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Managing to low-density lipoprotein particles compared with low-density lipoprotein cholesterol: A cost-effectiveness analysis

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BACKGROUND: Meta-analyses of clinical trials have shown that using statins to lower low-density lipoprotein cholesterol (LDL-C) reduces cardiovascular events, and more intensive lowering of LDL-C further decreases the risk of occlusive vascular events. Lipoprotein studies suggest treating patients more aggressively when low-density lipoprotein particle (LDL-P) number is discordantly high in the presence of normal LDL-C levels. Failure to manage LDL-P numbers may lead to additional direct and indirect costs.

OBJECTIVE: This analysis modeled direct and indirect costs associated with cardiovascular events due to suboptimal treatment resulting from discordance between LDL-C and LDL-P levels.

METHODS: The analysis was conducted from the payer perspective and the employer perspective, respectively, over a 3-year time period. Clinical data were obtained from the Multi-Ethnic Study of Atherosclerosis, a community-based population study. The employer perspective included indirect costs and quality-adjusted life years in addition to the direct costs and cardiovascular disease events considered in the payer analysis. All costs are reported in 2011 dollars.

RESULTS: From the payer perspective, managing LDL-C and LDL-P in comparison with LDL-C alone reduced costs ($21,212) and cardiovascular events (9 events). Similar patterns were observed for managing LDL-P alone in comparison with LDL-C. From the employer perspective, managing both LDL-P alone or in combination with LDL-C also resulted in lower costs, fewer cardiovascular disease events, and increased quality-adjusted life years in comparison with LDL-C.

CONCLUSION: This analysis indicates that the benefits of additional testing to optimally manage LDL-P levels outweigh the costs of more aggressive treatment. These favorable results depended on the cost of drug therapy.

Analyses of population risk led to the establishment of low-density lipoprotein cholesterol (LDL-C) goals, as defined in the National Cholesterol Education Program Adult Treatment Panel guidelines.[1] Meta-analyses of clinical trials have indicated that lowering LDL-C with statins

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reduces cardiovascular disease (CVD) in many patients[2,3] and that more intensive lowering of LDL-C further reduces the risk of occlusive vascular events.[4] However, even when LDL-C goals are met, more than one-half of patients continue to have CVD progression and clinical events,[5,6] particularly in patients with established coronary heart disease (CHD), low HDL-C, type 2 diabetes, and metabolic syndrome.[5] One large study of patients hospitalized for CVD events found that 56.5% of patients with CHD and 41.5% of patients without a prior history of CHD met the National Cholesterol Education Program LDL-C target of $<$100 mg/dL.[7]

LDL particles (LDL-Ps) contain a core of lipid, predominantly cholesterol, and some triglyceride, surrounded by a shell of phospholipids on which the major surface protein is apolipoprotein B (apoB). LDL-C measures the cholesterol content of the LDL-P. However, the LDL-C measure needs to take into account the dynamic relationship between the cholesterol and triglyceride content of LDL-Ps, which can vary widely and may change over time because of lifestyle changes and lipid-lowering therapy.[8]

LDL-P number was found to be a better discriminator of cardiovascular risk than LDL-C in several large epidemiologic studies, including EPIC-Norfolk,[9,10] Framingham Offspring,[11] Multi-Ethnic Study of Atherosclerosis (MESA),[12] Women's Health Initiative,[13,14] and the Veterans Affairs High-Density Lipoprotein Intervention Trial.[15] MESA examined concordant and discordant LDL-C and LDL-P levels as they relate to CVD events and reported that LDL-P number was a better predictor of CVD events in discordant patients.[12] Discordance between LDL-C and LDL-P levels may lead to either undertreatment or overtreatment with lipid-lowering pharmacotherapy. Patients with cholesterol-poor LDL-Ps who achieve recommended LDL-C goals may have correspondingly high LDL-P levels and therefore may remain undertreated.[12] Inefficient patient management may lead to additional costs from both direct health care costs and indirect costs related to lost labor productivity. However, lipid management of patients is becoming less costly because generic statins and other lipid-lowering therapies become more widespread.[16]

To assess the discordance between LDL-C and LDL-P, LDL-P level can either be measured by a blood test through nuclear magnetic resonance (NMR) spectroscopy[17] or through the LDL-P portion of the apoB measure. LDL-C is most commonly indirectly calculated with the Friedewald equation[17] derived from a lipid panel. Clinically, a discordantly high LDL-P measure is prevalent in patients with cardiometabolic risk such as diabetes and metabolic syndrome.[18]

A recent editorial examined the evidence for assessing the cardiovascular risk with the use of the apoB measure or the LDL-P level.[19] One of the limitations noted was the lack of economic evidence that examined the benefits of measuring LDL-P level compared with the additional costs.[19] The objectives of this study are to model direct and indirect costs associated with CVD events stemming from the common undertreatment scenario related to discordantly high LDL-P levels in the presence of normal LDL-C levels, to perform cost-effectiveness, and cost-utility analyses of managing LDL-C versus LDL-P, using data from published literature.

Methods

A decision-tree model was developed to assess the cost-effectiveness of the additional drug therapy and diagnostic testing required to assess and manage LDL-P levels to reduce CVD events and to improve the quality of life for discordant patients (Fig. 1). The model compares 2 alternative management cohorts, LDL-P number alone (group P) and LDL-C in combination with LDL-P number (group C&P) with the standard care of managing LDL-C alone (group C). All model inputs are described in Table 1 and discussed below.

The study incorporated sources from a "best evidence" literature review from peer-reviewed journals for model input values. The best evidence approach used for this study consisted of a literature search of English language articles from January 2000 to May 2012 indexed in PubMed. The inclusion criteria included studies that reported on LDL-P numbers, lipoproteins, testing for LDL-P numbers, and costs associated with cardiovascular events. The articles were ranked according to the impact factor of the journal, number of citations, and recentness of the article. A sensitivity analysis (described below) was performed to gauge the robustness of the results to alternative model input values.

Direct health care costs associated with patient management and complications from CVD events, as well as indirect job absenteeism costs associated with CVD events, were modeled, and the effect on quality-adjusted life years (QALYs) was also considered. Thus, the analysis was assessed from the following 2 separate perspectives: (1) a US payer (assessing direct health care costs and CVD events) and (2) a self-insuring employer (including indirect costs and QALYs in addition to direct costs and CVD events). Results for a 3-year time horizon are presented for both of these perspectives. A 3-year time horizon was chosen to be consistent with the third-party payer perspective, which is our primary analysis of interest. Payers tend to have a relatively short time horizon because of high turnover rates in their insured populations.

Treatment groups

The study computed net cost, incremental cost-effectiveness analyses (CEAs), and incremental cost-utility analyses (CUAs) from the payer and self-insured employer perspectives. Both perspectives compared management of LDL-C levels alone (standard of care) with management of LDL-P levels alone or in combination with LDL-C. The 3 treatment groups modeled in this analysis were based on the