals. For example, the utility of having a myocardial infarction is equal to $0.85 \times 0.88 = 0.75$.

hs-CRP = high sensitivity C-reactive protein; JUPITER = Justification for the Use of statins in Prevention: an Intervention Trial Evaluating Rosuvastatin.

We subtracted age- and sex-specific death rates from ischemic causes, which were explicitly modeled in our analysis, from the all-cause mortality rate (12).

EVENT RATES IN HS-CRP TEST-AND-TREAT ARM. In the test-and-treat arm, event rates for patients with elevated hs-CRP levels who received rosuvastatin were calculated using outcome-specific hazard ratios for all pre-specified primary and secondary outcomes evaluated in JUPITER, including venous thromboembolism and diabetes. Because the trial found no heterogeneity in treatment effects by age and sex, we used overall treatment effects. Although the trial was terminated after a median follow-up of 1.9 years, many patients were followed for longer, and the benefit of rosuvastatin appeared to increase over the 5-year trial period (13). Nevertheless, we assumed constant treatment effects for the first 5 years of treatment. The effects of statin therapy for patients with normal LDL and high hs-CRP levels beyond this time period are unknown. Thus, in our base case analyses, we assumed that treatment effects persisted for 15 years at the level observed during the trial and then tapered off to no effect after 25 years of follow-up, which is a more conservative assumption than that made in other recent cost-effectiveness analyses of lipid-lowering therapy (14). This assumption was tested in sensitivity analyses.

The JUPITER trial documented a 20% reduction in all-cause mortality in the test-and-treat arm ($p = 0.02$), but the cause of death was incompletely ascertained for some trial participants who died after their primary outcome event

Table 2 Event Rates Estimated by the Cost-Effectiveness Model Compared With the JUPITER Trial Results

Outcome	Number of Events With Usual Care		Number of Events With hs-CRP Screening and Rosuvastatin Treatment if Elevated	
	JUPITER	Estimated by Model*	JUPITER	Estimated by Model*
MI	68	68	31	31
Unstable angina	27	26	16	15
Stroke	64	62	33	32
Revascularization	131	129	71	70

*Model event counts are for the mean follow-up in JUPITER and were estimated assuming that patients were censored for occurrence of the primary event.

MI = myocardial infarction; other abbreviations as in Table 1.

(for example, patients who died after having a stroke). As a result, a model that measured the benefit of rosuvastatin on mortality entirely in terms of reductions in ischemic event related mortality underestimates the total benefit of this treatment on all-cause mortality. To adjust for this, we calibrated death rates for the test-and-treat arm to the actual rates of all-cause mortality in JUPITER observed during the first 5 years of follow-up. After this period, we conservatively applied the hazard ratios described in JUPITER without any correction factor.

COSTS. The cost of hs-CRP screening was based on the current Medicare payment rate for this test (15). Because we evaluated a cohort of patients already identified as having LDL levels below 130 mg/dl, we did not include the cost of cholesterol testing in our model. All patients in the test-

and-treat strategy, including those ultimately found to have a level ≤ 2.0 mg/l, were assumed to undergo hs-CRP testing and, therefore, to incur the cost of the test. In the base case analysis, we calculated rosuvastatin costs from a major online pharmacy (16). The cost until 2016 (i.e., the first 7 years of the model) was assumed to be the quoted price for branded rosuvastatin (\$3.63/day). After patent expiration, we assumed that the generic rosuvastatin price would be comparable to that of generic simvastatin beginning in 2018 (\$1/day), and halfway between branded Crestor and generic simvastatin (80 mg/day) prices during 2017 (\$2.32/day). Rosuvastatin-treated patients were assumed to receive liver function testing at treatment initiation, 1 month later, and once per year thereafter.

We calculated the costs of acute clinical events by summing the costs for acute hospitalization, physician services, medication use, and post-acute care for each outcome. Costs of ongoing care in cycles in which no acute event occurred were included for patients with a stroke, MI, angina, or diabetes. All costs were expressed in 2009 U.S. dollar values.

