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

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A B S T R A C T

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.

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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 35.7 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>
<thead>
<tr>
<th>Costs identified</th>
<th>Measurement of cost per patient</th>
<th>Valuation of costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Health care resources consumed</td>
<td>Cost per single adverse event multiplied by the number of adverse events</td>
<td>Depends on the adverse effect identified (no significant ones identified)</td>
</tr>
<tr>
<td>a. Costs of treating adverse events</td>
<td>Unit price of specific lipid-lowering agent multiplied by days in a year (365)</td>
<td>Prices obtained from the biggest drugstore in the country</td>
</tr>
<tr>
<td>b. Laboratory costs</td>
<td>Unit price (charge) multiplied by the frequency of screening tests in a year</td>
<td>Unit price/charge from laboratories range; minimum–maximum</td>
</tr>
<tr>
<td>c. Doctor’s fees</td>
<td>Outpatient fees multiplied by the number of visits in a year</td>
<td>Outpatient consultations fees (50%–100%); minimum–maximum fees</td>
</tr>
<tr>
<td>d. Travel costs</td>
<td>P100–P400 per visit × the number of visits in a year</td>
<td>Transportation charges by laboratory doing home visits</td>
</tr>
<tr>
<td>2. Cost of patient/patient’s family resources</td>
<td>1/2 d/visit multiplied by the number of visits in a year</td>
<td>GDP/average number of employed persons</td>
</tr>
<tr>
<td>a. Labor productivity</td>
<td>Same time spent as above (for those who will not use work time in doing outpatient consultations)</td>
<td>Overtime wage rate (150% of minimum daily wage in the national capital region)</td>
</tr>
<tr>
<td>b. Cost of leisure time</td>
<td></td>
<td>Cost of consultation = 0 (already part in the outpatient consultation – doctor's fees)</td>
</tr>
<tr>
<td>4. Cost due to the consumption of other resources/sectors</td>
<td>Number of consultations for lifestyle modification maneuvers</td>
<td></td>
</tr>
<tr>
<td>a. Lifestyle modification maneuvers education programs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- time spent on exercise</td>
<td>Number of hours spent</td>
<td>0 (leisure time not given a cost or value)</td>
</tr>
</tbody>
</table>

GDP, gross domestic product.

* Unit cost of medicine × number used/day × 365 (dose is 1 tablet/d; thus, unit cost × 365).
A summary is given in Table 1. The costs were expressed in Philippine peso using current prices as of the first quarter of 2010.

**Health care resources consumed**

This refers to the costs of setting up and running the program (variable and fixed or overhead costs), as well as the possible adverse events attributable to the program. In this article, however, this type of cost was not included because there is no need to create a dedicated facility for the screening and management of dyslipidemia. Patients’ consultations were done in existing outpatient clinics. Moreover, laboratory examinations for screening and monitoring of lipid levels and transaminases do not require setting up additional laboratory facilities. Furthermore, costs for clinic visits and laboratory examinations were included in out-of-pocket payments because the burden of these costs was on patients or their families. However, the costs of consultation for the lifestyle modification maneuvers were included in the fourth or last category of cost.

The costs of treating possible adverse effects were not included because no significant adverse events were reported for simvastatin, atorvastatin, pravastatin, and gemfibrozil.

**Cost of patient/patient’s family resources**

This refers to out-of-pocket payments incurred by the patient(s) and his family as well as value of resources allotted to the treatment process. Out-of-pocket payments included cost of medicines, laboratory examinations, doctor’s fees, and transportation costs of going to and from the doctor’s clinics. Some studies recommended using international prices of medicines, while others used the wholesale acquisition costs [14,15]. In contrast, this study used the prices obtained from the biggest drugstore chain in the country (with branches nationwide, controls 80% of the retail market, and claims uniform pricing scheme) [16]. Prices instead of cost of medicines were used because they represented the real costs borne through out-of-pocket payments. In instances in which a particular medicine was not available in this drugstore chain, the price was obtained from another store whose drug prices were almost similar to those of the biggest drugstore chain.

In view of the availability of lower-priced generic medicines, a list of the prices of similar generic medications from the above drug store chain was obtained. The lowest-priced drugs were used in the base-case analysis, while those of the innovator drug store chain was obtained. The lowest-priced drugs were used in the base-case analysis, while those of the biggest drugstore chain. However, because they represented the real costs borne through out-of-pocket payments, these were not included because there is no need to create a dedicated facility for the screening and management of dyslipidemia. The lowest-priced drugs were used in the sensitivity analysis.

