Available online at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: www.elsevier.com/locate/vhri

Generalized Cost-Effectiveness Analysis of Pharmaceutical Interventions for Primary Prevention of Cardiovascular Disease in Thailand

Panrasri Khonputsa, PhD[1,2,3,], Lennert J. Veerman, MD, PhD[3], Melanie Bertram, PhD[1,3], Stephen S. Lim, PhD[1,4], Nathorn Chaiyakunnaphruk, PhD[1,3,5,6], Theo Vos, PhD[1,3]*

[1]*The Setting Priorities using Information on Cost-Effectiveness Project, Ministry of Public Health, Mueang, Nontaburi, Thailand;* [2]*The Department of Pharmacy, Maharat Nakhonratchasima Hospital, Mueang, Nakhonratchasima, Thailand;* [3]*The University of Queensland, School of Population Health, Brisbane, Australia;* [4]*Institute for Health Metrics and Evaluation, University of Washington, Seattle, WA, USA;* [5]*Faculty of Pharmaceutical Sciences, Center for Pharmaceutical Outcomes Research, Naresuan University, Phitsanuloke, Thailand;* [6]*School of Pharmacy, University of Wisconsin-Madison, Madison, WI, USA*

A B S T R A C T

Objectives: To assess the cost-effectiveness of blood pressure (BP)-lowering and cholesterol-lowering drugs for cardiovascular disease (CVD) prevention. **Methods:** We constructed a Markov model in which the Thai population was classified by 10-year absolute CVD risk and modeled the use of BP- and cholesterol-lowering drugs, including a "polypill" (three BP-lowering drugs and a statin). We applied "do-nothing" as the comparator, a health sector perspective on lifetime cost-effectiveness, 3% discounting of costs and effects, and used probabilistic sensitivity analysis. Outcomes are expressed as average and incremental cost-effectiveness in Thai baht per disability-adjusted life-year averted. **Results:** The polypill would be a very cost-effective option for CVD prevention even in people at modest risk (10-year risk of 5%–9.9%). Use of the three most cost-effective BP drugs is also associated with a net cost saving and large health gain at risk levels greater than 5%. Adding a generic statin gives a price per disability-adjusted life-year of 0.5 (10-year risk at 20%+) to 1.5 (10-year risk at 5%–9.9%) times Thai per-capita gross domestic product using lowest available annual costs. However, at current average drug prices, adding a statin would be considered cost-effective only for those with a 10-year absolute CVD risk of 20% and more. **Conclusions:** Primary CVD prevention with the polypill or a combination of three generic BP-lowering drugs is very cost-effective in the Thai population.

Keywords: blood pressure–lowering drugs, cardiovascular disease, cholesterol-lowering drugs, cost-effectiveness, Thailand.

Introduction

Cardiovascular diseases (CVDs) are among the leading causes of health loss worldwide [1] and in Thailand [2,3]. CVD results in high case-fatality rates during the first few days following an event [4,5], an ongoing increased risk of death [6,7] among those who survive the initial event, and a high cost of treatment [8]. Exposure to important CVD risk factors such as raised blood pressure (BP) and cholesterol, tobacco use, and diabetes mellitus is rising in Thailand [9]. These factors are related to changes in lifestyle, including an increase in sedentary behavior and a change in diet. As observed in many Western countries, preventive action can reduce the incidence and premature mortality due to CVD [10,11].

BP- and cholesterol-lowering drugs have been proven to be effective in preventing ischemic heart disease (IHD) and stroke [12,13]. Given limited health care resources, Thailand's health policy needs to be based not only on effectiveness but also on associated costs to determine which intervention(s) should be publicly funded and what population should be targeted. Identifying population subgroup(s) that should be targeted with interventions can be based on estimates of future risks of CVD. Recent guidelines have advocated the use of individuals' "absolute CVD risks" as the criterion for the initiation of preventive drug therapies. For each individual, this absolute CVD risk is calculated on the basis of exposure to various determinants of CVD incidence and mathematical formulae such as the Framingham Risk Score, the Systematic Coronary Risk Evaluation, and cardiovascular risk prediction tools for populations in Asia [14–16].

Cost-effectiveness of BP- and cholesterol-lowering medications has been studied elsewhere; however, results differ from setting to setting [17–19]. Furthermore, studies on cost-effectiveness show differences in methodology, outcomes, cost components, and characteristics of the target population [17]. To our knowledge, there have been no studies reporting the cost-effectiveness of BP- and cholesterol-lowering drugs, singly or in combination, for CVD prevention in Thailand.

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

* *Address correspondence to:* Panrasri Khonputsa, 59/313 Piboonwattana Building, Rama 6 Road, Samsennai, Phayathai, Bangkok 10400, Thailand.

E-mail: panarasik@yahoo.com.

2212-1099/$36.00 – see front matter Copyright © 2012, International Society for Pharmacoeconomics and Outcomes Research (ISPOR). Published by Elsevier Inc.

doi:10.1016/j.vhri.2012.03.019

Table 1 – Effectiveness parameters used in cost-effectiveness analysis of blood pressure– and cholesterol-lowering drugs.