Results

For a cohort of men 50 years and older and women 60 years and older without known cardiovascular disease and LDL levels of <130 mg/dl, the model closely estimated the number of outcome events (Table 2) and rate of 5-year all-cause mortality (Fig. 2) observed in both arms of the JUPITER trial.

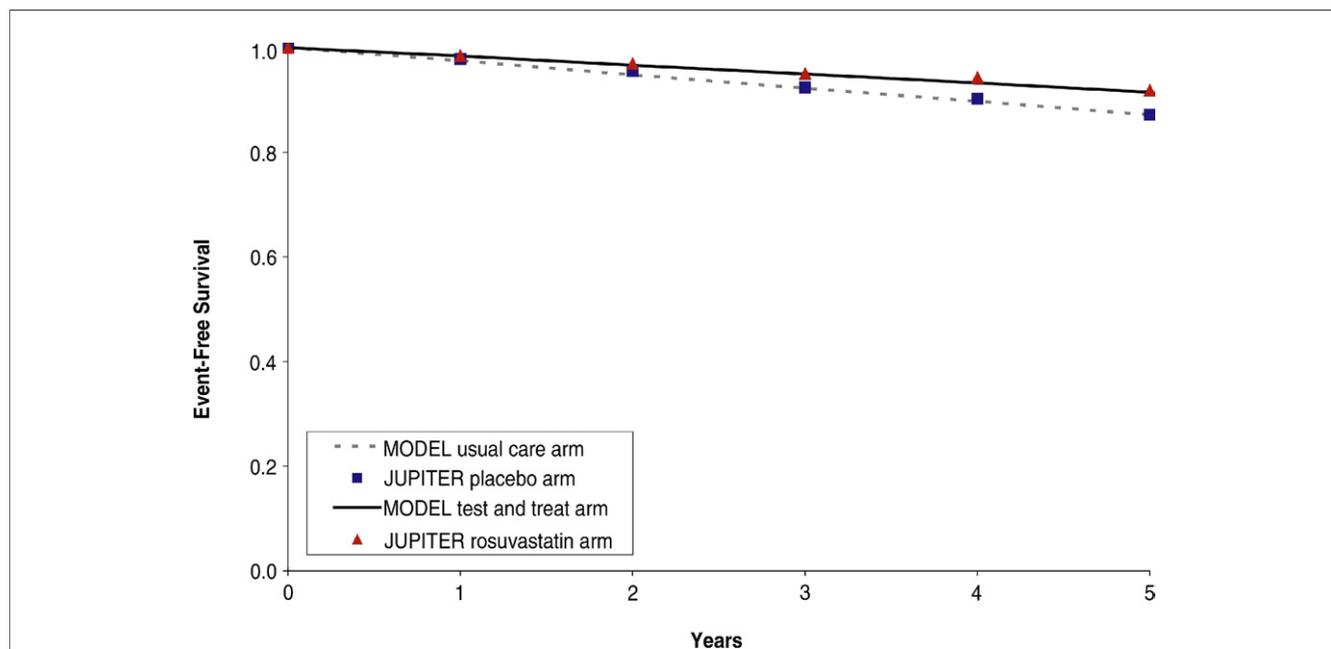


Figure 2 Event-Free Survival Predicted by the Cost-Effectiveness Model Compared With the JUPITER Trial Results

The solid black (test-and-treat) and dashed gray (usual care) lines represent the model estimates. The red diamonds (rosuvastatin) and blue squares (placebo) represent the observed event-free survival in JUPITER (Justification for the Use of statins in Prevention: an Intervention Trial Evaluating Rosuvastatin).

	Usual Care	hs-CRP Screening and Rosuvastatin Treatment if Elevated	Difference
Costs, \$*			
Screening and treatment	\$1,032	\$11,366	\$10,334
Vascular events	\$12,241	\$8,077	−\$4,164
Adverse events	\$6,444	\$8,173	\$1,729
Total	\$19,717	\$27,616	\$7,899
Effectiveness, QALY*	10.29	10.61	0.31
Incremental cost-effectiveness ratio (\$/QALY)	—	—	\$25,198

Values are in U.S. dollars. *All future costs and QALYs were discounted at a rate of 3% per year. QALY = quality-adjusted life year; other abbreviations as in Table 1.