**Production losses**

The value of production losses had been referred to as “wealth lost to society due to disease” [17]. However, the term “productivity cost” was recommended by the US Panel on Cost-Effectiveness in Health and Medicine, which refers to “the costs associated with lost or impaired ability to work or to engage in leisure activities due to morbidity and lost economic productivity due to death” [18].

Valuation of productivity cost or production losses varies. These issues are discussed lengthily in the CEA of the local guidelines [7]. Productivity cost or labor productivity is defined by the Organization for Economic Cooperation and Development (and adopted by the Department of Labor and Employment of the Philippines) as “the ratio of a volume measure of output to a volume measure of input” [19]. Thus, labor productivity was computed by dividing the gross domestic product by the number of employed persons (average of four survey rounds of the Labor Force).
either cost of labor productivity or cost of leisure time. Half a day’s work was used whether the basis of computation was examinations was estimated to be about 4 hours. Hence, wage for Philippines in 2008 was used in this study [20].

The time spent for outpatient consultation and laboratory examinations was estimated to be about 4 hours. Hence, wage for half a day’s work was used whether the basis of computation was either cost of labor productivity or cost of leisure time.

Cost due to consumption of other resources/sectors

This last category includes the cost of educating the patients with regard to lifestyle modifications and the cost of time spent on physical exercises. Some may argue that activities such as biking and the like are not only for exercise purposes but are pleasurable ways of spending “quality” time with family members or friends as well; hence, the monetary cost for “exercise time” was not determined. However, lifestyle modification maneuvers can be pursued through individual consultations or education campaigns. Advice on lifestyle modification maneuvers can be incorporated during physician visits without additional cost unless the patients are referred to nutritionists or dieticians. In addition, some education programs are carried out by government and nongovernment organizations on certain occasions. Participants, however, in such programs are not exclusive to the secondary prevention setting. In view of these, no cost for the fourth category was included in the base-case analysis.

Consequences/Outcomes Measured

The clinical end points required for inclusion in this article were nonfatal myocardial infarctions, death due to coronary heart disease, stroke, and revascularization. Utilities or health gains in the above outcomes were measured in a metric known as quality-adjusted life-years (QALYs), which were obtained from previous studies [21,22]. The values ranged from zero (0) to one (1), with 0 equating to death and 1 to full health [12].

Fig. 1 – Cost-effectiveness analysis (Table 2).

**Use of Markov Models for the Secondary Prevention Setting**

“A decision model is usually developed to assist decision-makers in making choices relating to the evaluated options. Typically, the objective of a decision model is to obtain a clearer understanding of the relationships between incremental costs and their consequences” [23]. Moreover, modeling is an “explicit, quantitative, prescriptive approach to medical decision-making and allows both clinical and economic consequences of medical actions and attitudes to be analyzed under conditions of uncertainty” [24]. Although modeling is not easy, “economists often build models that make simplifying assumptions to make the problem tractable, but hopefully capture sufficient detail to provide reasonably valid predictions of future events” [25].

In this study, the Markov models incorporated effectiveness data obtained from randomized controlled trials of the four lipid-lowering therapy with estimates of QALY weights and mortality rates in the local setting (life tables) [26]. Finally, modeling was accomplished through the use of the TreeAge software [27].

**Discount Rates**

The World Health Organization Guide for CEA recommends a discount rate of 3% for both costs and effects (or outcomes) in the base-case analysis and 6% for costs and 0% for effects in the sensitivity analysis [14]. However, other economists recommend using 3% and 5% in the base-case analysis and include 0%, 3%, and 5% in the sensitivity analysis (for both costs and effects) [12]. In this article, 3% and 6% were used in the base-case and sensitivity analyses for both costs and effects.

