The primary goals of treatment for patients with stable (chronic) coronary artery disease (CAD) include the prevention of death and myocardial infarction (MI) and the relief of ischemic symptoms. In this regard, medical therapy and revascularization comprise complementary approaches. Despite the dissemination of evidence-based practice guidelines (1–3) and appropriate use criteria (4), there is widespread recognition that clinical decision-making varies considerably among physicians, practice groups, and health systems, particularly with respect to the threshold at which percutaneous coronary intervention (PCI) is undertaken. As an example, in an observational cohort study of 2004 Medicare beneficiaries, less than one-half (44.5%) underwent stress testing in the 90 days before elective PCI (5). There is equal concern that the intensity and scope of medical therapy are often not accorded the attention they deserve. The reasons for these discrepancies are sometimes embedded in the context of an individual patient’s clinical course and its dynamic change. Certainly, no one size fits all. Several lines of evidence, however, suggest that opportunities remain to narrow the gap between recommended and applied management strategies for patients with chronic CAD.

In the more than 2 years since publication of its main results, the COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) trial has been the subject of intense scrutiny and editorial comment (6–8). That there was no difference in the primary composite outcome (death from any cause and nonfatal MI) between patients assigned to an initial strategy of percutaneous coronary intervention with optimal medical therapy (PCI + OMT) and those assigned to OMT had been consistently observed in other, smaller trials of this nature (9). There were also no significant differences between groups for the secondary composite end point of death, MI, and stroke; for hospital stay for acute coronary syndrome; and for MI. However, nearly one-third of patients in the OMT group required revascularization for clinical indications over the course of follow-up, and patients who underwent PCI initially reported better angina-specific health status and quality of life over the first 6 to 24 months of the study, differences that were no longer apparent at 3 years (10). A small substudy of the COURAGE trial suggested that PCI might provide relatively greater reduction in ischemic burden (11), an observation that merits further study.

The observed event rates in the COURAGE trial were substantially lower than predicted, due in part to the excellent background therapy provided to the study participants. Interestingly, the major outcomes in the COURAGE trial were similar to those reported in the EuroHeart Survey for a subgroup of patients with stable angina and angiographically confirmed CAD (rate of death or nonfatal MI 3.9 per 100 patient-years) (12). Overestimation of clinical event rates in medically managed patients has been observed in recent post-MI and acute coronary syndrome trials (13,14). The implication is clear that the aggressive medical and lifestyle interventions employed in such trials are effective and safe for large numbers of patients across the CAD spectrum. Whether they can be implemented in routine clinical practice, outside the confines of a well-executed clinical trial, remains to be seen.

In this issue of the Journal, the COURAGE investigators describe in greater detail the components of the multimodality treatment program used for both the PCI and OMT groups, adherence rates observed over the course of the trial, and the targets achieved (15). It is self-evident that the remarkable results seen across multiple domains were in no small measure related to regularly scheduled nurse manager visits and the provision of most medications (including
statins, clopidogrel, beta-blockers, and either angiotensin-converting enzyme inhibitors or angiotensin receptor blockers) at no cost to the patient. The degree to which patient demographics (85% male, 86% white, 42% U.S. veterans) might have influenced the results is unclear. The adherence rates observed for the use of evidence-based medications for secondary prevention and ischemia management establish a new benchmark for patients with chronic CAD. Significant improvements were noted for smoking cessation, dietary composition, and physical activity levels, yet body mass index increased slightly, the hemoglobin A1c levels of patients with diabetes at baseline did not change, and 8% of patients developed diabetes over the course of the study.

The blood pressure and lipid levels achieved were exemplary, although 30% to 40% of patients did not meet the pre-specified targets of <130 mm Hg systolic blood pressure and <85 mg/dl for low-density lipoprotein cholesterol, respectively, despite the disciplined manner in which patients were managed. Lastly, there were no differences between the PCI and OMT groups in the intensity with which the interventions were applied, the (surrogate) end points achieved, or treatment satisfaction scores.

The COURAGE trial reinforces several important concepts. Treatment programs that incorporate multi-versus uni-modality interventions are more likely to improve adherence rates (16). Prior work has established a plausible relationship between adherence and outcomes for several cardiovascular conditions and in several clinical settings, including hypertension, chronic CAD, heart failure, discharge after MI, and after PCI (17–21). Nonadherence can relate to patient (age, race), condition (depression), treatment (complexity), health system (fragmentation), and socioeconomic (cost) factors, either singly or in combination (22). The COURAGE trial was designed to lessen or eliminate the impact of several of these factors. Case management or chronic care supervision coordinated by nurses, 1 of several mechanisms to reduce fragmentation and identify modifiable patient-specific conditions, has had a salutary effect on both adherence and outcomes in patients with heart failure, chronic CAD, or at high risk for incident CV events (23). Adherence to prescribed medications varies inversely with the cost borne by the patient. Reductions in pharmacy benefits have been shown to result in lower adherence rates. Choudry et al. (24) have shown in a simulated Markov model that providing Medicare beneficiaries with free medications at time of discharge after MI would improve survival and save money from a societal perspective.

With very rare exception, individual practice groups and health care systems are not currently structured or financed to deliver the intensity of longitudinal care provided to COURAGE trial enrollees (15,25). Several barriers will need to be addressed and overcome, ranging from workforce shortages to the low prevalence of integrated health information technology platforms, drug cost, complexity of treatment regimens, patient education/empowerment, disparities, cultural competence, and reimbursement. The current battles surrounding health care reform do not engender much optimism, despite the emphasis on prevention in some of the proposed legislation. It would be easy to dismiss the COURAGE trial results as being too impractical, expensive, or difficult to replicate in practice, were it not for the fact that this is precisely the direction in which multiple programs for quality and performance improvement have pointed. It is also relevant to underscore the recognition that approximately one-half of the recent decline in U.S. deaths from coronary heart disease might be attributable to reductions in major risk factors (26). Implementation will require policymakers to make difficult but informed choices about what can be done to improve the public health in ways that are both predictable and affordable from patient-centered and societal perspectives.

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