Base care results. Patients treated with usual care (i.e., no hs-CRP testing or treatment) were estimated to have an average quality-adjusted life expectancy of 10.29 QALYs, and associated health care costs of \$19,717 (Table 3). A strategy of hs-CRP testing followed by rosuvastatin treatment for patients with hs-CRP levels ≥ 2.0 mg/l resulted in an average quality-adjusted life expectancy of

10.61 QALYs and costs of \$27,616. As a consequence, this strategy had an incremental cost-effectiveness of \$25,198 per QALY gained, compared with usual care. The cost per life year gained was \$22,160.

Sensitivity analyses. The base case results were robust to alterations in many model parameters (Fig. 3). Assuming a reduced effectiveness of rosuvastatin that is at the most unfavorable 95% confidence limit for the point estimates in JUPITER (for example, a hazard ratio of 0.70 for the reduction in myocardial infarction instead of the observed hazard ratio of 0.46) resulted in an incremental cost-effectiveness ratio of \$57,503 per QALY. Limiting the impact of the test-and-treat strategy on mortality to that resulting directly from its impact on preventing vascular events (i.e., removing the apparent effect of rosuvastatin on noncardiovascular mortality) yielded an incremental cost-effectiveness ratio of \$39,392. If the effect of rosuvastatin observed in JUPITER only persisted for 5 years with no subsequent effect, the cost-effectiveness of hs-CRP testing would be \$62,146 per QALY. In contrast, if the full effect of treatment persisted for 25 years and then tapered off to no effect by 35 years, the cost-effectiveness of the test-and-treat

