The scientific record required to support the approval of a new molecular entity, or in Canada a new active substance, typically amounts to hundreds of thousands of pages of densely written scientific reports. In vitro studies explore the mechanism of action. The chemical stability, human metabolism, and consistent manufacture of a new molecule require careful evaluation. Beneficial effects, high doses, and long-term exposure are examined in animal models that may or may not predict effects in humans. Hundreds to thousands of patients are exposed in preapproval clinical testing. Although many new drugs are intended for long-term use, the international standard requires that only a few hundred patients be exposed to these drugs for 12 months or more. Regulatory agency reviewers are faced with a formidable mass of scientific data that contain only modest amounts of information from direct patient testing. Therefore, important clinical questions may remain unanswered. There are increasing demands by legislatures, industry, medical professionals, and patients to make these difficult decisions even more quickly in both Canada and the United States.

The current FDA “Expedited Drug Development Pathway” now includes provisions to reduce the number and size of clinical trials, to accept more limited evidence of efficacy, and to initiate drug review before the completion of testing. It also sets short review deadlines. In fiscal year 2011, a total of 16 of 35 new molecular entities (46%) received a priority review from the FDA, 13 (37%) received additional fast-track treatment, and 24 (69%) were approved in the United States earlier than in Europe or Canada.

Getting faster access to newly developed, less thoroughly tested drugs is at best a mixed blessing. For the first 3 years after approval, new drugs should carry a special warning akin to the black triangle used in Britain. It should be prominent and mean to every physician, “New Drug: Caution Indicated.”

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Results. Quality-of-Life Outcomes. The mean (SD) age of the study population was 60 (10.6) years, and 53% were female, 49% were Hispanic, and 19% were African American. At the 6-month follow-up, greater improvements in health utility were observed in the intervention group compared with the usual care group, although were not statistically significant (0.60 vs 0.56; P = .07).

Use of Ambulatory Care. Among patients randomized to receive enhanced depression care, 51% reported using antidepressants or anxiolytics compared with 30% of patients receiving usual care, with mean costs of $261 compared with $236 (adjusted difference, $18; P = .81) (Table). Use of mental health care was also more frequent in the intervention arm, with 75% visiting a mental health specialist at least once, compared with 35% in usual care arm (mean cost $585 vs $58; adjusted difference, $535; P < .001). The frequency of visits to cardiologists and primary care physicians was similar in the intervention and control groups, with 88% and 92% of patients reporting at least 1 cardiology appointment and 95% and 92% of patients reporting at least 1 primary care appointment, respectively. Mean total costs for ambulatory care in the intervention group were $1083 compared with $554 in the usual care group (adjusted difference, $536; P < .001).

Use of Hospital Care. The higher costs of mental health care and higher use of psychotropic medications in the intervention group were offset by savings in hospitalizations for major adverse cardiac events and heart failure. Overall, 5% of patients receiving enhanced depression care compared with 16% of patients receiving usual care were hospitalized for stable angina, unstable angina, ST-segment elevation or non–ST-segment elevation myocardial infarction, or heart failure. This difference in hospitalization rates resulted in a cost difference of −$1782 (95% CI, −$3163 to −$402; P = .01).

Cost-effectiveness. Mean total health care costs, including costs for psychotropic medications, ambulatory care, and hospitalizations, totaled $1857 for the enhanced depression care group and $2797 for the usual care group (adjusted difference, −$1229 per patient; 95% CI, −$2652 to $195; P = .09). Because the intervention was cost saving on average, no mean cost-effectiveness ratio exists. Bootstrap analysis demonstrated that if society is willing to pay $30,000 per quality-adjusted life-year gained by enhanced depression care, the probability that this treatment approach will be considered cost-effective is 98%.

Comment. To our knowledge, this analysis is the first economic evaluation of enhanced depression treatment in patients with ACS and persistent depressive symptoms. A growing body of evidence suggests that mental health problems complicate physical health conditions and that this relationship worsens clinical outcomes, increases hospitalizations, and adversely affects quality of life. Another recent study of patients with depression and poorly controlled diabetes mellitus or coronary heart disease found that a multicomponent treatment program, with particular emphasis on depressive symptoms, reduced health care costs. The findings from our study support this conclusion, while highlighting the need for larger studies with longer follow-up to examine the robustness and durability of these findings.

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after an acute coronary syndrome (ACS). In the COPES trial, patients with ACS were evaluated soon after their acute cardiac event with the Beck Depression Inventory (BDI), and individuals with a score of 10 or more were then reassessed 3 months later. Patients with persistent symptoms (BDI score of $\geq10$ at 3 months) were then randomized to usual care by the patients’ treating physicians or to 6 months of a patient preference-based, stepped-care intervention that offered problem-focused psychotherapy or antidepressant medication. The COPES trial reported that enhanced depression care improved patient satisfaction with treatment and reduced depressive symptoms compared with usual care. The report by Ladapo et al suggests that these promising results can be realized while simultaneously reducing health care costs.

Just 2 decades ago, very few patients with ACS were treated with psychotherapy or antidepressant drugs despite the common occurrence of depression in this setting. For example, in the landmark study by Frasure-Smith et al that first called attention to the association of depression and mortality after a myocardial infarction, only 3 of 222 patients (1%) were taking antidepressants at the time of enrollment into the study. Now, however, the train has left the station; a recent study suggests that more than 13% of patients with ACS in North America are prescribed antidepressants and that this rate of antidepressant prescription may be increasing. However, as this train cruises down the tracks at break-neck speed, another train is headed in the opposite direction. Rising health care costs have led medical specialty societies to recommend reducing unnecessary tests and procedures as part of the “Choosing Wisely” campaign. Indeed, this very journal has initiated the “Less Is More” series that highlights situations in which less care may result in better health. So the question is, which train is the COPES trial on?

The COPES intervention was associated with a striking reduction in hospitalization costs ($1782 per patient) that more than made up for ambulatory care expenses, calculated as the cost of ambulatory visits plus psychotropic medications ($536 per patient). The true cost of the ambulatory care in the COPES trial, however, is not just the cost of ambulatory visits plus psychotropic medications. It must include all the costs that would be required to implement the intervention in clinical practice. One cannot compare the cost of coq au vin and a glass of pinot noir at a local French restaurant to the same meal in Paris without including the cost of airfare and hotel. The cost of enhanced depression care is like the cost of the French meal; the real cost must include all other expenses for the trip to get us there. Enhanced care interventions, such as the COPES trial and the Improving Mood-Promoting Access to Collaborative Treatment (IMPACT) trial on which it was based, include systems for identification and assessment of patients, ongoing case management, and coordination of services. These costs would be core expenses in an actual care setting but do not appear to have been included in the economic evaluation of the COPES intervention.

On the other side of the equation, caution must be used in interpreting cost savings based on reduced hospitalizations, since the COPES trial was not powered to as-

**INVITED COMMENTARY**

**Coping With Rising Health Care Costs**

The Coronary Psychosocial Evaluation Studies (COPES) randomized controlled trial examined patient satisfaction with depression care (the primary outcome) and depressive symptom reduction, major adverse cardiac events that required hospitalization, and death (secondary outcomes) associated with treatment of depressed mood that persisted at least 3 months...