Parameter	Point estimate (uncertainty range) Distribution			Source
First-year discontinuation rate	50% (37.5%–62.5%) for single drugs, 40% (30%–50%) for polypill Uniform distribution			Estimate
Relative risk	Ischemic heart disease	Ischemic stroke	Hemorrhagic stroke	
Diuretic	0.86 (0.75–0.98 Lognormal distribution	0.62 (0.53–0.72) Lognormal distribution	0.62 (0.53–0.72) Lognormal distribution	Law et al. [13]
ACEI	0.83 (0.78–0.89) Lognormal distribution	0.78 (0.66–0.92) Lognormal distribution	0.78 (0.66–0.92) Lognormal distribution	Law et al. [13]
BB	0.89 (0.78–1.02) Lognormal distribution	0.83 (0.70–0.99) Lognormal distribution	0.83 (0.70–0.99) Lognormal distribution	Law et al. [13]
CCB	0.78 (0.62–0.99) Lognormal distribution	0.66 (0.58–0.75) Lognormal distribution)	0.66 (0.58–0.75) Lognormal distribution	Law et al. [13]
Statin	0.77 (0.74–0.80 Lognormal distribution	0.78 (0.70–0.87) Lognormal distribution	1.00	Cholesterol Treatment Trialists' (CTT) Collaborator [12]
ARB	0.86 (0.53–1.40) Lognormal distribution	0.79 (0.69–0.90) Lognormal distribution	0.79 (0.69–0.90) Lognormal distribution	Law et al. [13]
Polypill*	0.44 (0.34–0.54) Lognormal distribution	0.32 (0.24–0.41) Lognormal distribution	0.41 (0.31–0.52) Lognormal distribution	Estimate based on the multiplicative effects of drug components
Current practice (men, women)	0.99, 0.98	0.99, 0.97	0.98, 0.97	Estimate based on proportion using drugs currently

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin-receptor blocker; BB, beta blocker; CCB, calcium channel blocker.
* Polypill cost is based on the sum of the costs for each drug component. However, the true cost is likely to be less because of economies of scale in drug preparation.

Objectives

We assessed the cost and effectiveness of different BP- and cholesterol-lowering drugs targeting population subgroups with varying absolute CVD risk levels.

Methods

This study was carried out as part of Setting Priorities using Information on Cost Effectiveness project, a collaborative project between the Ministry of Public Health of Thailand and the University of Queensland, School of Population Health, Australia.

Definitions, incidence, and case-fatality rates of CVD

We defined a new case of CVD as a first-ever fatal or nonfatal IHD or stroke event, including unstable angina pectoris, myocardial infarction, ischemic stroke, or hemorrhagic stroke.

There was no direct information on the incidence and case-fatality rates of CVD in Thailand; we estimated these by using hospital admissions data and mortality data. These two locally available data sources provided estimates of the incidence of fatal and nonfatal IHD/stroke. Hospital admission data were provided by the Ministry of Public Health, which uses these data to reimburse public hospitals. Because the database does not capture private hospital admissions, we inflated all admissions to reflect the total number of self-reported hospital admissions by age, sex, and hospital level from the 2005 Health and Welfare Survey (National Statistics Office, Bangkok, Thailand). The vital registration system has unacceptably high proportions of deaths coded to ill-defined causes, and so we used data from a recent cause-of-death study. The study was well designed and conducted by using standard methods [3,20–22].

Current practice

To assess the cost-effectiveness of current practice, we first estimated its average yearly cost by adding the weighted yearly cost of the three drug components currently used: BP-lowering drugs, cholesterol-lowering drugs, and the combination. Similarly, the overall effects of current practice on IHD, ischemic stroke, and hemorrhagic stroke were calculated, separately, as the sum of the effects of BP-lowering drugs as one group, cholesterol-lowering drugs as another group, and the combination of these as a third group.

Interventions analyzed

We selected BP- and cholesterol-lowering drug interventions that have been proven in clinical trials to be effective in preventing IHD and stroke [12,13]. BP-lowering drugs were classified into five subclasses: thiazide diuretics (Ds), calcium channel blockers (CCBs), beta blockers, angiotensin-converting enzyme inhibitors (ACEIs), and angiotensin receptor blockers (ARBs). Statins were selected as the most cost-effective cholesterol-lowering drugs available as a generic in Thailand. The analysis was conducted for single drug interventions and combinations of drugs from different classes. When two or more drugs were used together, their effects, measured as the relative risk (RR) of disease incidence, were combined by using a multiplicative equation (e.g., RR1 × RR2 × RR3) [23]. We also analyzed the cost-effectiveness of a theoretical "polypill" [11] composed of a statin [12] in full dose and three BP-lowering drugs in half standard doses (D, CCB, and ACEI) [13]. This combination was selected on the basis of superior effects of the three drugs and their cost-effectiveness over beta blockers and ARBs (Table 1).