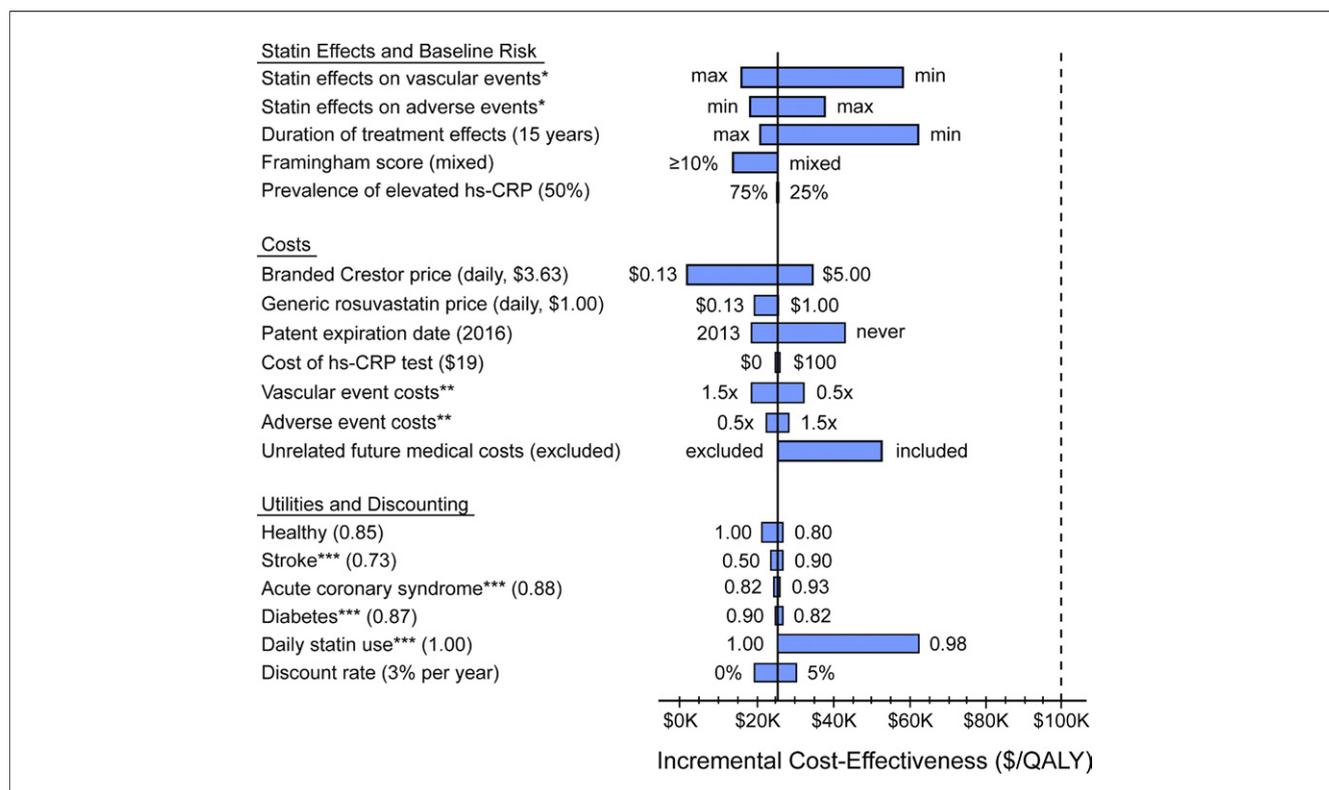


Figure 3 1-Way Sensitivity Analyses

Each bar represents the incremental cost-effectiveness ratio of the test-and-treat strategy for different assumptions concerning the parameter listed. The vertical line depicts the incremental cost-effectiveness ratio when all parameters are set at their base case values (listed in parentheses beside the parameter name). *For statin effects, “min” and “max” represent the weakest and strongest effects, respectively, based on the 95% confidence interval of the point estimates observed in JUPITER. For the duration of treatment effects, “min” represents the scenario in which the statin effects from the JUPITER trial were assumed to persist for 5 years only, whereas in the “max” scenario, full treatment effects were assumed to persist for 25 years and then taper off over the subsequent 10 years. **Sensitivity analyses values represent multiples of base case values. ***Utilities for patients with vascular and adverse events were calculated by multiplying utilities for the specific event with age-specific utilities for healthy individuals. For example, the utility of having an MI is equal to $0.85 \times 0.88 = 0.75$. QALY = quality-adjusted life year; other abbreviations as in Figure 1.

strategy would be \$20,962 per QALY. In JUPITER, a greater proportion of myocardial infarctions were fatal among patients treated with rosuvastatin as compared placebo; incorporating this differential fatality rate into our model resulted in an incremental cost-effectiveness ratio of \$31,559 per QALY. Restricting the hs-CRP test-and-treat strategy to patients with a Framingham risk score predicting a $\geq 10\%$ risk of myocardial infarction or coronary death over 10 years would lead to an incremental cost-effectiveness ratio of \$14,205 per QALY. The cost-effectiveness of restricting rosuvastatin to patients with Framingham risk scores of $< 10\%$ would be \$54,961 per QALY. If consuming rosuvastatin on a daily basis were associated with a utility of 0.98, a JUPITER-based strategy would have a cost-effectiveness of \$62,633 per QALY.

The results of 2-way sensitivity analyses are shown in Figure 4. If treatment efficacy were 50% of JUPITER estimates but was restricted to patients with a Framingham risk score $\geq 10\%$, it would have an incremental cost-effectiveness ratio of \$34,190 per QALY (Fig. 4A). If statin treatment were 50% as effective as observed in JUPITER but statin costs were \$1 per day, the test-and-treat strategy would be associated with an incremental cost-effectiveness of \$22,874 per QALY for all patients (Fig. 4C) and \$13,509

per QALY in patients with a Framingham risk score $\geq 10\%$ (Fig. 4D). At statin costs less than \$0.11 per day, the test-and-treat strategy would be cost-saving for intermediate-risk patients even if treatment were only 50% as effective as observed in JUPITER. If testing and treatment were restricted to patients with a Framingham risk score of $\geq 10\%$, and the daily cost of rosuvastatin were reduced to $< \$0.86$, this strategy would improve outcomes and would save money compared to usual care (Fig. 4B).

