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Economic Evaluation of Lipid-Lowering Therapy in the Secondary Prevention Setting in the Philippines

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ABSTRACT

Objective: To determine the cost-effectiveness of lipid-lowering therapy in the secondary prevention of cardiovascular events in the Philippines. **Methods:** A cost-utility analysis was performed by using Markov modeling in the secondary prevention setting. The models incorporated efficacy of lipid-lowering therapy demonstrated in randomized controlled trials and mortality rates obtained from local life tables. Average and incremental cost-effectiveness ratios were obtained for simvastatin, atorvastatin, pravastatin, and gemfibrozil. The costs of the following were included: medications, laboratory examinations, consultation and related expenses, and production losses. The costs were expressed in current or nominal prices as of the first quarter of 2010 (Philippine peso). Utility was expressed in quality-adjusted life-years gained. Sensitivity analyses were performed by using variations in the cost centers, discount rates, starting age, and differences in utility weights for stroke. **Results:** In the analysis using the lower-priced generic counterparts, therapy using 40 mg simvastatin daily was the most cost-effective option compared with the other therapies, while pravastatin 40 mg daily was the most cost-effective alternative if the higher-priced innovator drugs were used. In all sensitivity analyses, gemfibrozil was strongly dominated by the statins. **Conclusions:** In secondary prevention, simvastatin or pravastatin were the most cost-effective options compared with atorvastatin and gemfibrozil in the Philippines. Gemfibrozil was strongly dominated by the statins.

Keywords: cholesterol, cost-effectiveness, cost-utility, lipid-lowering therapy.

Introduction

In the Philippines, ischemic heart disease and cerebrovascular disease accounted for 10% and 5% of total deaths, respectively, in 2002 while in 2004, heart and vascular system diseases were the top two causes of mortality, accounting for 85.7 and 62.5 deaths per 100,000, respectively [1,2]. Moreover, in 2009, diseases of the heart and the cerebrovascular system were the top two causes of mortality, accounting for 21% (100,908) and 11.8% (56,670) of deaths, respectively [3]. In a global case-control study that included the Philippines, dyslipidemia and smoking were found to be the two most important risk factors for acute myocardial infarction [4]. Meanwhile, in the national nutrition and health surveys, the prevalence of hypercholesterolemia increased by twofold between 1998 and 2003 [5]. Unfortunately, this has further increased in the 2008 survey, which showed that 10% of Filipino adults have high total cholesterol levels while 14.6% have high triglyceride levels [6]. Thus, the problem of dyslipidemia needs to be addressed.

The cost of treating dyslipidemia represents an additional economic burden to a population in which four out of five live below the poverty line [4]. Also, the national government provision for health care delivery is limited. In contrast to the World Health Organization recommendation of 5% of the gross national product to be spent on health care, the national health care expenditure was 3.3% of the gross national product in 2006 [2]. Furthermore, health care is usually obtained through out-of-pocket payments as seen in 2006 when it represented 56% of the total health care expenditures [7].

Faced with the increasing problems of dyslipidemia as a cardiovascular disease risk factor, the country's limited health resources, variations in clinical practice, and the difficulty of adopting foreign clinical practice guidelines, the Philippine Heart Association together with the International Clinical Epidemiology Network developed and published in 2005 "The Clinical Practice Guidelines for the Management of Dyslipidemia in the Philippines" [4].

However, increasing awareness that effectiveness alone is not sufficient for decision making, whether in the individual patient setting or in the broader context of policymaking, a cost-effectiveness analysis (CEA) of the local guidelines was performed in 2008 [8]. This CEA reported the cost of preventing mortality and the cardiovascular events reported in the clinical trials expressed as cost-effectiveness ratios (CERs), either as average CERs or incremental CERs (ICERs). Several methods were used to determine the ICERs including Markov modeling, though in a limited manner.

Conflict of Interest: The authors have indicated that they have no conflicts of interest with regard to the content of this article.

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The promulgation and implementation of the Cheaper Medicine law and maximum drug retail prices of some of the essential medicines led to a decrease in the cost of lipid-lowering drugs by as much as 50%. Because the cost of medicines is a significant factor in the computation of ICERs of pharmacologic options, a drastic change in the cost of drugs would result in a significant change in the ICERs for secondary prevention.