**Results**

**Base-Case Analysis**

The base-case analysis included the following assumptions: 1) lowest range of costs, 2) 6% discount rate for costs and effects, and 3) 35 years as starting age. Moreover, the utility weight for moderate stroke (0.68) [22] was used, and when data for fatal stroke were lacking, it was assumed to be 20% (fatal strokes were reported

| Table 4 – Average and incremental cost-effective ratios of lipid-lowering therapy (base-case analysis; 3% discount rate). |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| **Strategy**    | **Cost**        | **Incremental cost** | **Effect** | **Incremental effect** | **Average CERs** | **ICERs** |
| Simvastatin     | Php 135K       | Php 15K          | 6.02 QALY  | −1.27 QALY           | 22,508/QALY      | Dominated    |
| Gemfibrozil     | Php 150K       | Php 18K          | 4.75 QALY  | −0.30 QALY           | 31,633/QALY      | Dominated    |
| Pravastatin     | Php 154K       | Php 28K          | 5.72 QALY  | 0.12 QALY            | 26,182/QALY      | Dominated    |
| Atorvastatin    | Php 164K       | Php 15K          | 4.28 QALY  | 0.23 QALY            | 26,182/QALY      | 122,990/QALY |

CERs, cost-effectiveness ratios; ICERs, incremental cost-effectiveness ratios; QALY, quality-adjusted life-year.
to be about 20% of all strokes in one of the trials [8]. Unfortunately, there is no country-specific data for fatal strokes in the Philippines (data obtained through personal communication with a neurologist revealed that in a study conducted in a tertiary government hospital on noncardioembolic ischemic strokes, mortality after first stroke and second stroke was 11% and 18%, respectively).

The corresponding CERs (average) and ICERs are seen in Tables 2 and 3. The comparator for the CERs is the specific drug versus placebo, while for the ICERs, the pharmacologic options were compared as to their incremental cost and QALYs. This analysis showed that simvastatin was the most cost-effective option and that it dominated the option of using pravastatin because the latter cost more and had less QALYs. In addition, gemfibrozil was dominated by atorvastatin. However, if atorvastatin would be used instead of simvastatin, the incremental cost would be Php 121,654 for every QALY gained.

The cost-effectiveness frontier (Fig. 1) links the ICERs of the different options. Gemfibrozil and pravastatin are easily seen as the dominated options because they lie above and to the left (northwest) of the other options (simvastatin and atorvastatin). The slope of the line connecting simvastatin and atorvastatin represents the ICER of choosing atorvastatin over simvastatin (Php 121,654 for every QALY gained).

### Sensitivity Analysis

Sensitivity analyses could be one-way or multiway. One-way sensitivity analysis means that one variable was changed during the analysis, while multiway analysis refers to changing more than one at a time.

One-way sensitivity analysis using different utility weights for stroke (minor to severe) resulted in similar CERs and ICERs at the same discount rate of 6%.

The results using 3% discount rate are shown in Tables 4 and 5. This analysis showed that both gemfibrozil and pravastatin were dominated by simvastatin. Moreover, the incremental cost of choosing atorvastatin over simvastatin would be Php 122,990 for every additional QALY gained. As expected, as compared with the base-case analysis, changing the discount rate resulted in a significant change in the average CERs, but not the ICERs. Tables 6 and 7 show the results when the highest value in the range of costs for all cost centers and 6% discount rate were used. If the cost of medicines was the only variable that was changed, that is, the lowest value was maintained for the other cost centers, and the discount rate at 6%, the magnitude of the change in CERs and ICERS was large. This proved that the cost of medicines was a key determining factor for the CERs and ICERS.
It can be seen that with changing the cost of the medicine alone or of all the cost items, the most cost-effective option shifted from simvastatin to pravastatin. Moreover, both simvastatin and gemfibrozil were dominated by atorvastatin. However, choosing atorvastatin over pravastatin would entail an incremental cost of Php 66,757 (Tables 6 and 7) or Php 57,142 (Tables 8 and 9) for every QALY gained.

The last sensitivity analysis generated involved changing the initial age of the population, that is, from 35 years to 45 years, when it entered the model. This starting age was chosen because it is generally accepted that the majority of patients in the secondary prevention setting are older compared with those in the primary prevention setting. This analysis resulted in Tables 10 and 11, in which all the assumptions for the base-case analysis were used except for using 45 years as the entry age in the model. The resulting most cost-effective option was the same as in the base-case analysis, that is, simvastatin. In addition, the incremental cost for every QALY gained if atorvastatin would be used instead of simvastatin was Php 130,389.

However, using the same starting age of 45 years, but using 3% discount rate and the higher cost in all the cost centers (same assumptions for the rest of the variables), the most cost-effective option had again shifted to pravastatin. Simvastatin and gemfibrozil, however, were dominated by atorvastatin, but if atorvastatin would be used instead of pravastatin, the incremental cost for every QALY gained was Php 64,612. These CERs and ICERs and the dominated options are shown in Tables 12 and 13 and Fig. 2.