Figure 5 presents the results of our probabilistic sensitivity analysis. The mean cost-effectiveness from these simulations was \$27,575 per QALY with a 95% credible interval of \$10,400 to \$62,782 per QALY. Ninety-four percent of the probabilistic simulations produce cost-effectiveness ratios below a willingness to pay of \$50,000 per QALY, suggesting that at this threshold, there is a high likelihood that the intervention would be cost-effective.

Discussion

This analysis found that hs-CRP testing and rosuvastatin treatment for hs-CRP ≥ 2.0 mg/l in healthy individuals with LDL levels < 130 mg/dl is cost-effective compared with conventionally used thresholds of \$50,000 to \$100,000 per

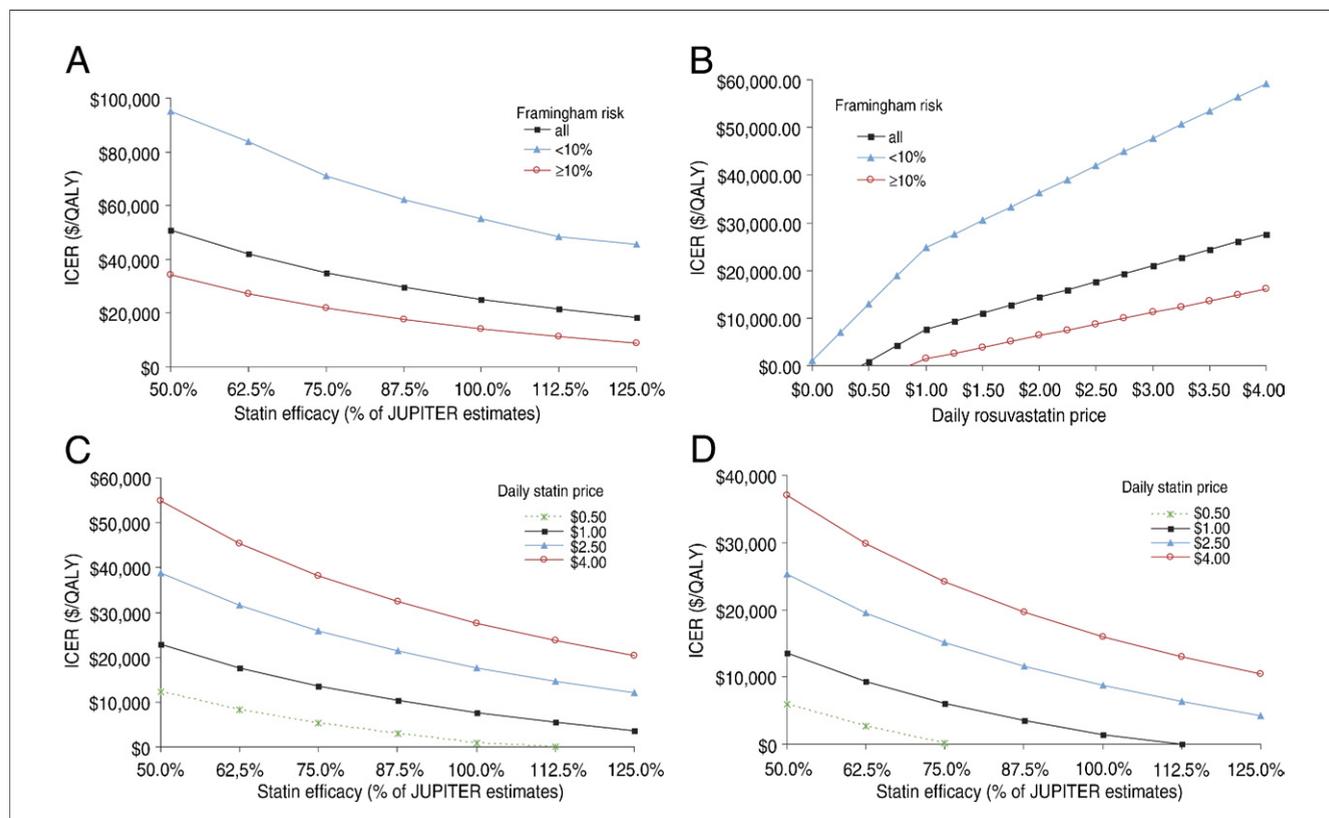


Figure 4 2-Way Sensitivity Analyses

Assessment of the impact of treatment efficacy and Framingham risk score (A), rosuvastatin cost and Framingham risk score (B), treatment efficacy and rosuvastatin price for all patients (C), and treatment efficacy and rosuvastatin price for patients with a Framingham risk score of $\geq 10\%$ (D). In the top right panel, the inflection point at \$1 is the result of the assumed fall in the price of rosuvastatin to this level when generics become available. ICER = incremental cost-effectiveness ratio; JUPITER = Justification for the Use of statins in Prevention: an Intervention Trial Evaluating Rosuvastatin; QALY = quality-adjusted life year.

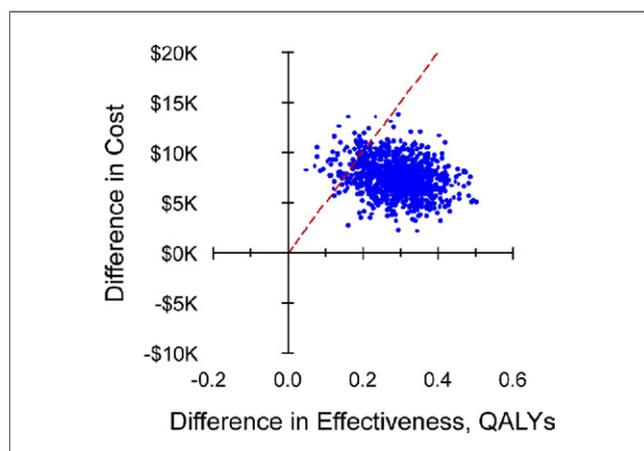


Figure 5 Probabilistic Sensitivity Analyses

The sensitivity ranges tested for each variable are shown in Table 1. Each point represents the incremental cost and incremental effectiveness of a test-and-treat strategy versus usual care for one simulation. The red dashed line depicts a societal willingness to pay threshold of \$50,000 per quality-adjusted life year (QALY).

