

Clinical and Economic Considerations of Coronary Heart Disease: A Managed Care Approach—Introduction

This Special Report supplement to *The American Journal of Managed Care* presents the latest findings on prevention and management of coronary heart disease (CHD), lipid-lowering therapy, and the pharmacoeconomics of lipid-lowering therapy in a managed care environment. Clinical

CHD is the leading cause of death among American men and women and the leading driver of healthcare costs. In 1996 alone, CHD cost an estimated \$90.6 billion. The future risk to managed care organizations will increase dramatically as Americans age and government shifts the healthcare burden to the private sector. Evidence-based medicine, whereby treatment decisions are based on proven clinical outcomes, is a cost-effective method of determining whom to treat, when to treat them, and which therapies to use.

presentations cover the scope of the CHD problem in the United States, mechanisms of acute coronary events, primary prevention, and secondary prevention. CHD is the leading cause of death among American men and women and the leading driver of healthcare costs. In 1996 alone, CHD cost an estimated \$90.6 billion. The future risk to managed care organizations will increase dramatically as Americans age and government shifts the healthcare burden to

the private sector. Evidence-based medicine, whereby treatment decisions are based on proven clinical outcomes, is a cost-effective method of determining whom to treat, when to treat them, and which therapies to use.

A paradigm shift has occurred in the mechanisms of acute coronary events, which are far more complex than once believed. Clinical trials over the last few decades have not supported the old paradigm—disease progression over years and decades resulting in coronary plaques that became flow-limiting and stenotic, often causing symptoms and acute coronary events. It is now known that 70% of all acute coronary events result from rupture of unstable plaques with less than 50% stenosis. Rupture causes occlusive thrombosis, and unstable plaques are not flow-limiting. Much remains to be learned about the mechanisms for reducing and preventing acute coronary events under this new paradigm.

Each year, 30% to 50% of the 1.5 million American men and women who have a myocardial infarction (MI) die as a result. Most of these MIs occur with no warning or previous symptoms, making a strong case for primary prevention. Identifying and treating people who are at high risk for CHD, but do not yet manifest symptoms, is the greatest challenge in the management of CHD. Many of those at risk have elevated cholesterol levels. The West of Scotland Coronary Prevention Study, a landmark trial in primary prevention, was the first study large enough (6596 participants) and long enough (5 years) to demonstrate

a relation between lowering low-density lipoprotein cholesterol (LDL-C) and reducing CHD events. Middle-aged men with moderately high lipid levels and no history of CHD who underwent pravastatin therapy demonstrated statistically significant reductions in risk for nonfatal MI or CHD death, first MI, and cardiovascular death. The study results have the potential to drive primary prevention. A post hoc analysis, the Pravastatin Event Reduction Analysis, examined the relations between baseline lipid levels and treatment efficacy, changes in LDL-C levels and reduction in CHD risk among patients taking pravastatin and whether LDL-C reduction alone explained the trial results. It was concluded that risk reduction with pravastatin is independent of baseline lipid phenotype; reduction in LDL-C was necessary for event reduction, but the benefit was maximized with about a 25% reduction; and that LDL-C reduction alone does not account entirely for the benefits of pravastatin therapy.

Sixty to seventy million Americans have some form of cardiovascular disease and are prime candidates for secondary prevention. Landmark clinical trials with the statins—the Scandinavian Simvastatin Survival Study, the Cholesterol and Recurrent Events Study, and the Long-term Intervention with Pravastatin in Ischaemic Disease Study—have consistently demonstrated that lowering LDL-C reduced the number of coronary events among patients with CHD. Most of these trials involved pravastatin, which has been proved to limit progression of atherosclerosis and reduce the number of secondary MIs, cardiovascular deaths, and coronary interventions. It also has been proved to be cost effective in the care of most patients with CHD and compared with other cardiovascular interventions. Despite the well-known relations between an increasing cholesterol level and increasing coronary events and the body of clinical trial evidence to support the link between reductions in cholesterol and reductions in clinical events, much work

remains to make secondary prevention routine in American healthcare.

The pharmacoeconomics presentations in this symposium address the debate over whether LDL-C reduction should be the outcome of choice in CHD. The biologic basis of and epidemiologic studies on lipoproteins and cardiovascular disease and a review of landmark lipid trials set the stage for the debate over the optimal level of LDL-C reduction necessary for maximum benefit. No definitive conclusions are reached. The methods and mindsets associated with pharmacoeconomics and the controversies surrounding this discipline are examined. Current pharmacoeconomics methods—cost effectiveness, cost minimization, cost benefit, and cost utility—are described and compared. Issues in pharmaco-

ACRONYM LIST

The following acronyms are used in this Special Report:

4S	Scandinavian Simvastatin Survival Study
CARE	Cholesterol and Recurrent Events
CHD	coronary heart disease
FATS	Regression of Coronary Artery Disease as a Result of Intensive Lipid-Lowering Therapy in Men with High Levels of Apolipoprotein B
HDL-C	high-density lipoprotein cholesterol
HMG	3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor
HMO	health maintenance organization
IDL-C	intermediate density lipoprotein
KAPS	Kyopio Atherosclerosis Prevention Study
LDL-C	low-density lipoprotein cholesterol
LIPID	Long-term Intervention with Pravastatin in Ischaemic Disease Study
MI	myocardial infarction
NCEP	National Cholesterol Education Program
PLAC I	Pravastatin Limitation of Atherosclerosis in the Coronary Arteries
PLAC II	Pravastatin, Lipids, and Atherosclerosis in the Coronary Arteries
REGRESS	Regression Growth Evaluation Statin Study
WOSCOPS	West of Scotland Coronary Prevention Study

economics to be resolved include developing appropriate methods for tracking illness, improving patient compliance, and improving external validity of studies and presentation of modeling results. The perspectives of the key participants in pharmacoeconomics—payers, providers, and patients—are provided.

The articles are based on presentations delivered at two conferences—Cardiovascular Event Reduction:

Defining the Role of HMG Therapy in Managed Care, hosted by Bristol-Myers Squibb, November 14-16, 1997, in Philadelphia; and Pharmacoeconomics & Outcomes Issues of Lipid Therapy, hosted by the International Society for Pharmacoeconomics and Outcomes Research (formerly known as the Association for Pharmacoeconomics and Outcomes Research), November 5-7, 1997 in Orlando, Florida.