In view of these issues, this study was undertaken with the following objectives: General Objective: To determine the cost-effectiveness of the lipid-lowering therapy in the secondary prevention setting in the Philippines using the societal perspective. The specific objectives were to determine 1) the average and incremental cost-effectiveness ratios of the lipid-lowering therapy in the secondary prevention setting and 2) the most cost-effective option among the lipid-lowering therapies in the secondary prevention level.

This economic analysis chose the societal perspective because it reflects a broader evaluation of both costs and effects (health and nonhealth aspects) of an intervention or program.

Methods

Effectiveness data were obtained from randomized controlled trials in the secondary prevention setting. The trials that were appraised by the technical research committee of the local guideline developers were considered. This appraisal included issues on the applicability of foreign studies to the local setting by utilizing the International Clinical Epidemiology Network Guideline Development Cycle, otherwise known as the Knowledge Management Plus [4]. Knowledge Management Plus incorporated included questions on "equity lens," that is, those involving access to a particular health care intervention [4].

However, the trials must include the following end points: nonfatal myocardial infarctions, death due to coronary heart disease, stroke, and revascularization. Based on these criteria, the following were chosen to be the basis for this economic analysis: 1) MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomized placebo-controlled trial [9]; 2) Treatment with atorvastatin to the National Cholesterol Education Program goal versus usual care in secondary heart disease prevention: the GREek Atorvastatin and Coronary-heart-disease Evaluation (GREACE) study [10]; 3) Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels (the Long-term Intervention with Pravastatin in Ischaemic Disease (LIPID) study [11]); and 4) The Veterans Affairs High-density lipoprotein cholesterol Intervention Trial (VA-HIT) study [12]: Gemfibrozil for the secondary prevention of coronary heart disease in men with low levels of cholesterol.

Description of Competing Alternatives

Using the above-mentioned trials, the pharmacologic options analyzed in this article were comparisons of any of the following pharmacologic maneuvers versus placebo:

1. Simvastatin 40 mg/d
2. Pravastatin 40 mg/d
3. Atorvastatin 20 mg/d
4. Gemfibrozil 1200 mg/d

Daily doses of 10, 20, 40, and 80 mg were used in the GREACE study [9]; however, the 20 mg daily dose was chosen because 85% of the study population received this dose.

Identification, Measurement, and Valuation of costs

The classification of cost recommended by Drummond et al. [13] into four types was utilized in this study and is described below.

Table 1 – Summary of the societal costs for the diagnosis and treatment of dyslipidemia.

Costs identified	Measurement of cost per patient	Valuation of costs
1. Health care resources consumed - Costs of treating adverse events	Cost per single adverse event multiplied by the number of adverse events	Depends on the adverse effect identified (no significant ones identified)
2. Cost of patient/patient's family resources		
a. Cost of medicines	Unit price of specific lipid-lowering agent multiplied by days in a year (365)*	Prices obtained from the biggest drugstore in the country
b. Laboratory costs	Unit price (charge) multiplied by the frequency of screening tests in a year	Unit price/charge from laboratories range; minimum–maximum
c. Doctor's fees	Outpatient fees multiplied by the number of visits in a year	Outpatient consultations fees (50%–100%); minimum–maximum fees
d. Travel costs	P100–P400 per visit × the number of visits in a year	Transportation charges by laboratory doing home visits
3. Production losses		
a. Labor productivity	$^1/_2$ d/visit multiplied by the number of visits in a year	GDP/average number of employed persons
b. Cost of leisure time	Same time spent as above (for those who will not use work time in doing outpatient consultations)	Overtime wage rate (150% of minimum daily wage in the national capital region)
4. Cost due to the consumption of other resources/sectors - lifestyle modification maneuvers education programs	Number of consultations for lifestyle modification maneuvers	Cost of consultation = 0 (already part in the outpatient consultation – doctor's fees)
- time spent on exercise	Number of hours spent	0 (leisure time not given a cost or value)

GDP, gross domestic product.
* Unit cost of medicine × number used/day × 365 (dose is 1 tablet/d; thus, unit cost × 365).