QALY (17). This strategy compares favorably with the cost-effectiveness of fully implementing existing National Cholesterol Education Program (NCEP) lipid-lowering guidelines, which has been estimated at \$42,000 per QALY (14). Hs-CRP testing and rosuvastatin treatment, if indicated, appear most cost-effective for those with Framingham risk scores of $\geq 10\%$. This finding is consistent with recommendations from the Canadian Cardiovascular Society (18), the U.S. National Academy of Clinical Biochemistry (19), and the American Heart Association/Centers for Disease Control and Prevention (20), that a test-and-treat strategy be restricted to intermediate-risk patients. In contrast, the U.S. Preventive Service Task Force has recommended against a JUPITER-based strategy even in intermediate-risk patients, citing the absence of cost-effectiveness data and uncertainty about whether statin treatment based on hs-CRP testing provides incremental value beyond treatment based on Framingham risk assessment alone (21). Our results may help to clarify some of these uncertainties and inform the ongoing evolution of lipid-lowering treatment guidelines.

Our analysis used statin effect estimates from the JUPITER trial, which are higher than those seen in other statin trials (22). It has been argued that the JUPITER results overestimate true treatment effects because the trial was stopped early for efficacy (5). Others contend that clinical trials with principled monitoring plans yield valid estimates of treatment effects (23). Because of the uncertainty surrounding this influential model parameter, we repeated our analyses using more conservative assumptions of treatment effects and found incremental cost-effectiveness ratios that remain below typical willingness-to-pay thresholds.