**Discussion**

The results of this cost-utility analysis showed that simvastatin or pravastatin was the most cost-effective options compared with atorvastatin and gemfibrozil. Atorvastatin, however, was not dominated by either of the two, and if one would decide to use atorvastatin over simvastatin or pravastatin, the ICER was about Php 65,000 to Php 130,000.

Having obtained the above results, the most important consideration is how they will affect decisions in the management of dyslipidemia as clinicians, patients, or health policy makers. However, before a decision is made, a threshold value (threshold or ceiling ratio or willingness-to-pay) must be set. This value corresponds to “shadow price per unit effectiveness in the absence of a market” [28]. This means that if an ICER of Php 100,000 is set as the threshold ratio, therapies or options with values higher than this threshold are not considered cost-effective.

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**Table 9 – CERs and ICERs (without dominated options).**

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Cost</th>
<th>Incremental cost</th>
<th>Effect</th>
<th>Incremental effect</th>
<th>Average CERs</th>
<th>ICERs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pravastatin</td>
<td>Php 96K</td>
<td></td>
<td>5.10 QALY</td>
<td></td>
<td>18,836/QALY</td>
<td></td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>Php 121K</td>
<td>Php 25K</td>
<td>5.53 QALY</td>
<td>0.44 QALY</td>
<td>21,870/QALY</td>
<td>57,142/QALY</td>
</tr>
</tbody>
</table>

CERs, cost-effectiveness ratios; ICERs, incremental cost-effectiveness ratios; QALY, quality-adjusted life-year.

**Table 10 – Average and incremental cost-effective ratios of lipid-lowering therapy (sensitivity analysis, starting age = 45 y, 6% discount rate).**

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Cost</th>
<th>Incremental cost</th>
<th>Effect</th>
<th>Incremental effect</th>
<th>Average CERs</th>
<th>ICERs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simvastatin</td>
<td>Php 119K</td>
<td></td>
<td>5.27 QALY</td>
<td></td>
<td>22,508/QALY</td>
<td></td>
</tr>
<tr>
<td>Gemfibrozil</td>
<td>Php 134K</td>
<td>Php 15K</td>
<td>4.23 QALY</td>
<td>−1.04 QALY</td>
<td>31,633/QALY</td>
<td>Dominated</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>Php 135K</td>
<td>Php 17K</td>
<td>5.03 QALY</td>
<td>−0.24 QALY</td>
<td>26,893/QALY</td>
<td>Dominated</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>Php 143K</td>
<td>Php 24K</td>
<td>5.46 QALY</td>
<td>0.19 QALY</td>
<td>26,182/QALY</td>
<td>130,389/QALY</td>
</tr>
</tbody>
</table>

CERs, cost-effectiveness ratios; ICERs, incremental cost-effectiveness ratios; QALY, quality-adjusted life-year.

**Table 11 – CERs and ICERs (without dominated options).**

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Cost</th>
<th>Incremental cost</th>
<th>Effect</th>
<th>Incremental effect</th>
<th>Average CERs</th>
<th>ICERs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simvastatin</td>
<td>Php 119K</td>
<td></td>
<td>5.27 QALY</td>
<td></td>
<td>22,508/QALY</td>
<td></td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>Php 134K</td>
<td>Php 15K</td>
<td>5.46 QALY</td>
<td>0.19 QALY</td>
<td>26,182/QALY</td>
<td>130,389/QALY</td>
</tr>
</tbody>
</table>

CERs, cost-effectiveness ratios; ICERs, incremental cost-effectiveness ratios; QALY, quality-adjusted life-year.

**Table 12 – Average and incremental cost-effective ratios of lipid-lowering therapy (sensitivity analysis, starting age = 45 y, highest cost in all, 3% discount rate).**

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Cost</th>
<th>Incremental cost</th>
<th>Effect</th>
<th>Incremental effect</th>
<th>Average CERs</th>
<th>ICERs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pravastatin</td>
<td>Php 160K</td>
<td></td>
<td>5.64 QALY</td>
<td></td>
<td>28,452/QALY</td>
<td></td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>Php 194K</td>
<td>Php 33K</td>
<td>6.15 QALY</td>
<td>0.52 QALY</td>
<td>31,485/QALY</td>
<td>64,612/QALY</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>Php 201K</td>
<td>Php 7K</td>
<td>5.93 QALY</td>
<td>−0.22 QALY</td>
<td>33,903/QALY</td>
<td></td>
</tr>
<tr>
<td>Gemfibrozil</td>
<td>Php 468K</td>
<td>Php 274K</td>
<td>5.06 QALY</td>
<td>−1.47 QALY</td>
<td>99,793/QALY</td>
<td></td>
</tr>
</tbody>
</table>

CERs, cost-effectiveness ratios; ICERs, incremental cost-effectiveness ratios; QALY, quality-adjusted life-year.
ICERs below or equal to this value are considered cost-effective, and thus should be undertaken. In contrast, options with ICERs greater than the ceiling ratio are considered not cost-effective and should not be adopted. In many Western countries in which health care delivery is usually through a third-party payor, threshold ICERs influence health policy decisions [29–32] and vary from country to country. In the Philippines, however, no explicit ceiling ratio exists. Thus, faced with the above ICER of atorvastatin, divergent views are expected, especially in a setting in which health care provision is largely dependent on out-of-pocket payments.

However, economists do not agree on setting threshold values. Some countered that because this ratio could be influenced by societies or one’s ability to pay, it may further promote health inequity. To help resolve this issue, the WHO Commission on Macroeconomics and Health recommended using a country’s gross domestic product per head as the basis for the following classification: very cost-effective, cost-effective and not cost-effective [33].

It should be noted that the cost of pravastatin remained the same due to the availability of a single brand (the generic counterpart) at the time of the study, leading to almost similar CERs in the base-case and sensitivity analyses for pravastatin. Compared with the cost of the innovator drug that was used in the previous local economic evaluation for dyslipidemia [7], the nominal cost of pravastatin (first quarter of 2010) was just about 11% of the cost of the innovator drug. In view of this tremendous drop in the cost of medicine, the corresponding CERs for pravastatin significantly decreased; hence, pravastatin was the most cost-effective option in the sensitivity analysis. This is in contrast to the previous study in which simvastatin remained the most cost-effective option in all the analyses among the lipid-lowering therapies included [7]. The exact CERs of the previous study, however, cannot be compared with the CERs of the present analysis because of the difference in the type of economic evaluation that was conducted. In the previous study, a cost-consequence analysis was done to come up with a multidimensional outcome required for the CEA. However, a cost-utility analysis was performed for the present study.

Economic evaluation studies performed in several developed countries using the same secondary prevention setting showed different CERs and ICERs [34–37]. These variations are expected and may be attributed to 1) difference in the identification, measurement, and valuation of costs from country to country and 2) changes in disease prevalence leading to differences in the magnitude of effects of the intervention. Inevitably, this would lead to different CERs and ICERs in different settings. Moreover, if a threshold ratio is adopted by some countries, imposing the same threshold value in a developing country setting such as the Philippines will not be realistic.

**Conclusions**

This study showed that among the four included options of lipid-lowering therapy in the secondary prevention level, simvastatin was the most cost-effective option if the cost of the lower-priced generic counterpart was used in the analysis. However, if the cost of the higher-priced innovator drugs was used except for pravastatin (of which there was just one brand available then), it was found that pravastatin was the most cost-effective therapy. The incremental cost of using atorvastatin either over simvastatin or over pravastatin ranged from about Php 65,000 to Php 130,000 for every QALY gained (base-case analysis and sensitivity analysis). The choice of any of these three statins would be influenced by a threshold ratio or one’s willingness to pay and one’s ability to pay.

In all analyses, gemfibrozil was strongly dominated by the statins, being more costly and less effective.

There were several limitations recognized in this article. First, the analysis was limited to the four lipid-lowering therapies and the corresponding trials that serve as the basis for the economic evaluations. Other lipid-lowering therapies that were considered for inclusion in the analysis were rosuvastatin, ezetimibe, and nicotinic acid. However, they were not included in the analysis because of the lack of the required end points at the time of the study. Moreover, the above trials were conducted in the Western population; thus, applicability to the local setting may be problematic. Although local data were used whenever possible, for example, life tables, the existing life table is for the general population; none exist for those in the secondary prevention setting. The article was also constrained by the presence of many generic counterparts and the possibility of differences in bioavailability and bioequivalence. The article tried to limit the generic counterparts to those available in the drugstore chain, which was discussed in the Methods section.

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**REFERENCES**