Only 1 prior estimate of the cost-effectiveness of statin treatment for patients with elevated hs-CRP has been published (24). This analysis found cost-effectiveness ratios of

\$48,100 and \$94,400 per QALY for 58-year-old men and women, respectively, who were on average at lower baseline risks than the population we modeled. The study relied on statin treatment effects derived from post hoc analyses, which found smaller reductions in the risk of stroke from statins than was observed in JUPITER and did not consider other important pre-specified outcomes, such as venous thromboembolism or diabetes. Sensitivity analyses altering the model assumptions to be more similar to those that we used yielded results that are very consistent with ours.

As expected, rosuvastatin treatment for patients with an elevated hs-CRP level becomes more cost-effective as the price of rosuvastatin is lowered. If a JUPITER-based strategy were restricted to intermediate-risk patients, it dominates usual care (i.e., improves health outcomes and reduces overall spending) at rosuvastatin prices below \$0.86 per day. This price is similar to that of simvastatin and is more than those of pravastatin and lovastatin, which are both widely available in the U.S. for as little as \$10 for a 90-day supply (i.e., \$0.11 per day). Of course, the JUPITER trial specifically evaluated rosuvastatin, and the efficacy of other statins in this setting remains unclear. Lovastatin may reduce vascular events in patients with low LDL and elevated hs-CRP levels to a similar degree to those observed in JUPITER, but this observation was based on post hoc data (25). Even if other statins were less effective than rosuvastatin, our analysis suggests their use could still be cost-effective, if not cost-saving, because of their much lower cost. For example, if 1 of the generically available statins were only 75% as effective as rosuvastatin, its use as part of a test-and-treat strategy in patients with a Framingham risk score of $\geq 10\%$ would be cost-saving at a daily drug cost of \$0.49 per day. This finding is very consistent with cost-effectiveness estimates of generic simvastatin based upon results from the Heart Protection Study (26).

Study limitations. First, we did not evaluate the cost-effectiveness of treating all patients with below-target cholesterol levels. This practice is not recommended by current guidelines, and we sought to evaluate the next incremental step in cardiovascular risk reduction. Further, no randomized trial has prospectively assessed the value of statin treatment for patients with low LDL and low hs-CRP levels, and post hoc data suggest that these patients do not benefit from statin treatment (25). Accordingly, Blake et al. (24) found that treating all patients with normal LDL levels was associated with incremental cost-effectiveness ratios that were much less favorable than those we observed ($> \$100,000$ per QALY compared with usual care and $> \$500,000$ per QALY compared with a test-and-treat strategy).

Second, we relied on data from the JUPITER trial to build our model (2). This trial did not provide all of the necessary data to perform a cost-effectiveness analysis of a test-and-treat strategy from a societal perspective over a lifetime horizon. In addition to uncertainty surrounding the treatment effects observed in JUPITER, data on resource

utilization, health care costs, and utilities were not prospectively collected. It is reassuring that our results were robust to our modeling assumptions. Third, most patients in the U.S. receive pharmacy benefits through third-party insurers who negotiate substantial rebates from drug manufacturers. Because the magnitude of these discounts is not publicly disclosed, we relied on retail prices charged to individual consumers, which tend to be the highest prices paid for a given drug. This would lead to an underestimation of the cost-effectiveness of an hs-CRP test-and-treat strategy.

Conclusions

Our analysis demonstrates that a strategy of rosuvastatin treatment for apparently healthy patients with low LDL and elevated hs-CRP levels is cost-effective relative to typical willingness-to-pay thresholds. As expected, more conservative estimates of the treatment effects from the JUPITER trial lead to less attractive cost-effectiveness ratios, although even these appear to be relatively cost-effective. The value of this strategy appears greatest for patients with Framingham risk scores $\geq 10\%$, and thus our findings are consistent with several current practice guidelines. If the price of rosuvastatin were reduced to \$0.86, treatment of intermediate-risk individuals with elevated hs-CRP levels may not only be cost-effective, but also cost-saving.

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Key Words: cost-effectiveness ■ hs-CRP ■ statin.

APPENDIX

For an expanded Methods section and a supplemental table, please see the online version of this article.